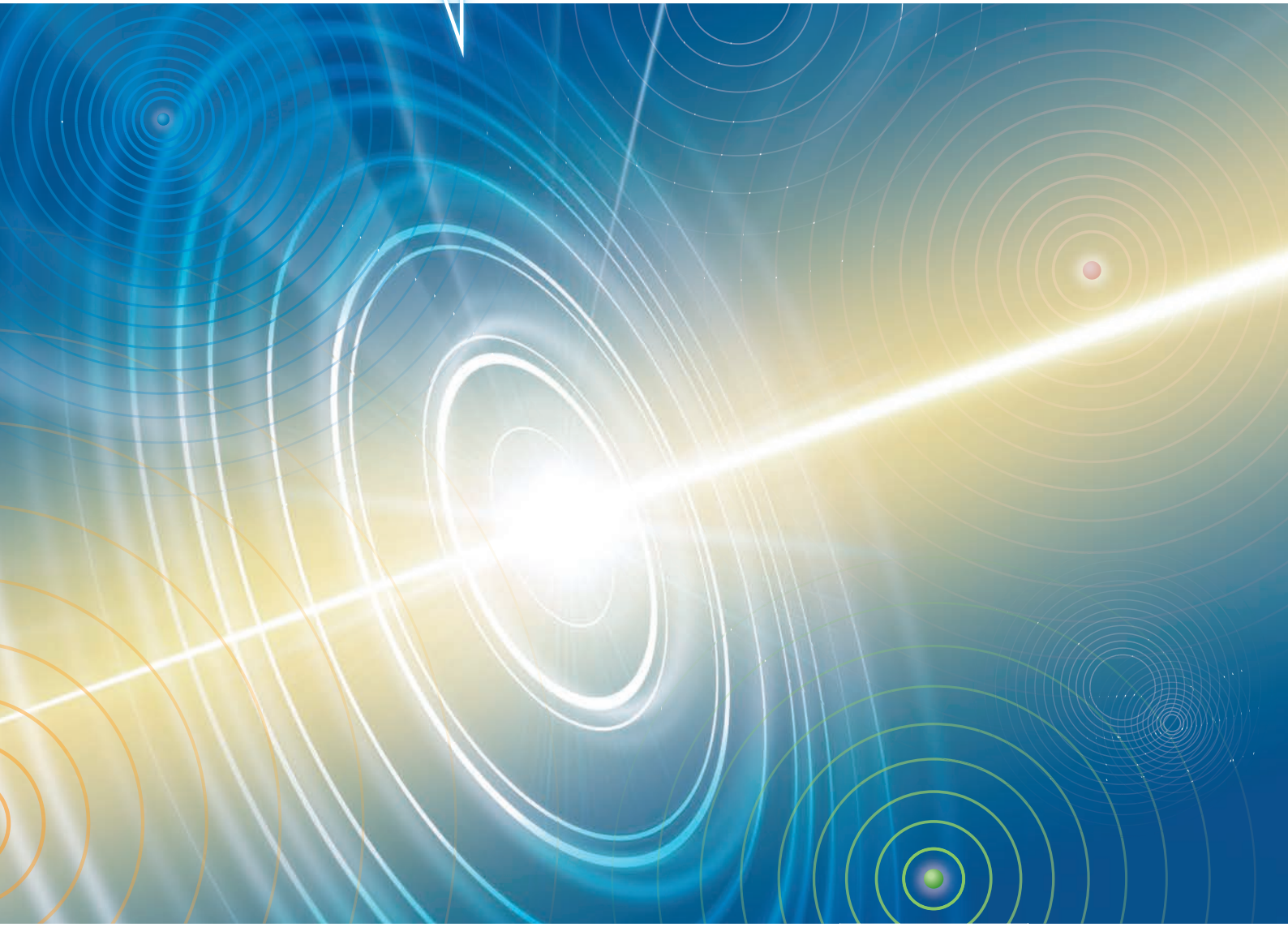
ImPACT Impulsing PAradigm Change through disruptive Technologies

Photoacoustic Imaging
~Opens a Door to the Future~

Innovative Visualization Technology to Lead to Creation of a New Growth Industry



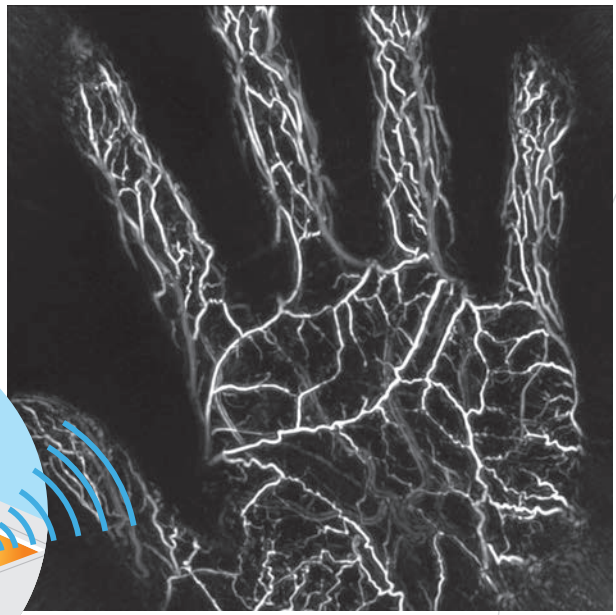
Beginning of Vascular Health Science Through Photoacoustic Imaging

In Japan's super-aging society, extending the healthy life expectancy of its population is an urgent issue, and activities related to early detection, treatment, and prevention of diseases are gaining importance. The main aging-related diseases are cancer, arteriosclerosis, diabetes, and locomotive syndromes due to motor disorders caused by arthropathy, which are known to cause blood vessel disorders. Photoacoustic imaging is a technique that combines light and ultrasound to form images of the vascular network and hemoglobin oxygen saturation in a noninvasive manner without X-ray exposure. This technique makes it possible to detect abnormalities in blood vessels before the symptoms become aggravated, and is giving birth to a new health science that will lead to early detection and prevention of various diseases.
We will call this new health science "Vascular Health Science" and describe the applicability of photoacoustic imaging.

Over the course of history, when a new measurement technology makes it possible to comprehend a previously incomprehensible phenomenon or a condition that could not be measured, new fields of science and industries have been created. For example, magnetic resonance imaging (MRI), which is based on nuclear magnetic resonance spectroscopy, gave birth to a new field of science and a new industry after over 40 years of continuous innovative technological development and development for clinical application since the first successful imaging in 1973.
The photoacoustic imaging being developed in the "Innovative Visualization Technology to Lead to Creation of a New Growth Industry" program (hereafter referred to as "this program") is a new imaging technique that provides visualization of the vascular network and hemoglobin oxygen saturation the physiological properties of blood in an organism by detecting the hemoglobin in its interior using the photoacoustic phenomenon. The technique is noninvasive and does not require X-ray exposure. With this technique, a three-dimensional image of the blood vessels is created as a new indicator of conditions in the body. This makes it possible to obtain a comprehensive understanding of health conditions before and after disease since its onset through the healing process, based on the morphological and functional information of the blood vessels.

Possibilities of Photoacoustic Imaging

Photoacoustic imaging consists of detecting ultrasonic waves generated by laser irradiation (pulsed laser light) with an ultrasonic sensor, thereby allowing the formation of an image. It is a noninvasive and nondestructive technique that allows one to map the "whole picture" of organisms or objects as an image.
By processing a huge volume of ultrasonic signals in parallel, this technique can construct three-dimensional images in real time and provides a visualization of how they change over time. In addition, not only can the organism or object be analyzed as an image, but the existence of a specific component, as well as its variations, can be determined by color differences. With this technique, it will be possible to image fine vascular networks and the physiological properties of blood such as oxygen saturation in a noninvasive manner and without X-ray exposure, as well as to visualize internal damage and defects in food items and commercial products. These examinations are not possible with the current diagnostic methods.



▶ Vascular network of the hand shown in a three-dimensional image as constructed with photoacoustic imaging

The creation of Vascular Health Science

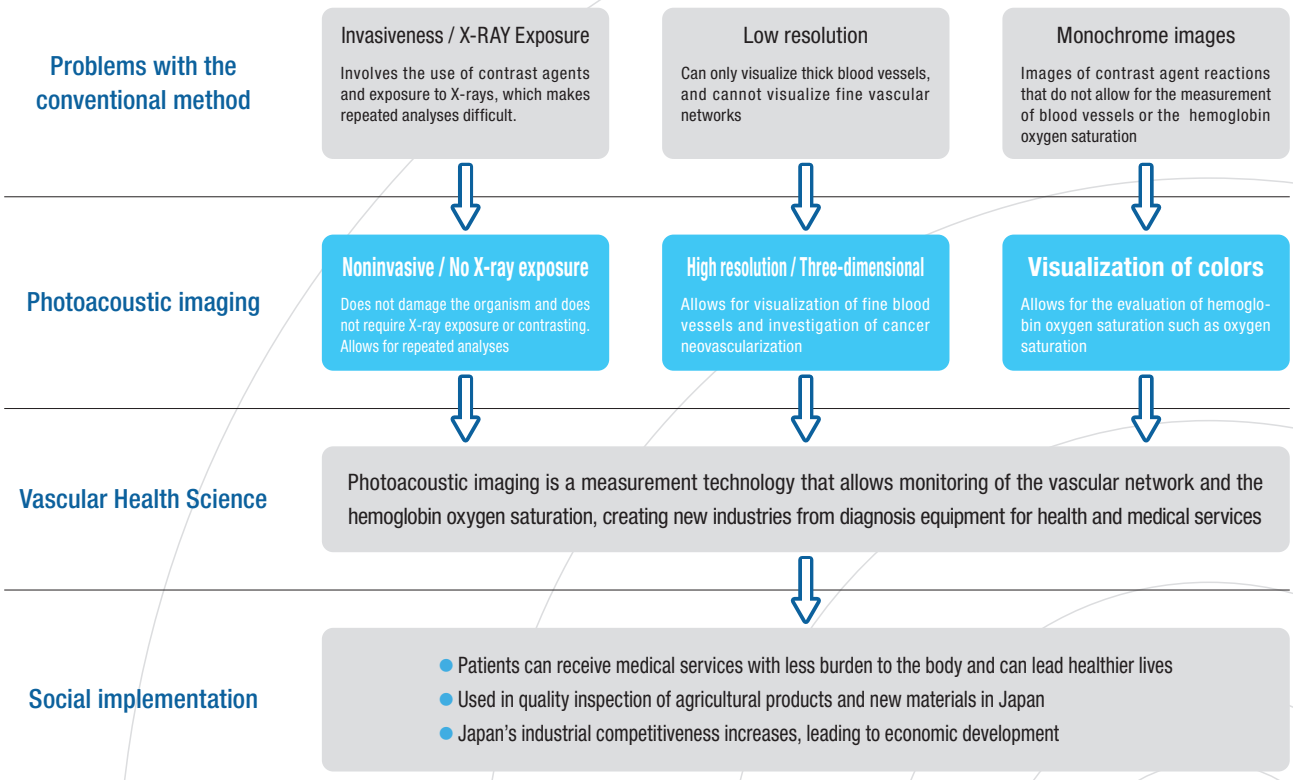
Cabinet Office
ImPACT (Impulsing PAradigm Change through Disruptive Technologies) program
Program Manager

Takayuki Yagi

With the arrival of a super-aging society, the morbidity rate and the number of persons in need of nursing care are increasing rapidly, spreading concerns about diseases and care. Meanwhile, more people seek a life in which they can work safely. It is also important to provide the population with security and safety by improving the quality of food and other products.
It is known that the onset and symptoms of diseases such as cancer, arteriosclerosis, diabetes, and arthropathy affect a large part of the population and manifest in the vascular network and hemoglobin oxygen saturation.
Blood vessels are traditionally imaged using a contrast agent. If the blood vessels can be imaged in a noninvasive manner and without X-ray exposure, it will be possible to detect many diseases and diagnose the symptoms at an earlier stage. With this information, everyone from children to the elderly can expect to be healthy and receive healthcare and services with less burden to the body.
This is how the new medical treatments and maintenance of health will look when the visualization of the vascular network and hemoglobin oxygen saturation becomes a reality.
Early diagnosis of various diseases with photoacoustic imaging, followed by the creation of an image database, should pave the way for prediction of disease risks through big data analysis.
If photoacoustic imaging can be applied to evaluate skin aging, it may also be possible to expand the technique to beauty treatments.
Furthermore, we believe that if we devise a simple method for taking advantage of the characteristics of light to generate high-definition images of structural and physical properties, we will be able to increase the reliability and quality of Japanese products, thereby strengthening their competitiveness.

In this program, we are creating “Vascular Health Science” using a blood vessel imaging technique and we are developing photoacoustic imaging in the hope that we can contribute to the creation of a new industry. We hope this brochure provides you with a better understanding of this technique.

Social implementation diagram of Vascular Health Science brought about by Photoacoustic Imaging



Basic Principle of Photoacoustic Imaging

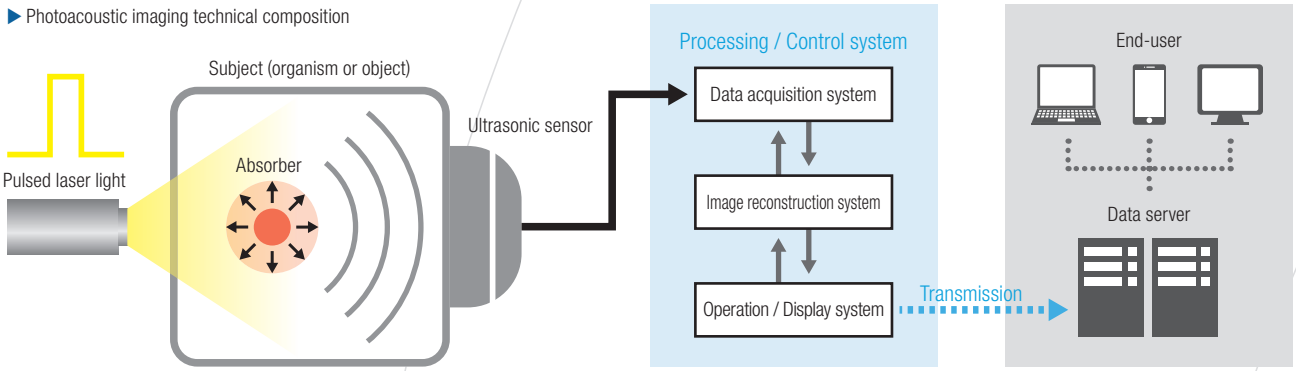
Photoacoustic imaging is a new, noninvasive, and X-ray exposure-free imaging method that combines the advantages of optical imaging, measuring optical characteristics, with the advantages of deep area visualization of ultrasonic imaging. By appropriate placement of ultrasonic sensors with wavelengths adjusted to the subject (organism or object), it is possible to visualize the internal structure and texture properties of the subject. Because it is a noninvasive technique that involves no exposure to X-rays or harmful energies, it does not require facilities that shield radiation and magnetism, nor does it require restricted areas. This can lead to the development of diagnostic devices that can be easily used anytime, anywhere, by any person.

In photoacoustic imaging, a pulsed laser light with a wavelength adjusted with the absorber to be visualized is irradiated, which generates ultrasonic waves that are detected by ultrasonic sensors. A three-dimensional distribution of the absorber inside the subject can then be constructed. This section explains the technical composition of photoacoustic imaging, the principle of imaging, and “visualization of color,” the most remarkable characteristic of the technique.

Photoacoustic Imaging System

Photoacoustic imaging systems consists of the following technologies: a “variable wavelength laser” which irradiates a subject, “ultrasonic sensors” which receive the ultrasonic waves generated by the absorber in the interior of the subject, a “data acquisition system” which converts the signal detected by the ultrasonic sensor into a digital signal, “image reconstruction” which calculates the position and size of the absorbing body, and the “operation / display system” which displays the processed images and controls the entire system. Moreover, connecting the processing / control system to a data server makes it possible to analyze large amounts of data along with various types of medical information. Personalized treatments can be developed, and automatic and remote diagnoses can be performed. In order to meet one of the objectives of this program, an imaging technique must be developed that can be applied to a wide range of subjects. We are developing a Wide-Field Visualization System (tomographic type), which provides broad visualization, and a Micro-Visualization System (microscope type), which has micron-order resolution. In parallel, we are also developing a high-output variable wavelength laser, designed for deeper imaging with higher resolution, as well as a multi-channel ultrasonic sensor.

▶ Photoacoustic imaging technical composition

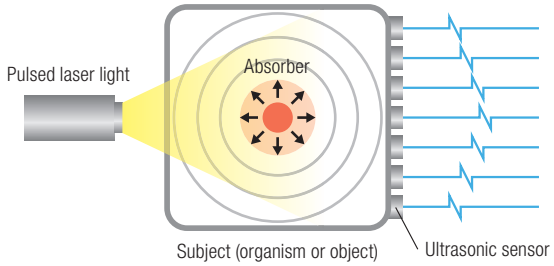


Principle of Photoacoustic Imaging 1 Fusion of Light and Ultrasound

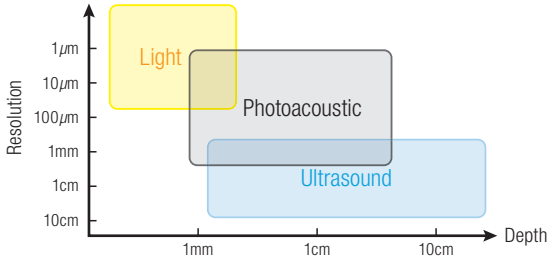
Photoacoustic imaging occurs by taking advantage of the photoacoustic effect, in which a subject emits ultrasonic waves when irradiated with light. The emitted ultrasonic waves can be gathered with multiple ultrasonic sensors, and the data can be used to construct an image. Pulsed laser light from a variable wavelength laser is irradiated on a subject, and the absorber inside this subject absorbs light. The ultrasonic waves are generated by volume expansion, which is caused by a temperature rise in the subject.

When generating ultrasonic waves with light, it is possible to determine the characteristics of the color of the absorber (i.e., its absorbing properties) as image information, just as in optical imaging.
With the introduction of ultrasound, which can propagate through living bodies, a high spatial resolution is maintained even at deeper parts, providing clear visualization that was difficult to obtain with conventional optical imaging.

▶ Basic Principle of Photoacoustic Imaging



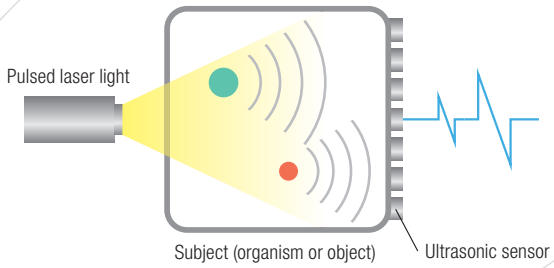
▶ Combination of the properties of light and ultrasound



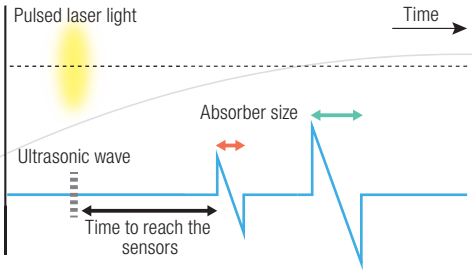
Principle of Photoacoustic Imaging 2 Reconstruction / Three-dimensional imaging

To form three-dimensional images, the ultrasonic waves generated by absorption of pulsed laser light from the variable wavelength laser are received by multiple sensors arranged facing the absorber. The time required for the ultrasonic waves to reach each sensor is calculated by the timing between the emission of a laser pulse from the variable wavelength laser and its reception at the ultrasonic sensor array. Based on this arrival time, the position information for each ultrasonic sensor and the speed of wave propagation in the subject, it is possible to form a three-dimensional image of the absorber using an image reconstruction method known as the back-projection method. The shape of the absorber is reflected in the form of the ultrasonic wave generated. If the shape of the absorber is small, the generated wave has a narrow time axis, and vice versa. It is possible to use this kind of waveform information to measure the size of the absorber.

▶ Measurement of ultrasonic waves with sensors



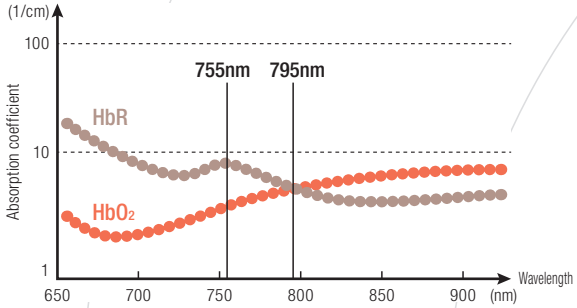
▶ Measurement of ultrasonic waveforms with multiple ultrasonic sensors to form three-dimensional images



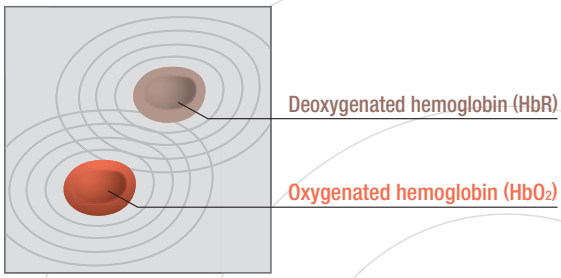
Principle of Photoacoustic Imaging 3 Visualization of color

In photoacoustic imaging, it is possible to visualize material properties based on the color of the absorber (i.e., light absorption properties) by irradiating it with multiple laser pulses with wavelengths adjusted to the optical characteristics of the absorber. For example, the light absorption spectrum of hemoglobin varies with oxygen saturation. Focusing on the light absorbance difference of two wavelengths of hemoglobin (e.g., 755 nm and 795 nm) dependent on the hemoglobin oxygen saturation value, laser pulses with these different wavelengths generate photoacoustic waves with different intensities. By visualizing the intensity ratio of the photoacoustic waves, it is possible to map oxygen saturation in hemoglobin.

▶ Light absorption spectrum of hemoglobin varies according to its oxygen saturation



▶ Different hemoglobin colors due to different oxygen saturation levels



Advantages of Photoacoustic Imaging

In this section, we present the advantages of photoacoustic imaging in the medical field and its application to visualizing blood vessels in living bodies and diagnosing related diseases. We also mention the advantages of photoacoustic imaging compared to other imaging devices (modalities) currently used for examination of blood vessels and the blood stream—ultrasound, contrast-enhanced MRI, contrast-enhanced computed tomography (CT), contrast-enhanced X-ray.

In this program, we are developing two types of devices: a microscope-type device, which can provide high-resolution visualization of capillary vessels up to a depth of a few millimeters below the surface of the body and the skin texture, and a tomographic-type device, which offers a broad visualization of vascular networks ranging from sub-millimeter size to a depth of a few centimeters. Our objective is to demonstrate the efficacy of these devices for disease diagnosis and study by using them in clinical research.

Advantages of the blood vessel imaging technique

Noninvasive / No X-ray exposure

Photoacoustic imaging is capable of imaging finer blood vessels than other existing techniques. Compared to other imaging techniques such as ultrasound, MRI, CT, and X-ray (angiography), a contrast agent is not required. It is a noninvasive technique that performs measurements using a variable wavelength laser with an intensity that does not harm the skin. Because photoacoustic imaging irradiates specimens and detects ultrasonic waves with no X-ray exposure involved, it is possible to repeat the measurements multiple times. This makes it applicable to a wide range of subjects, ranging from children to the elderly. In addition, unlike MRI and CT, it does not require shielding against radiation or magnetism, nor does it require restricted areas, which makes it easier to introduce devices in a clinical setting.

High resolution / Visualization of hemoglobin oxygen saturation / Three-dimensional imaging

With this technique, a large number of ultrasonic sensors are placed around the subject for ultrasonic measurement. This eliminates the need for moving the sensors, as well as the dependence on the practitioner, which is an issue in ultrasound diagnosis. Therefore, it provides results that are not influenced by the ability of the technician and generates three-dimensional images of blood vessels with high resolution and excellent reproducibility. If we apply the technique of combining multiple laser wavelengths introduced in the previous section, images of hemoglobin oxygen saturation can be obtained, allowing clinicians to observe details of the vascular networks and hemoglobin oxygen saturation that cannot be visualized with current diagnostic equipment. Our goal is to implement an imaging technique that is simultaneously real-time, such as ultrasound diagnosis, and high-definition, to allow three-dimensional imaging of blood vessels.

▶ Photoacoustic imaging provides noninvasive three-dimensional visualization of hemoglobin oxygen saturation with high resolution and without X-ray exposure.

	Photoacoustic imaging	Ultrasound		Contrast-enhanced MRI	Contrast-enhanced CT	Contrast-enhanced X-ray
		Doppler ultrasound	Contrast-enhanced ultrasound			
Noninvasive / No X-ray exposure	◎	◎	○	○	×	×
Visualization of vascular network	Fine blood vessels	>1mm	Fine blood vessels	>1mm	~1mm	Fine blood vessels
Visualization of blood stream without contrast	△	○	×	×	×	×
hemoglobin oxygen saturation (oxygen saturation)	○	×	×	×	×	×
Three-dimensional imaging	○	△	△	○	○	×
Convenience / Promptness	○	○	×	×	×	×

Types of Photoacoustic Imaging devices

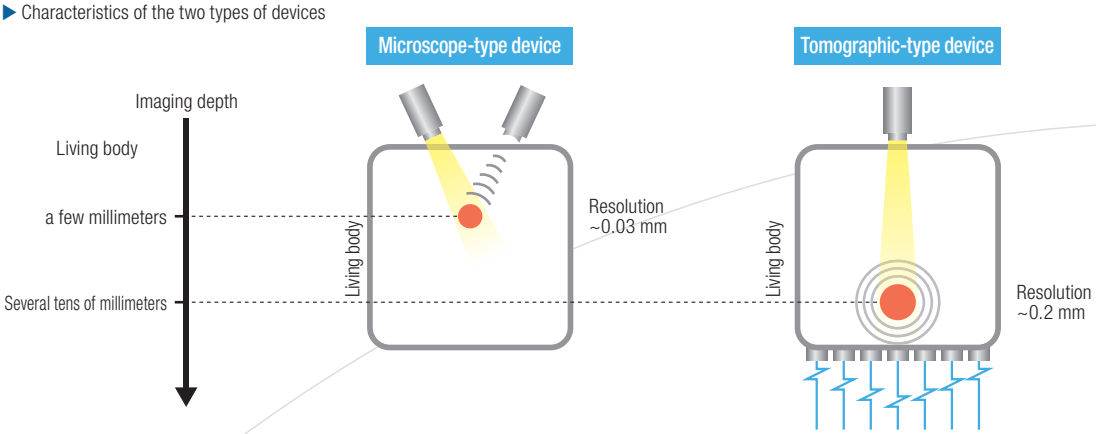
Microscope-type device

The method involving the microscope-type device is a method in which the living body is irradiated with pulsed laser light and, while the body surface is scanned, ultrasonic waves generated near the focal point of an acoustic lens are captured by ultrasonic sensors and the measured signal is used to form images. It is possible to obtain high-resolution images by measuring high-frequency ultrasonic waves. The imaging becomes shallow with a depth of just a few millimeters. In this program, we use the microscope-type device to image skin tissue.

Tomographic-type device

The method involving the tomographic-type device is a method in which a large number of ultrasonic sensors cover only the portion of the living body to be scanned. Laser pulses irradiate this area, generating ultrasonic waves inside the living body that are captured in a wide range. Because a large number of ultrasonic sensor are combined to reconstruct the images, they can detect very weak signals, and the depth of imaging reaches several tens of millimeters. The resolution is up to around 0.2 mm. In this program, we use tomographic-type device to examine blood vessels for diagnosis of breast cancer, circulatory system diseases, arthropathy, and others.

▶ Characteristics of the two types of devices



Photoacoustic Imaging Capabilities

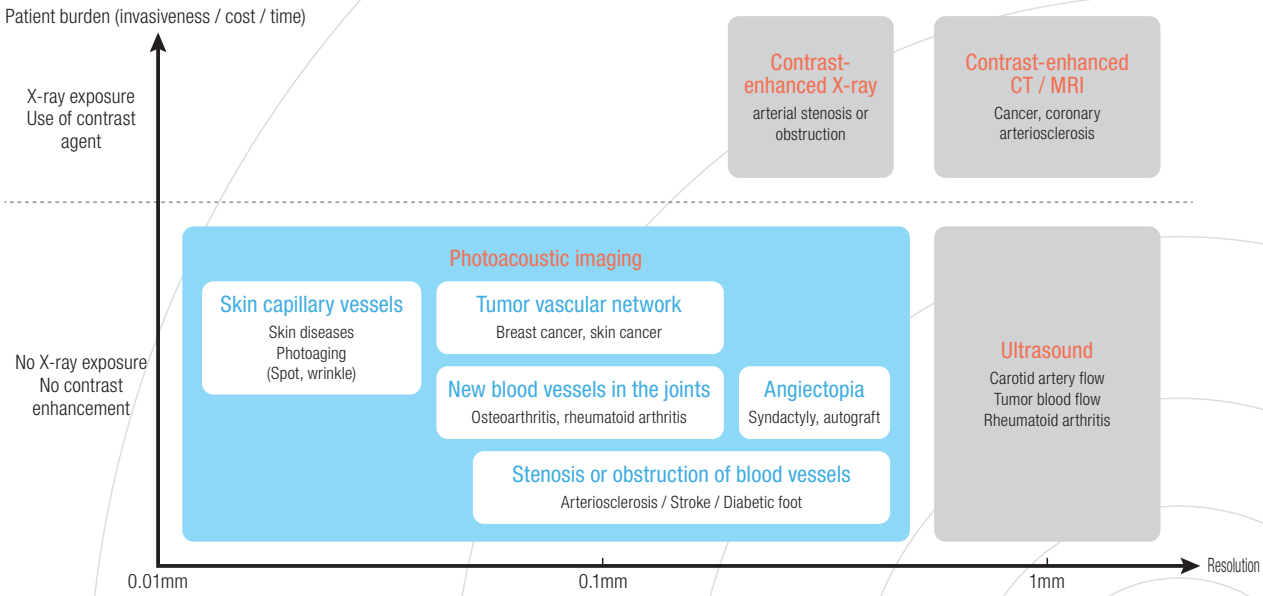
It is known that the onset and symptoms of the main diseases in the Japanese population—cancer, arteriosclerosis, diabetes, and locomotive syndrome—are manifested in the vascular network and in the physiological properties of blood. However, barely any progress has been made in studies that apply the evaluation of the vascular networks and the physiological properties of blood to early diagnosis and prevention using existing imaging modalities since the use of contrast agents and X-ray exposure is to be avoided.

Through the use of photoacoustic imaging, it is possible to noninvasively visualize the vascular network (tumor vascular network) related to the growth of cancer cells without X-ray exposure; neovascularity of joints related to osteoarthritis and rheumatoid arthritis; stenosis or obstruction of blood vessels related to foot lesions caused by arteriosclerosis, stroke, or diabetes; angiectopia related to syndactyly and autograft; and skin capillary vessels related to skin diseases.

Early diagnosis of blood vessel disorders, which are known to be signs of diseases, can not only facilitate early treatment, but also increase the patient's survival rate and quality of life (QOL), as well as reduce medical expenses.

In addition, visualization of skin vascular networks can be expanded into beauty treatment and cosmetic applications such as the identification of changes in spots and wrinkles caused by photoaging and measurement of operation effects.

▶ Blood vessel conditions related to diseases visualized by photoacoustic imaging



Possibilities of Vascular Health Science in Medical Treatment

"From cure to care"—It is said that in 2035, one in three persons in Japan will be over 65 years old and one in five persons will be over 75 years old. As in the government's vision, it is necessary to enhance the quality and efficiency of medical care and make effective use of medical resources. Instead of treating (curing) a disease after it aggravates, as done in the past, it is necessary to develop preventative medical care and the social infrastructure to support it. This requires detecting a disease before its onset or at an early stage and improving individual health awareness and cooperating with medical institutions to manage health and improve symptoms. By treating diseases that largely affect the Japanese population, such as cancer, arteriosclerosis, and locomotive syndrome—which commonly result in the need of nursing care—before the symptoms appear or in the initial stages, it is possible to create a society where people have healthier lives and greatly reduce social security expenses. Photoacoustic imaging, a noninvasive and X-ray exposure-free technique that can be used in children and the elderly, is an imaging tool that embodies Vascular Health Science. Below is a description of potential applications of Vascular Health Science in the medical field.

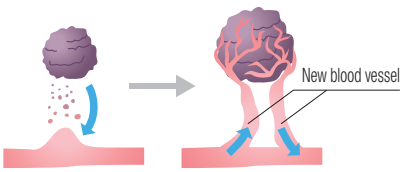
Possibility Medical treatment 1 Cancer (Breast)

Tumor vascular network

According to the vital statistics from 2015, the top cause of death was cancer. While breast cancer ranks 5th among female cancer victims of all ages, it has the highest percentage of death among middle-aged women in their 40s and 50s.
The number of deaths from breast cancer increased from 12,455 in 2010 to an estimated 14,000 in 2016. The number of patients also increased from 68,071 to 90,000 in the same period*1.
Mammography is the primary inspection method used today, but it shows difficulty in detecting cancer because of dense breast tissue, which is commonly seen among Asians. There are also many people who feel pain from the pressure applied to the breast and therefore ask for an inspection method that detects a tumor more easily, with less burden, and without exposure to X-rays.
With diagnosis by photoacoustic imaging, we aim to visualize cancer-specific vascular networks (angiogenesis) and hemoglobin oxygen saturation in order to detect cancer at an even earlier stage. It will also be quick and free of compression or exposure to X-rays, thus allowing patients to be examined as many times as necessary. With photoacoustic imaging, it is possible to identify the vascular network and hemoglobin oxygen saturation in the tumor and its surroundings and thereby perform treatment with minimal resection and medication. For instance, if the anti-cancer agent administered shows no effect, it can be quickly switched to a different medicine. Thus, the most effective treatment method can be selected for each patient. As a result, it is possible not only to preserve the patient's physical strength, but also to improve his or her QOL. In addition, patients can watch the monitor screen in the consultation room and check their own photoacoustic three-dimensional images in real time, which makes the treatment more reliable and secure.

*1: National Cancer Center Japan Press Release "Projected Cancer Statistics, 2016" 7/15/2016

▶ If a cancer cell grows, a new blood vessel is formed



Possibility Medical treatment 2 Arteriosclerosis / Stroke / Diabetes

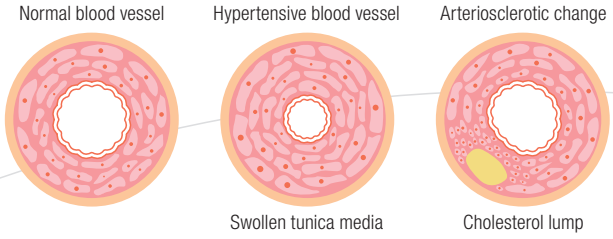
Stenosis or obstruction of blood vessels

According to the vital statistics from 2015, the second leading cause of death is heart disease, and the fourth is cerebrovascular disease and arteriosclerosis, all of which are diseases caused by vascular disorders due to hypertension, hyperlipidemia, and diabetes. In 2012, the combined number of pre-diabetic and diabetic people was approximately 20.5 million people*2. At a global scale, according to the "Diabetes Atlas 2012 Update" of the International Diabetes Federation, the number of diabetic patients both in China and India is expected to exceed 100 million by 2030. There are few subjective symptoms in the initial stage of arteriosclerosis, and most conventional methods required identifying signs

based on intermediate indexes such as blood pressure value, cholesterol value, and blood glucose level. Photoacoustic imaging with many different wavelengths makes it possible to distinguish between plaque in the blood vessel wall—the primary cause of arteriosclerosis—from a normal blood vessel wall based on its absorption spectrum. Since it is also capable of imaging the shape of blood vessels with high resolution, it becomes possible to identify arteriosclerosis as a morphological alteration of blood vessels and distinguish a stenosis or obstruction of arterioles based on the form of the blood vessels. This technique is particularly effective in diagnosing patients to whom it is not possible to administer a contrast agent due to conditions such as diabetic nephropathy. By mapping the vascular network and hemoglobin oxygen saturation using photoacoustic imaging, the narrowed portions of fine blood vessels can be measured and the existence of ischemia can be determined, allowing for diagnosis and lifestyle improvements before the appearance of symptoms. As a result, it avoids aggravation of symptoms and can reduce medical expenses. If the condition aggravates, the only choice may be to amputate the foot. But by determining the state of the arteries and veins in the affected area by photoacoustic imaging, it is possible to minimize the chances of amputation.

*2: Ministry of Health, Labor and Welfare “National Health and Nutrition Examination Survey 2013” 10/12/2014

▶ If the disease progresses, the blood vessel wall and properties of the plaque change



Possibility Medical treatment 3 Locomotive Syndrome

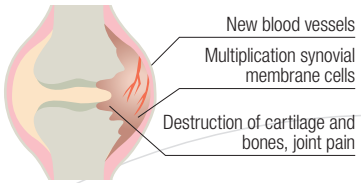
New blood vessel in the joints

If a person suffers a motor disorder (locomotive syndrome), it is likely that the execution of daily tasks becomes more difficult. Stroke, dementia, bone fracture, and arthropathy are some of the diseases that may cause motor problems. Among patients who need support, the leading causative disease according to the degree of care is “arthropathy.” In particular, the number of osteoarthritis and rheumatoid arthritis patients in Japan is said to be 25.3 million and 700,000, respectively *3*4. While contrast-enhanced MRI is an effective technique to diagnose arthropathy, because of the burden it causes to the body and its high inspection cost, it cannot be applied repeatedly before the onset of the disease. Inflammation causes joint destruction in osteoarthritis and rheumatoid arthritis patients. Rheumatoid arthritis is a disease that causes swelling and pain in the joint due to an inflammation caused by an immunity disorder, leading to deformation in the joint. In rheumatoid arthritis, new blood vessels generated in the synovial membrane are thought to be the predictors of joint destruction, and it is now possible to detect those new blood vessels by Doppler ultrasound and perform an early treatment. However, diagnosing a joint by Doppler ultrasound has the problem of dependence on the practitioner in that the diagnosis result changes depending on the ability of the laboratory technician, as well as the long time it takes to diagnose each joint individually. In photoacoustic imaging, there is no dependence on the practitioner's experience and it is possible to visualize new blood vessels generated in the synovial membrane of all joints of the hand in real time. With the visualization of the three-dimensional structure of new blood vessels, photoacoustic imaging is expected to become a diagnostic method capable of providing early detection of arthropathy before it reaches the point of joint deformation or wear. When preventive medical care becomes widespread, after 2025, it will also be possible to monitor the condition of a patient’ s motor system and select the most adequate treatment to prevent motor disorders.

*3: Ministry of Health, Labour and Welfare – Annual Health, Labour and Welfare Report 2013

*4: Noriko Yoshimura, Grant-in-Aid for Scientific Research Project Final Report “Epidemiology of Knee Osteoarthritis, Lumbar Spondylosis and Osteoporosis in Japanese Men and Women: The Research on Osteoarthritis/Osteoporosis Against Disability (ROAD)” 06/07/2014

▶ If synovial membrane cells multiply, new blood vessels are generated



Possibility Medical treatment 4 Skin Disease

Skin capillary vessels

Human skin has a complicated three-dimensional structure that covers the entire body. Its blood vessels are very sensitive to environmental changes: its color tone quickly changes when the outside temperature drops and turns red with a little stimulation. Long-term exposure to strong sunlight (ultraviolet rays) and scars from burns or injuries suffered in the past are known causes of skin cancer, and both the onset risk and the number of patients in Japan are increasing as its population ages*5. The current method of diagnosing skin conditions requires examining the skin or a tissue diagnosis through a painful biopsy. With photoacoustic imaging, in the case of skin cancer, it is possible to visualize the capillary vessels of the skin in a noninvasive manner and determine the progress of cancer. Many other diseases besides skin cancer are closely related to blood vessel conditions. A few examples are Raynaud's disease, which causes a cool feeling and change of color in the fingers and toes; scleroderma, which hardens the skin; and burns; vasculitis; and angioma. Photoacoustic imaging is expected to become a new diagnostic method for skin conditions.

*5: Cancer Information Services “Cancer Registration and Statistics” (2015) http: //ganjoho.jp/reg_stat/index.html

Possibilities of Vascular Health Science in health and beauty treatment

Photoacoustic imaging will advance into a technique capable of visualizing and quantifying photoaging of skin and weakening of body functions based on the vascular network and hemoglobin oxygen saturation. As research on Vascular Health Science progresses, it is expected to expand into a new concept of beauty treatment and promotion of health.

In this program, we are developing a technique that evaluates the deterioration of skin functions, such as spots and wrinkles caused by photoaging, by imaging the capillary vessels and skin texture. The microscope-type device (micro-visualization system) is a device that can directly image the skin capillary vessels. It is applicable to anti-aging measures in skin care and to evaluate health conditions.

Possibility Beauty Treatment Positive Aging

New research shows that photoaging of the skin produces “new blood vessels” and increases spots and wrinkles on the skin surface. There are countless capillary vessels in the dermis near the skin surface, and that the number and blood flow influence the clarity and gloss of the skin surface. If blood flow is too low, the skin loses its gloss and its metabolism also declines. The capillary vessels, which provide nutrition, moisture, and regulate body temperature, play an important role in keeping the skin youthful. When photoacoustic imaging is used to determine the condition of capillary vessels in the skin, skin measurements will clarify the relationship between skin conditions and blood vessels. It is possible that these studies will give birth to beauty treatments such as “blood vessel beauty,” which regenerates skin through the improvement of blood vessel conditions. Perhaps we will see many cosmetic or medical treatments based on the concept of obtaining beautiful skin by maintaining healthy blood vessels by deriving the best blood vessel conditions and blood flow in the skin surface. Similar to cosmetic therapy, caring for one's skin is said to be effective against dementia. We predict that anti-aging will eventually produce a paradigm shift toward positive aging. By 2035, it will be easy to have a skin diagnosis by photoacoustic imaging. Cosmetics and manufacturers of beauty equipment, beauty dermatology, esthetic treatment, and even food and sleep-related products and services for positive aging will be offered.

▶ Measurement of the healthiness of skin by photoacoustic imaging

Possibility Health Sports Injury Prevention / Highly Effective Training

After an intense match or competition, top athletes employ various methods to regulate and maintain their body, especially their muscles and joints. They have massages according to their fatigue level, carry out training developed to prevent injuries, balance the content of their daily meals, and constantly maintain optimal physical condition. For example, blood vessels that supply oxygen play an important role in the improvement of stamina. In fact, it is known that endurance exercises increase the number of capillary vessels. In addition, the effect of low oxygen training is verified by measuring oxygen saturation of arteries with a pulse oximeter and estimating fatigue from blood glucose. When it is possible to visualize the vascular networks and hemoglobin oxygen saturation in the body, it will be possible manage training up to an even higher level. Moreover, photoacoustic imaging allows monitoring of different body parts such as muscle, knee joint, and skin blood vessels in real time, it will likely be used in the development of new training methods. It has the potential of not only improving the potential of athletes but also in creating new sports industries.

▶ Keep up an effective training while preventing injuries

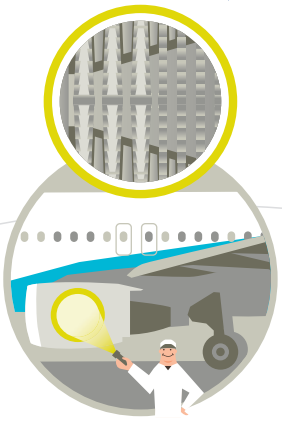
Further applications of photoacoustic imaging

With conventional optical imaging, it was possible to visualize the shape and property changes of material surfaces. With photoacoustic imaging, it will be possible to optically inspect and image the internal structure and property changes of objects without destruction. It can be applied to check for small scratches in industrial materials that demand high quality, as well as to inspect fruits at high capacity, which is currently done visually by sampling.

In this program, we are also conducting research that aims to expand the use of photoacoustic imaging to nondestructive inspections of Carbon Fiber Reinforced Plastics (CFRP), which are used in parts of cars and airplanes, and in ceramic structure components. If these studies progress and the device becomes compact and easy to handle, it will be applicable for inspection of industrial materials and for safety inspection of food products.

Possibility Industry Quality inspection of New Materials

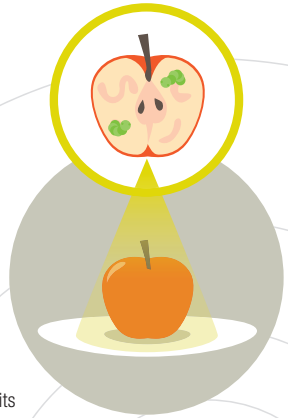
CFRP is a strong and lightweight composite material that is widely used as a structural material for airplanes, rockets, wind turbines, etc. It is also being incorporated into accessories of fuel cell vehicles, such as hydrogen tanks and engine parts.
While composite materials have advantages over single materials, their structure is complex and requires close inspection. If photoacoustic three-dimensional imaging successfully generates images of cracks in the multilayer structure of carbon fiber, it will be possible to expand its application from materials and press production lines to inspection sites for airplanes and cars.
This technique will increase the reliability of products, reduce costs, and improve manufacturing techniques.
As new materials are developed in the field of composite materials, photoacoustic imaging is expected to be used as its measurement technique.



▶ Inspection of CFRP on airplane wings

Possibility Agriculture Food Inspection

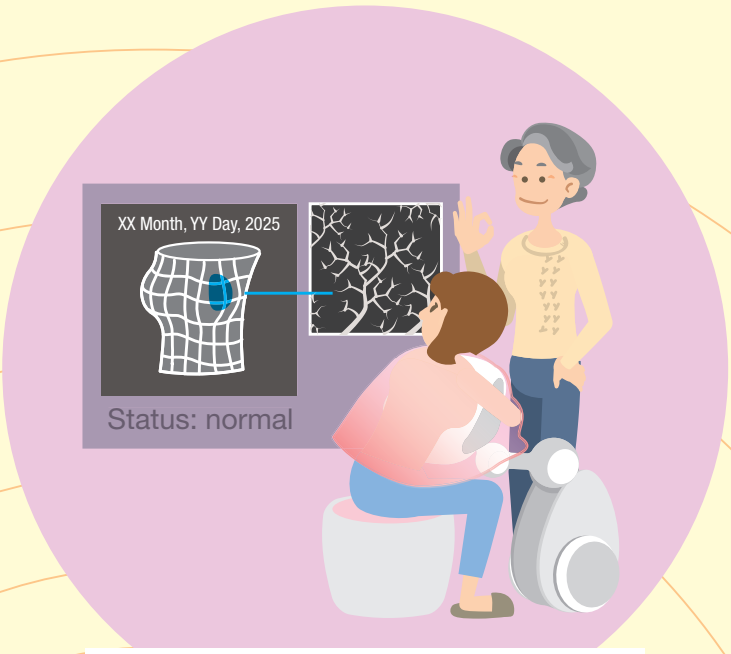
In recent years, there was a global boom in Japanese food that led to an increase in exports of Japanese agricultural and marine products. In particular, exports of apples and other fruits to China and Southeast Asia have seen exceptional growth, promoting policies for increased exports. The fruits to be exported are visually inspected both at the cultivation and export sites, but there is a limit in inspection processing capacity, which is beginning to inhibit the growth of exports. Meanwhile, some export partner countries and regions have adopted embargos to prevent the invasion of diseases and pests, which is also inhibiting exports.
With photoacoustic imaging, it is possible to visualize pests hiding inside fruits by using the difference in light absorption properties between the fruit and the pest. If the device becomes more compact and cheaper, it can be incorporated in the sorting process, which will allow for preselection of all products and making quarantines more reliable.
Moreover, in food processing factories, the contamination of food products with the body hair of workers has been a long-standing problem that led to the adoption of various measures. The current methods, however, are not capable of completely detecting all body hairs, and for this reason, it has not been possible to eliminate the contamination of processed foods.
Since body hair contains a lot of melanin pigment, photoacoustic imaging can detect melanin using its light absorption properties. By incorporating this technique into the food processing line and combining it to an image processing technique for body hair extraction based on its shape, it will be possible to perform an automatic total inspection for body hair mixed into processed food products.



▶ Inspection for pests in fruits

Toward a future where Photoacoustic Vascular Health Science

Children, the elderly, healthy, and diseased people will be able to see three-dimensional images of their vascular networks and hemoglobin oxygen saturation with a low burden using this technique. Patients can also check their conditions before and after the appearance of symptoms, as well as determine how individual patients responded to treatment. In addition to early diagnosis followed by early treatment, photoacoustic imaging is expected to pave the way for personalized medical treatments, such as individually selected medicines and prescriptions, as well as the development of new therapeutic drugs.



Locomotive Syndrome

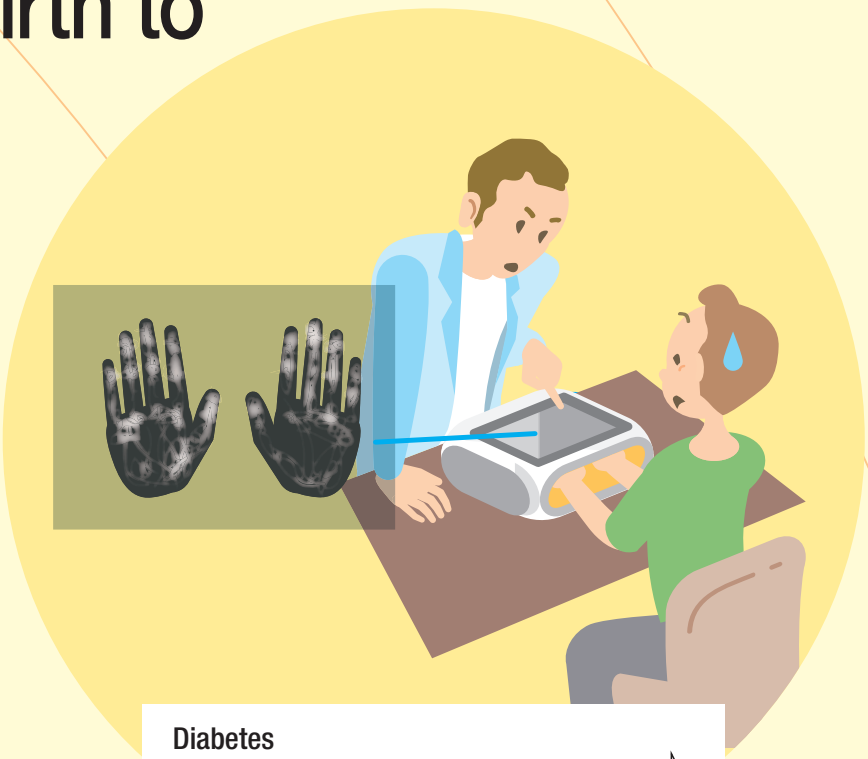
The technique will be able to detect arthropathy in advance through three-dimensional visualization of the entire joint.

Breast Cancer

A quick process that works just by gently pressing the diagnosis device against the breast, without painful pressure or X-ray exposure. Patients with dense breast tissue and young women can safely use it.

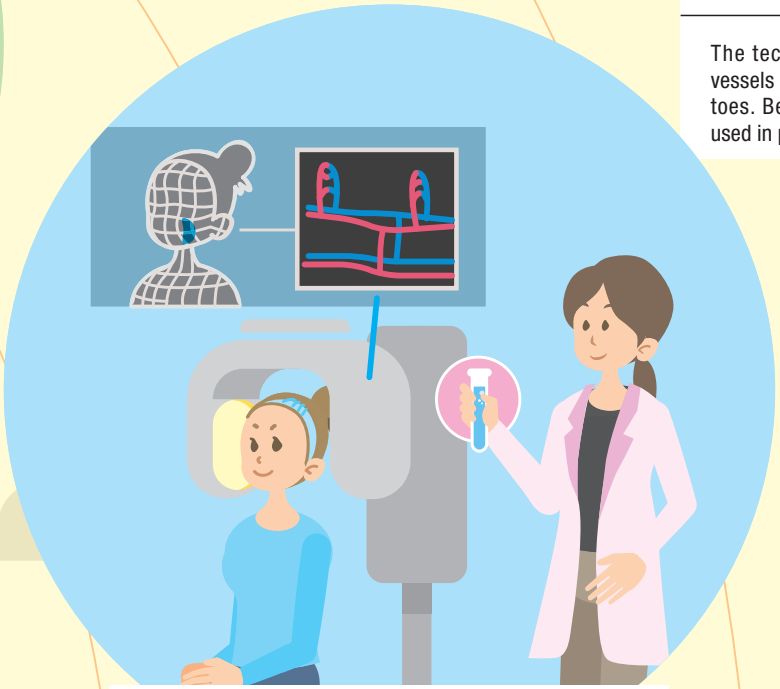
Photoacoustic Imaging → 2025

Imaging gives birth to



Diabetes

The technique will form 3D images of peripheral blood vessels and hemoglobin oxygen saturation in the fingers and toes. Because it does not use a contrast agent, it will be used in periodic medical examinations.



Cosmetics Development site

It will be possible to analyze the relationship between capillary vessels and skin conditions, leading to the development of new cosmetics and treatments.

Future image of 2035, when Vascular makes people healthier and happier

Nondestructive Analysis

Periodic inspection of fuel cell taxis. Checks for scratches in the CFRP body and accessories of a fuel cell system.

Beauty Aging Doc

As part of a one-stop service from skin care to hair care aimed at maintaining beauty even at advanced ages, the doctor analyzes the condition of capillary vessels of the skin, sebum, melanin and others, and also evaluates the effect of beauty treatments.

2035

Health Science

Positive Aging Village

As one of the measures to revitalize the country, a tourism base of positive aging, targeting an influx from overseas, will be born in Japan. The effect of various therapies, including Oriental medicine, will be quantitatively evaluated through the visualization of vascular networks and hemoglobin oxygen saturation.

Sports Gym

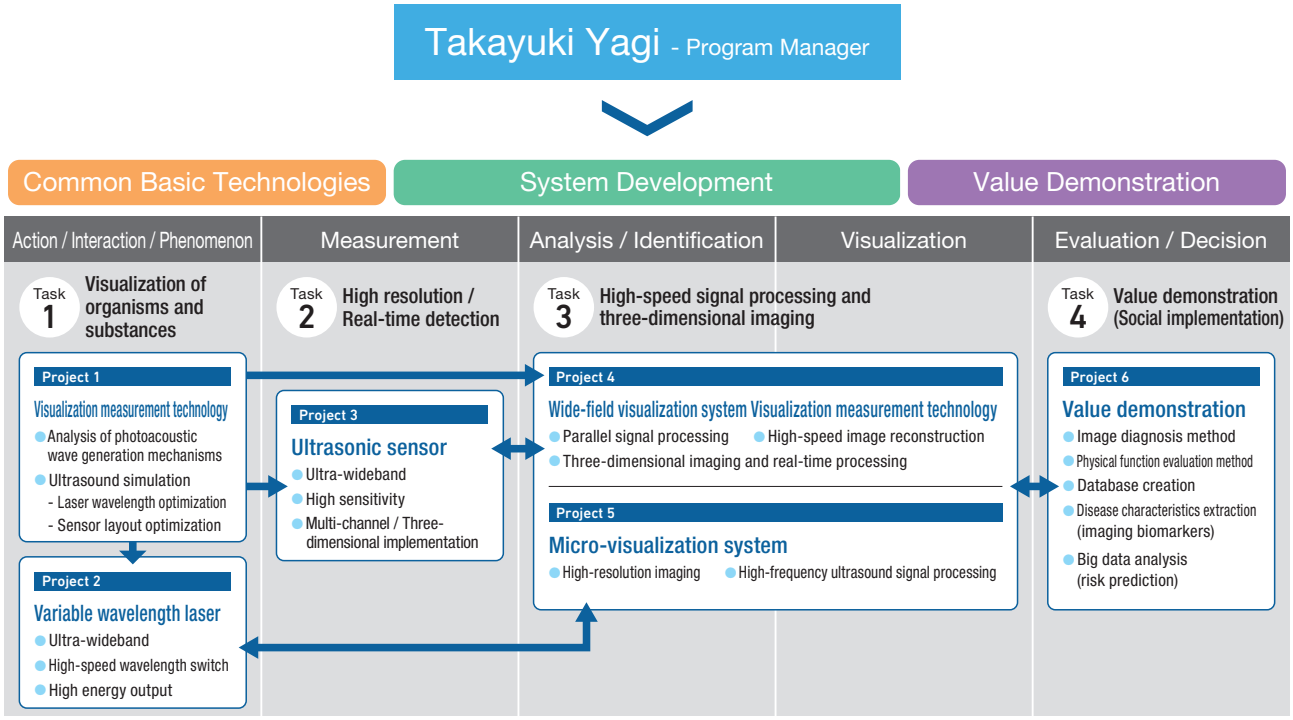
Checks the condition of blood vessels and joints to prevent injuries and accidents. Athletes under rehabilitation feel motivated by monitoring the effects and progress of rehabilitation.

Impulsing PAradigm Change through Disruptive Technologies Program (ImPACT)

Program name **"Innovative Visualization Technology to Lead to Creation of a New Growth Industry"**

- It allows real-time and three-dimensional visualization of morphological, functional, and structural changes in the interior of organisms and materials in a noninvasive and nondestructive manner by combining the most advanced types of laser and ultrasonic technologies.
- It allows for early diagnosis and health assessment through visualization of vascular network morphologies and changes in hemoglobin oxygen saturation associated with cancer, arteriosclerosis, diabetes, and arthropathy, as well as for inspection of defects in the interior of objects such as composite materials.

Organization chart of this program



Participating institutions

(As of April 2018)

Project 1	Visualization measurement technology	Kyoto University, Ehime University
Project 2	Variable wavelength laser	Riken, Megaopto Co. Ltd.
Project 3	Ultrasonic sensor	Japan Probe Co. Ltd.
Project 4	Wide-field visualization system	Canon Inc., Hitachi, Ltd.
Project 5	Micro-visualization system	Tohoku University, Shiseido Co. Ltd., Advantest Corporation
Project 6	Value demonstration	Kyoto University, Keio University, National Institute of Informatics, Kyushu University, Shiseido Co. Ltd., Ricoh Co. Ltd.

ImPACT is a program led by the Cabinet Office's Council for Science, Technology and Innovation (CSTI). The program was founded in 2014 with the objective of creating discontinuous innovations. The program manager (PM) is given high authority on planning, team formation, and budget allocation, and engages in the management of entire R&D as a general producer, casting researchers and R&D institutions.

ImPACT Impulsing PAradigm Change through Disruptive Technologies Program

"Innovative Visualization Technology to Lead to Creation of a New Growth Industry" Website
http://www.jst.go.jp/impact/hp_yagi/index.html

For inquiries regarding the organization, please contact the Cabinet Office.

ImPACT Program Promotion Office, Cabinet Office

Impulsing Paradigm Change through Disruptive Technologies Program Office

1-6-1 Nagatacho, Chiyoda-ku, Tokyo, 〒100-8914
TEL: 03-6257-1339
E-mail: g.sentan.pro@cao.go.jp

内閣府

For inquiries regarding the program manager or the program, please contact JST.

JST ImPACT Office

Japan Science and Technology Agency
Office for the Impulsing Paradigm change through Disruptive Technologies Program

K's Gobancho, 7, Gobancho Chiyoda-ku, Tokyo, 〒102-0076
TEL: 03-6380-9012
E-mail: impact@jst.go.jp URL: http://www.jst.go.jp/impact/

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