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EDITORIAL

Eiichi Tanaka, Ph.D. (1927–2021): pioneer of the gamma camera and PET in nuclear medicine physics

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1 Introduction

Dr. Eiichi Tanaka passed away on August 21, 2021, at the age of 93. The photo (Fig. 1) is a portrait of him when he was approximately 70 years old. Dr. Tanaka often said that he was "the same age as nuclear medicine." He is regarded as a great pioneer in nuclear medicine physics. His research activities were in a wide range of fields, from hardware to software, beginning with radiation measurement methods and extending to research on environmental radioactivity measurements, research and development of nuclear medicine imaging equipment, and medical image-reconstruction methods. Among them, the development of large-area gamma camera and positron emission tomography (PET) equipment significantly contributed to the diagnosis of diseases in many people through nuclear medicine examinations.

Dr. Tanaka was born on October 17, 1927, in Hyogo, Japan. In the same year, H. L. Blumgart co-authored a paper with O. C. Yens detailing the successful measurement of human blood flow using RaC (^{214}Bi) [1], and a nuclear medicine device was born. However, Dr. Tanaka's first encounter with radiation was a painful event during the detonation of the Hiroshima atomic bomb. As a high school student, he was in Hiroshima on August 6, 1945, approximately 6 km from the hypocenter of the atomic bomb. He graduated from the Department of Physics, Faculty of Science, Kyoto University. Between 1951 and 1957, he worked at the Electrotechnical Laboratory, the predecessor research institute of the National Institute of Advanced Industrial Science and Technology, where he developed a highly sensitive vibration capacitance electrometer. This paved the way for the domestic production of vibration capacitance electrometers by several manufacturers.

2 Very weak radioactivity measurements

In 1957, he moved from the Electrotechnical Laboratory to the National Institute of Radiological Sciences (NIRS), which was established in the same year. The NIRS aimed to (1) promote the medical applications of radiation and (2) to ultimately investigate the health effects of radiation and radiation protection. During the Cold War, the world's military powers were in a race to develop nuclear bombs and weapons. Dr. Tanaka started the development of a whole-body radioactivity measurement system to monitor radioactivity contamination due to radioactive fallout.

Dr. Tanaka also developed a coincidence-type spectrometer for highly sensitive measurements of very weak radioactivity (Fig. 2) [2]. In the device, a small recess (diameter 26 mm, depth 10 mm) was provided at the lower end of a large cylindrical plastic scintillator, and a mylar film with a thin gold-vapor deposition of approximately 1.3 mg·cm^{-2} was attached to the lower end as a beta-ray incident window to form the Geiger–Müller (GM) counter section. A stainless-steel loop electrode (wire diameter 50 µm) was placed as an anode, and gold was vapor-deposited on the inner surface of the depression to serve as a cathode. Q gas was poured into the depression from the outside to make it function as the GM counter. The sample was placed near the beta-ray incident window of the GM counter, and it was measured in coincidence using a plastic scintillation detector and GM counter. The invading background could be excluded, enabling the measurement of very weak radioactivity levels with high sensitivity. This device was commercialized by a company under the trade name "Pico-beta" in 1968 and is still marketed today by Fuji Electric Co., Ltd. It

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Fig. 1 Photo portrait of Eiichi Tanaka, Ph.D., courtesy of his family

has been used to measure not only environmental radioactive contamination, but also residual radioactivity from atomic bombs in Hiroshima and Nagasaki. Dr. Tanaka's experience in the devastated Hiroshima was his "residual radioactivity," as he stated that his invention reminded him of the tragic scenes of 1945.

In January 1960, Dr. Tanaka was appointed as Section Head of the Physics First Laboratory, Measurement of Radioactivity and Radiation under the physics division of the NIRS, and he oversaw the project entitled "Investigation on Radiation Measurements of Humans and Other Living Things." Research on the prevention and countermeasures against internal exposure to plutonium produced by nuclear power generation has been an urgent task of the NIRS, for which a long-term project was organized between 1963 and 1968. During this time, Dr. Tanaka was involved in the research and development of plutonium measurement methods, lung monitors, wound monitors, and dust monitors, and he devised and successfully built a prototype of a pocketable personal radiation alarm meter. This novel invention utilizes the howling oscillation of a vibration electrostatic electrometer [3]. The device was commercialized by Riken Keiki Co., Ltd.

3 Research and development of gamma cameras

In the late 1960s, as nuclear medicine gained momentum worldwide, hopes grew to improve the performance of gamma cameras (Fig. 3). In the Anger-type gamma cameras of the time, the position at which a gamma ray entered a scintillator and emitted light was calculated through the center-of-gravity calculation, in which the output of each photomultiplier tube (PMT) was weighted by the PMT's position. Dr. Tanaka considered the position calculation of the emission point from each PMT output as an inverse problem and succeeded in deriving the conditions that must be satisfied for the calculation of the ideal position.

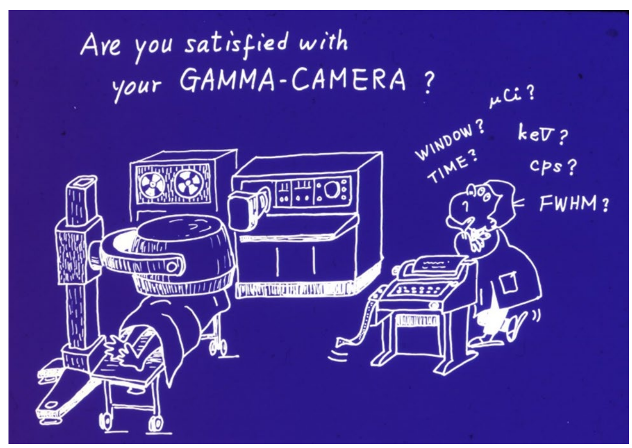
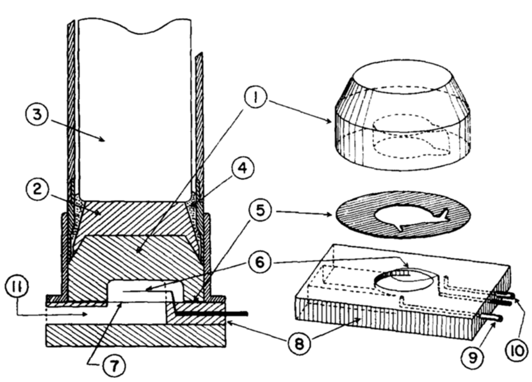


Fig. 3 Cartoon drawing done by Dr. Tanaka in 1967 of a scientist improving the performance of a gamma camera, courtesy of Dr. Tanaka's family

Fig. 2 Cross section and exploded views of the detector assembly. The detector is a low-level beta-ray scintillation detector using a coincidence method with a GM counter. The figure is reprinted from the work of Tanaka [2] (© 1961), with permission from Elsevier



1. Plastic scintillator
2. Lucite light pipe
3. Photomultiplier tube
4. MgO powder light reflector
5. Vinyl packing
6. Anode wire of GM counter
7. Window of GM counter
8. Lucite plate
9. Counting gas inlet tube
10. Counting gas outlet tube
11. Sample inlet

Based on these conditions, Dr. Tanaka and his colleagues discovered that the resolution and effective field of view could be improved using a new optimal position-calculation method to determine the incident position of the gamma rays. This discovery was published in 1970 [4]. Furthermore, he devised an implementation method in which the optimal position was calculated by converting position information into time information using a delay line, and he proposed a delay-line-type gamma camera (Fig. 4). After prototyping and demonstration, he succeeded in developing the world's first large-area high-resolution gamma camera, GCA-202, in 1972, in cooperation with Toshiba Co., Ltd., through the mediation of the New Technology Development Corporation (Fig. 5). Dr. Tanaka presented these results at the 1973 International Atomic Energy Agency symposium [5]. The device had a field-of-view diameter of 34 cm, and its resolving power was 30% higher than that of the conventional method. It was commercialized by the company and exported. That same year, the Mainichi Newspaper awarded Dr. Tanaka the 25th Mainichi Industrial Technology Award for his achievements. In 1978, he was awarded a Medal with Purple Ribbon by the Cabinet Office. In 1977, Dr. Tanaka's optimal position-calculation method was found to be equivalent to the position-calculation method based on the maximum-likelihood method [6].

The delay-line-type gamma camera was a reasonable device for analog circuits in their heyday. Owing to the advent of microprocessors in the 1980s, rapid advances in digital circuits have changed from analog processing to digital processing, and with the advancement of the digitalization of gamma cameras, delay-line-type gamma cameras have become redundant. However, the principle of the position-calculation method elucidated by Dr. Tanaka is still used today as a guideline for equipment design.

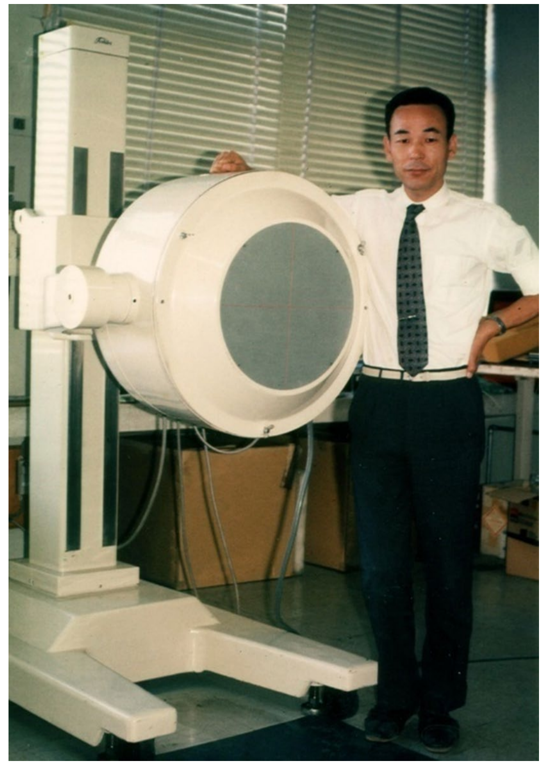


Fig. 5 Dr. Tanaka with the first GCA-202 produced by Toshiba Co., Ltd. in 1972 (© 1972 QST), courtesy of the National Institutes for Quantum Science and Technology. This was a large-area, high-resolution scintillation camera based on delay-line time conversion

4 Research and development of PET

In 1970, Dr. Tanaka and his team began research on positron imaging to utilize the short-lived positron-emitting isotopes produced by the medical cyclotron at the NIRS for nuclear medicine. First, they prototyped a positron camera with two

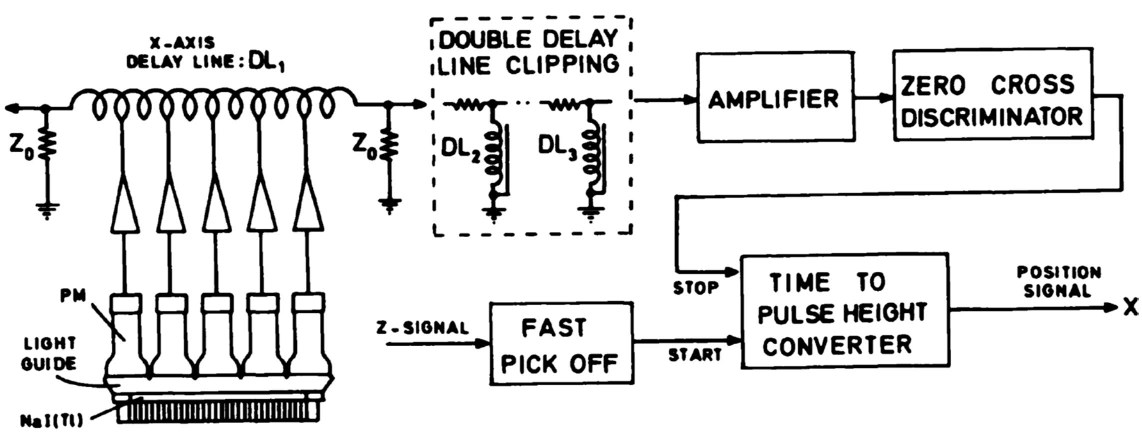


Fig. 4 Simplified block diagram of delay-line position computer using the time conversion method. The Y-axis position computer is omitted for simplicity. This research was originally published in JNM [4] (©1970 SNMMI)

two-dimensional (2D) detectors facing each other for coincidence detection. Subsequently, with the advent of X-ray CT, they moved to the research and development of positron CT (i.e., PET). A bismuth germanium oxide (BGO) scintillator developed by Hitachi Chemical Co., Ltd. was used, and the development of PET for brain studies proceeded with the cooperation of Hitachi Medical Co., Ltd. and the Central Research Laboratory of Hitachi, Ltd. In this context, Dr. Tanaka proposed an ingenious method (i.e., "Positology"). Figure 6 is a cartoon drawing by Dr. Tanaka, which was presented at an international conference in 1978 to propose this new scanning method. The method was characterized by improved resolving power owing to the intentional placement of detectors at unequal intervals around the circumference and the continuous rotation of the detector ring [7]. In 1979, approximately 4 years after Dr. Ter-Pogossian and his colleagues developed the world's first PET, the device was completed, and the Positologica-I (Fig. 7) for human brain studies started operation at the NIRS as the first PET device in Japan. Figure 8 shows the unequal detector array of Positologica-I obtained by the Positology method and the density distribution of its linear sampling [8].

Between 1979 and 1982, as part of a government-supported research and development project, the NIRS, Hitachi Medical Co., Ltd., the Central Research Laboratory of Hitachi, Ltd., and Hamamatsu Photonics Co., Ltd., under the guidance of Dr. Tanaka, collaborated to develop two whole-body PET systems. The first PET system, Positologica-II, was installed at the NIRS in 1982 (Fig. 9), and the second PET system, Positologica-III, was installed at Kyoto University in 1983 and used for clinical application research. The detectors in these PET systems were the first to use a coding technique that electrically discriminates gamma-ray-detected crystals from the two output signals. Positologica-II uses a four-crystal-coupled BGO detector with a coding scheme. In this system, two PMTs

Fig. 7 Positologica-I for human brain studies (© 1979 QST), courtesy of the National Institutes for Quantum Science and Technology

Fig. 6 Cartoon drawing done by Dr. Tanaka in 1978 of a scientist with the idea of Positology, courtesy of Dr. Tanaka's family

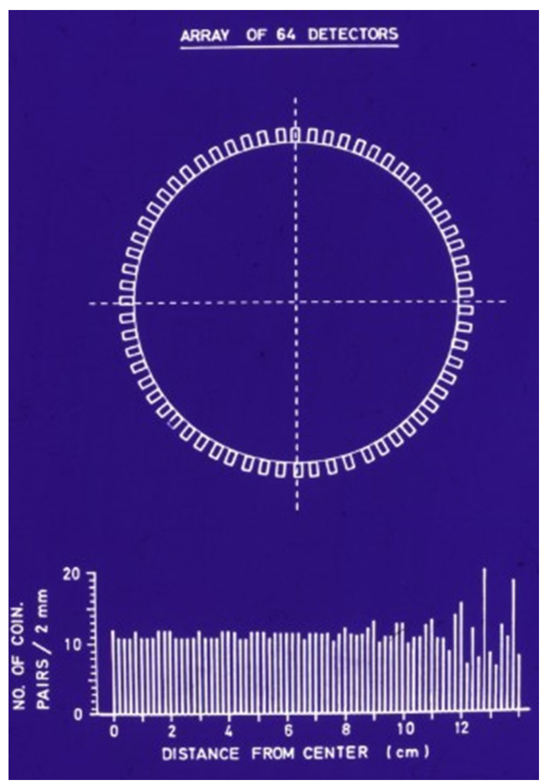


Fig. 8 An array of unequally spaced detectors and the linear sampling density distribution of the array when implemented in the Positologica-I. The figure is courtesy of Dr. Norimasa Nohara

Fig. 9 Photo of Positologica-II for human body studies, courtesy of Dr. Tanaka's family

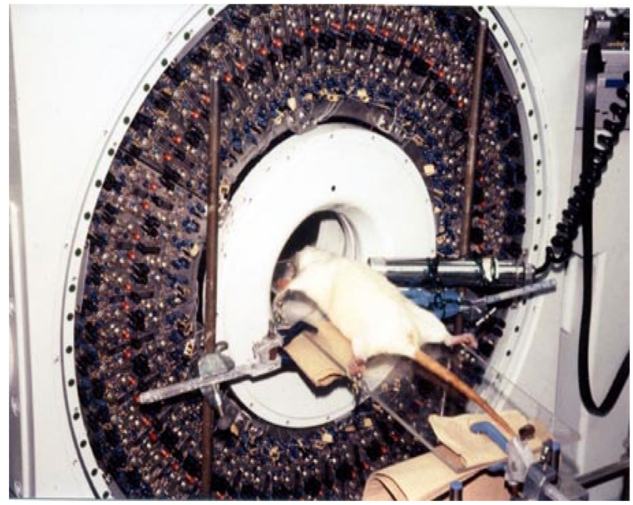


Fig. 10 Photo showing a mouse during brain measurement with the Positologica-IV, courtesy of Dr. Tanaka's family

were coupled to four BGO crystals, and each emission from each crystal was distributed to two photodetectors at different light levels, such that the ratio of the two output signals could be used to discriminate the crystals. This method allows the number of photodetectors to be halved relative to the number of crystals, making it possible to arrange crystals without gaps, achieving both high sensitivity and resolution. In addition, Hamamatsu Photonics Co., Ltd. developed a square dual-PMT that incorporated two PMTs in a square glass tube, which was used in the Positologica-III as a light-receiving element in the coding method. The coding method was extended to become a 2D coding method, which later became the forerunner of the block detectors that became mainstream in commercial PET.

As the demand for PET dedicated to animal studies increased with the progress in PET research, the NIRS collaborated with Hamamatsu Photonics Co., Ltd. in 1983 to develop the world's first small-animal (mouse) PET, Positologica-IV (Fig. 10). A gated PMT developed by Hamamatsu was used to achieve the world's highest resolution (3 mm) at that time. In 1984, Dr. Tanaka was awarded the 3rd Shimadzu Award by the Shimadzu Science and Technology Foundation in recognition of his achievements in radioisotope imaging equipment. Research on PET equipment and its development have been highly evaluated. As a development consignment project of the New Technology Development Corporation, the development of a high-performance, high-resolution head PET for researching higher order functions of the human brain was approved. Between 1986 and 1989, Hamamatsu Photonics Co., Ltd. and the NIRS collaborated to conduct development research under the guidance of Dr. Tanaka. Using a unique PMT "Quad-PMT" with four independent photomultiplier dynode structures in a single rectangular glass container, that is an extension of the "Dual-PMT", the entrusted project PET for brain studies completed in 1988, and achieved a resolution of 3.5 mm in the center of the field of view.

5 Basic research and SPECT research

In the 1970s, the commercialization of X-ray CT with EMI scanners spurred extensive research on tomographic imaging methods. Dr. Tanaka researched analytical image-reconstruction methods and independently developed a filter-corrected back-projection method. When he courageously submitted his paper, he was surprised to find that the content had already been presented. However, he resubmitted his paper after determining the optimal filter for reconstructing images from projection data containing statistical noise from a new perspective. This study was approved in 1975 [9]. His research is truly original, as noise optimization had not been explored in existing studies. Dr. Tanaka further considered image reconstruction, expanding the scope of applications from conventional 2D to 3D by introducing superfunctions, and successfully derived a filter for the 3D filter-corrected back-projection method [10].

In parallel with the above PET developments, Dr. Tanaka also conducted extensive basic research, including the development of a variable sampling time technique to improve the high-count rate characteristics of scintillation detectors (1979) [11], theoretical research on the design of multi-slice PET (1982) [12], theoretical research on PET reconstruction using gamma-ray time-of-flight information (1982) [13], and research on the reduction of total noise in PET images by an iterative image-reconstruction method (1982) [14]. It is worth noting that Dr. Tanaka was the first to show that improving the measurement accuracy of gamma-ray time-of-flight differences not only reduced the random coincidence but also improved the quality of the reconstructed images.

In the mid-1980s, Dr. Tanaka also undertook the challenge of attenuation correction, which had been a long-standing issue in single photon emission computed tomography (SPECT), and proposed a weighted back-projection (WBP) method [15]. In SPECT, the 360-degree projection data are redundant. There are many solutions with different noise propagation characteristics owing to differences in handling redundancy. However, Dr. Tanaka derived the WBP method as a method that considers noise propagation characteristics, in addition to the rigor of image reconstruction. The following year, he proposed a radial post-correction method that simplified and accelerated the WBP method and conducted a detailed comparison between the WBP method and other SPECT image-reconstruction methods for correcting uniform attenuation [16]. By highlighting the importance of redundancy in SPECT image-reconstruction methods at an early stage, Dr. Tanaka contributed significantly to subsequent research on analytical SPECT attenuation correction. Simultaneously, between 1983 and 1985, Dr. Tanaka served as the principal investigator of the "Research on the Development of a High-Performance Single Photon ECT Device," a group study funded by the Ministry of Health and Welfare Cancer Research Grant, working vigorously with the group members.

In 1988, after retiring from the NIRS, he relocated his research to the Tokyo branch office of Hamamatsu Photonics Co., Ltd., where he worked as an advisor. The company opened a Central Research Laboratory in 1990. In 1992, the PET Center was constructed and the development of PET and applied research using animals commenced. Dr. Tanaka was enthusiastic about training and instructing young engineers, and he researched image-reconstruction methods with young colleagues [17, 18]. From 1993, he was also a lecturer at Seikei University Graduate School, where he lectured on medical physics measurements for 9 years and enjoyed a very good reputation among the students.

6 Dr. Tanaka's final research

Dr. Tanaka had an unresolved issue in his research on very weak radioactivity measurements in the 1960s. The study of a magnetic levitation ionization chamber using permanent magnets failed several times and yielded no results. However, he conceived a new idea in 1990 to overcome these difficulties by exchanging permanent magnets with electromagnets and researching ionization chambers using a magnetically suspended electrode. He levitated the center electrode of the ionization chamber in a non-contact manner, prototyped all high-sensitivity ionization chamber radiation measuring instruments without electrical leakage by hand, and evaluated their performance [19]. As a result, Dr. Tanaka realized an extremely high-performance environmental radon concentration-measuring instrument, which gave him a great sense of accomplishment.

In 1993, Dr. Tanaka was appointed to the Board of Directors of Hamamatsu Photonics Co., Ltd. and was given heavy responsibility from a technical viewpoint in the company's management team. Dr. Tanaka had long been interested in and researched successive approximation image-reconstruction methods [20]. After he retired as an advisor in 2003, he focused his research on accelerating iterative image reconstruction, specifically considering how to speed up the block-type iterative method, and developed a new iterative reconstruction method with excellent convergence, known as the dynamic row-action maximum-likelihood algorithm (DRAMA) [21]. The algorithm was put into practical use in PET devices from Shimadzu Corporation and Hamamatsu Photonics Co., Ltd. Dr. Tanaka viewed this as one of the best research results that he had achieved. Furthermore, in 2010, Dr. Tanaka and his colleagues analyzed the convergence of the DRAMA method in detail and obtained research results that extended to the iterative image reconstruction of 3D PET. They detailed the research in a paper, which they submitted to Phys. Med. Biol. [22]. This was the last publication in which he was the leading author. Dr. Tanaka continued his research with young people, even past the age of 80, until he retired from Hamamatsu Photonics Co. Ltd. in 2014.

In 1993, 1994, and 1996, he became an honorary member of the Japanese Association of Radiological Physicists (the predecessor society of the Japan Society of Medical Physics), Japanese Society of Medical Imaging Technology, and Japanese Society of Nuclear Medicine. In 1997, he was awarded the Order of the Sacred Treasure, Gold Rays with Neck Ribbon, in recognition of his many years of achievements in medical imaging technology. In 2013, Dr. Tanaka was certified by the International Organization for Medical Physics as one of the top 50 medical physicists in the world, who have attained remarkable achievements in medical physics in the last half-century.

The research trail of Dr. Tanaka reveals the surprising fact that his achievements covered various fields, such as radiation measurements, nuclear medicine, and imaging engineering with astounding insight in each area. His greatest achievements were the development of the world's first large field-of-view gamma camera and Japan's first PET system and subsequent systems. Dr. Tanaka made a significant contribution to the development of nuclear medicine equipment, which is indispensable for modern medicine. He was an outstanding scientist who was globally unparalleled for his achievements from choosing the direction of his research by paying attention to the demands of the times and benefiting society. He was also an excellent mentor to researchers and engineers in the field of nuclear medicine physics, and his teachings live on among the younger generations. In his 2018 lecture [23], Dr. Tanaka revealed that his favorite quote was a saying by Leonardo da Vinci: “Inspiration comes only to those who keep thinking.” This quote has been carried over to the current Imaging Physics Group at QST, which is rooted in Dr. Tanaka’s Physics First Laboratory in the Division of Physics at the NIRS.

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Data Availability This is not applicable to this article because this is not an original article.

Declarations

Conflict of interest The authors declare that they have no conflict of interest.

Research involving human participants and/or animals (if applicable) Not applicable.

Informed consent (if applicable) Not applicable.

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