■Project Introduction

Advanced Biomedical Technology: Micro tomographic diagnosis using multi-functional OCT

~ Application to the diagnoses of skin and cartilage diseases, arteriosclerosis, cancer and regenerative medicine ~

profile
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Obtained a doctoral degree (Engineering) at the Department of System Quantum Engineering, Graduate School of Engineering, University of Tokyo in March 1999. He became a doctoral researcher at MIT in 1999, a lecturer of the Department of Mechanical Engineering, Graduate School of Engineering, Yamaguchi University in 2001, an associate professor of the Department of Applied Medical Engineering, Graduate School of Medicine, Yamaguchi University in 2004, a guest associate professor of the Department of Mechanical Engineering, MIT in 2008, and an associate professor of the Department of Mechanical and Physical Engineering, Graduate School of Engineering, OCT in 2013.

Wrinkles and sagging of the skin, which are caused by aging and ultraviolet rays, are also related to a decrease in the metabolism of skin tissue; therefore, micro circulation system including exchanges of interstitial fluid from/to tissues and cells are regarded as an important evaluation index for skin care and anti-aging.The skin tissue consists of the three main layers of epidermis, dermis and hypodermis, and capillaries with a diameter of 10μm to 20 μm run from the papillary layer under the epidermis to the subpapillary layer at the upper dermis, covering a depth of 500 microns from the skin surface.The properties of micro blood flow and diapedesis of interstitial fluid may change the viscosity and elasticity of the skin as well as metabolic functions. Hence, it is necessary to conduct non-invasive measurement of micro blood flow in order to clarify skin mechanisms such as the generation of wrinkles.

Also, in malignant tumors, which are the top cause of death, metastasis via neovascularization as well as the invasion depth of the tumor determine the cancer stage. Neovascularities grow around tumors, and they transmit more interstitial fluid and activate more exchanges of interstitial fluid compared with normal blood vessels; therefore, the risk of lymph node metastasis increases before that of blood metastasis. Accordingly, the blood dynamics of neovascularities is an important factor in determining treatment policies.The NBI endoscopic system, which is generally used for the diagnosis of cancer of digestive organs, only provides a surface image including overlapping mucosal layers that display the running status of blood vessels. Therefore, it is impossible to evaluate the invasion depth quantitatively or evaluate blood flow mechanisms, and the rate of correct diagnoses depends on doctors' skills.Optical coherence tomography (OCT) was developed recently [1], and it has enabled in vivo non-invasive visualization of morphological distribution of biological tissue. However, this system is based on the low-coherence interferometer; therefore, although it is possible to visualize biological tissue structures on a micro scale, it is impossible to evaluate the functional properties of biological tissue by visualizing blood flow dynamics.

We proposed the optical coherence Doppler velocigraphy (OCDV) system [2], which allows for precise detection of Doppler modulation frequencies in OCT interference signals. We are now developing an instrument for micro tomography that measures blood flow velocity distribution in the capillaries based on video signal rates.Our OCDV system is a low-coherence interferometer based on the fiber-type Michelson interference optical system, using the light source of a near-infrared band of 1,300nm. The reference arm optical system adopted the system that reflects light emitted from the diffracting grating on a curved mirror and conducts tomographic scanning by means of a resonant mirror. It realized high-speed optical path scanning and dispersion compensation.In addition, the adjoining self-correlation method has been introduced to detect phase changes in rear incoherence interference signals from biological tissues, and Doppler modulation generated by the dynamic changes of red blood cells, which indicate the blood flow dynamics, is examined by means of high-precision micro tomographic visualization.As shown in Fig. 1, a system using this technology was produced in cooperation with Takaoka Toko Co., Ltd. and is to be exhibited in Medical Japan 2017 in Osaka this February. It is scheduled to be on the market starting next year.

Figure. 2 shows examples of tomographic images produced by means of our OCDV. These are the images produced by means of micro tomography at 6cm from the wrist of a human forearm flexor for examining the morphological distribution in the skin surface layer and capillary blood flow distribution. Figures. 2 (a) and (b) show the normal condition and avascularization condition using tourniquet respectively.Since the diameter of red blood cells is about the same as the capillary diameter (10 micron), red blood cells flow very slowly (approx. 100 μm/s) and intermittently while deforming, and intermittent Doppler modulation signals are observed. This figure shows the images at the maximum blood flow speed in the data for about two seconds, which are projected on OCT tomographic images.It has been confirmed that the flow speed of blood that comes up from the upper dermis to the bottom of the epidermis is lower in the avascularization condition than in the normal condition. Also, in morphologic distribution of OCT tomographic images, Doppler modulation was detected in the low-brightness part, which was presumed to be blood vessels. Doppler modulation generated from red blood cells flowing in the capillaries was thought to be detected.Hence, this system was found to be effective in the quantitative evaluation of micro circulation mechanisms (metabolism) of skin tissues by visualizing in vivo blood flow speed. This result is expected to become an important evaluation index for skin mechanisms for anti-aging and smart aging. This research is expected to be important not only for medicine but also for the cosmetics industry, and we have been receiving inquiries from transdermal medicine companies and cosmetic companies.We are also studying the appropriateness of micro tomography for examining the blood flow speed distribution and neovascular network blood vessels in micro tumors by applying this method to the animal model of gallbladder cancer. We aim to diagnose the invasion depth of tumors, based on blood flow speed and 3D blood vessel images. This method is expected to be applied to the diagnosis of not only cancers of digestive organs, but also malignant neoplasms of skin cancer and brain tumors. It is also useful in the evaluation of medicine that prevents generation of neovascularization, and can be used for the monitoring of brain blood behavior in neurosurgery for brain infarctions, etc. We are now engaged in the application of this technology to neurosurgery and plastic surgery.

Meanwhile, the main factor leading to cardiac disease, which is one of the three main causes of death, is arteriosclerosis. In this regard, it is important to identify the changes in dynamic properties of biological tissue. Also, it is estimated that 40 million people in Japan suffer from osteoarthritis of the knee, and the understanding of viscosity and elasticity of cartilage is a key to early diagnosis; however, it has not been realized yet.We have developed a multi-functional OCT system, which contains our OCDV system [3] [4] [5], and we are developing a micro tomographic instrument for the diagnosis of dynamic properties of biological tissue (biomechanics, viscosity and elasticity). This can also be used to examine the skin in the fields of cosmetic skin care and plastic surgery and we are working jointly with a cosmetic company.In particular, evaluation of the dynamic quality of regenerative tissues is key to the realization of regenerative medicine and related business plans. We have already obtained the results of experiments using cultured skin models, and this method is expected to be effective for the evaluation of tissue quality.As stated above, we aim to realize a diagnosis system using micro tomography to visualize the functional properties of biological tissue such as blood flow speed, viscosity and elasticity, through collaboration of medicine, engineering and the private sector, and apply the accomplishments to the medical instrument industry, pharmaceutical industry and aesthetic and health industry, thus contributing to society through our support for the treatment of patients.

[1] Joseph M. Schmitt, "Optical Coherence Tomography (OCT) : A Review", Interface Focus, 1, (2011), IEEE Journal on Selected Topics in Quantum Electronics, Vol. 5, No. 4, (1999), pp.1205-1215.
[2] D. Furukawa, S. Saeki, R. Nishino, S. Mishima: "Accuracy verification of the micro tomography for flow speed distribution, using the high-frequency modulation low-coherence interferometer", Experimental Mechanics, in printing
[3] S. Saeki, D. Furukawa, Y. Sakata: "Micro tomographic visualization of dynamic properties (multi-functional OCT)", Optronics, in printing
[4] S. Saeki, Y. Nakamichi: "Application of the functional OCT using two wavebands to DDS (multi-functional OCT)", Hikari Alliance, 2015
[5] Souichi Saeki, "In vivo and in situ Tomographic Micro-Diagnosis using Functional OCT", Japanese Society of Mechanical Engineering, 26th Bioengineering Conference, Korea and Japan Symposium, 2014, (on CDrom).

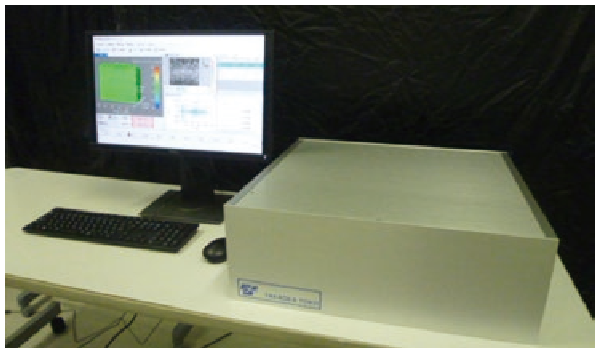

Fig. 1: Smart aging skin diagnosis instrument (OCDV system)
The system based on the accomplishment of this project was produced in cooperation with Takaoka Toko Co., Ltd. and is to be exhibited in Medical Japan 2017 in Osaka this February.

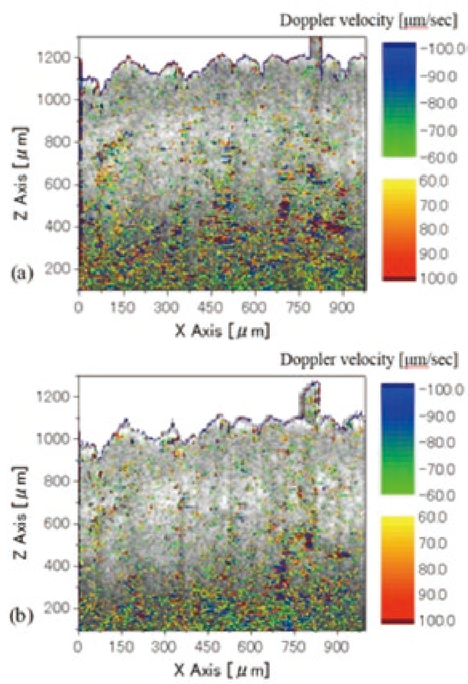

Fig. 2: Micro tomography of tissue morphological distribution and capillary blood flow velocity distribution on the wrist side of a human forearm flexor
The blood flow velocity is lower in avascularization condition using tourniquet (b) than in normal condition (a).