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The 456th International Symposium on Therapy

The 456th International Symposium on Therapy was held by the Zoom Webinar on September 15, 2022. Dr. Ko Ichihashi, Director of the International Medical Society of Japan (IMSJ), presided over the meeting.

Medical ultrasonics
-From POCUS to front-end technology-

Introductory Message from the Chair

Ko Ichihashi, MD, PhD
Director, IMSJ

The theme of the 456th International Symposium on Therapy has been set as "Medical ultrasonics -From POCUS to front-end technology-". Ultrasound in medicine is primarily used for diagnosis. Previously, technicians and physicians familiar with examinations ordered performed examinations in physiology laboratories for detailed observations, which was highly valued. Recently, however, the usefulness of Point of Care Ultrasound, which is performed at the bedside by the attending physician, has been pointed out. Akira Tada MD., Clinical director, National health insurance kuniyoshi/hasekebara clinic, who is a graduate of Jichi Medical University, has been practicing efficient community medicine by making full use of ultrasound examinations. Today, he will explain the usefulness of POCUS mainly with actual case presentations.

Katsuro Tachibana M.D., Ph.D., Professor, Dept of Anatomy, Fukuoka University School of Medicine, has been researching the use of ultrasound for treatment for two generations. He will talk about new world-leading technologies, starting with thrombolysis, then microbubbles, and further ultrasound gene therapy using nano-bubbles.

I hope that you will learn about the wide range of usages of ultrasound in medicine by listening to their lectures on the two extremes - the usefulness of ultrasound in daily medical practice and the front-end technology of ultrasound used in gene therapy.

Lecture I

POCUS (Point of care ultrasound) spreading in- to out-of-hospital for all the patients in Japan

Akira Tada MD.
Clinic director
National health insurance kuniyoshi/hasekebara clinic

Point of care ultrasound (POCUS) refers to ultra sonography performed and interpreted by a clinician at the patient's bedside.

【Differences between POCUS and comprehensive ultrasonography】

Comprehensive ultrasonography is mainly performed by organ-specific ultrasound specialists and ultrasound technologists using high-performance ultrasound equipment installed in ultrasound examination rooms.

POCUS, on the other hand, is a quick ultrasound examination performed at the bedside by a clinician focusing on findings necessary for diagnosis or treatment. For this purpose, the ultrasound device used in POCUS should be small and portable.

【POCUS development】

The earliest POCUS protocol was FAST (focused assessment with sonography for trauma) for intra-abdominal hemorrhage following blunt trauma.

Since then, POCUS protocols have been developed and utilized in clinical practice.

POCUS was initially developed for use in emergency departments and hospitals, and has since been used in a wide range of settings, including disaster situations and home care.

In recent years, the multifaceted use of POCUS in COVID-19 has also attracted attention. While there are limitations in the use of imaging tests with droplet and contact infection prevention, POCUS, which is easy to perform in the field, can be used to detect pneumonia, myocarditis, and thromboembolism, which are serious complications of COVID-19, as well as for respiratory management and transfusion management.

【The evolution of hand-held ultrasound devices】

Furthermore, POCUS has progressed along with the evolution of portable ultrasound devices.

The improved portability of POCUS due to its smaller size allows for ultrasound examinations at any location, and the improved image quality has led to a variety of applications.

In addition, the ICT function of the ultrasound device itself facilitates information sharing with colleagues and supervisors and makes it easier to consult with patients in and out of the hospital and at home.

These technological advances are changing home care as well as emergency medicine.

As of 2022, there will be more than 800,000 patients in home care in Japan, and the number is increasing every year. Although there are limitations on the tests and treatments in home healthcare, the use of POCUS has greatly expanded the possibilities.

On the other hand, in home healthcare, it is difficult to perform POCUS on all indicated patients due to the lack of manpower of physicians.

Therefore, home-visiting nurses are expected to be the POCUS providers. They are regularly involved in the medical and nursing care of patients at home and can more closely assess patients' changes.

The benefits of using POCUS for home-visiting nurses are as follows. The visualization of patient complaints provides reassurance to both patients and health care providers, and the use of ultrasound images facilitates the communication of information between professions.

【The issues of POCUS】

First, there are some barriers to evidence creation.

Although data on the efficiency and economics of POCUS are increasing, data on patient outcomes are still insufficient. On the other hand, the variation in skill levels of clinicians performing POCUS and the difficulty of standardizing scanning protocols are barriers to clinical research and are issues to be

addressed in the future.

Next is the issue of the payment system for POCUS.
Concerning medical fees, POCUS is partially distinguished from comprehensive ultrasonography in home healthcare in Japan, but in hospitals, there is no distinction between them.
In addition, POCUS performed by visiting nurses is currently not reimbursed, which is an obstacle to its widespread use.
Thus, for POCUS to be widely utilized in the future, it is considered necessary to establish a payment system.

Thirdly, educational opportunities should be secured under the SARS-CoV-2 epidemic.
The most desirable learning for POCUS is hands-on training, in which participants hold the probe and receive instruction, rather than just listening to lectures.
On the other hand, the number of hands-on seminars rapidly declined after the SARS-CoV-2 epidemic, and securing educational opportunities became an urgent issue. In response to this problem, online lectures, remote live demonstrations, and hands-on activities are gradually increasing by utilizing ICT devices. The search is on for more effective educational methods, combining traditional and new educational methods.

Lecture II

New horizons in ultrasound gene therapy with nanobubbles

Katsura Tachibana, MD. Ph.D.
Professor, Dept of Anatomy
Fukuoka University School of Medicine

Gene therapy has been intensively investigated as a new treatment for various cancers as well as for rare diseases. Therapeutic genetic materials such as DNA or RNA are required to reach the target cells in sufficient quantities to yield beneficial outcome. The use of nanobubbles (NBs) for ultrasound-mediated gene therapy has recently attracted much attention. The word “nanobubble” is officially termed by ISO as “ultrafine bubble” and defined as bubbles smaller than 1 micrometer. Few studies have evaluated the effect of different NB size distribution to the efficiency of gene delivery into cells. We studied, various size of albumin stabilized sub-micron bubbles and examined in an in vitro ultrasound irradiation setup in the aim to compare and optimize gene transfer efficiency (1). Results with pDNA showed significant increase of gene transfer efficiency in the presence of NB. Similarly, carrier-free mRNA transfer efficiency increased in the same conditions. It is suggested that NB size contributed more to the delivery of genes into the cytoplasm with ultrasound. Although further experiments are needed to understand the underlying mechanism for this phenomenon, the present results offer valuable information in optimizing of NB for future ultrasound-mediate gene therapy. In addition, our experiments suggests that lower ultrasound intensity can be used to induce gene transfer thus opening possibility of miniaturization of the ultrasound device. In the future, hand-held, battery powered, portable ultrasound gene “injectors” may be used for gene vaccines and for various cancer therapy.

1) Kida H, Feril LB, Irie Y, Endo H, Itaka K and Tachibana K (2022) Influence of Nanobubble Size Distribution on Ultrasound-Mediated Plasmid DNA and Messenger RNA Gene Delivery. Front. Pharmacol. 13:855495. doi: 10.3389/fphar.2022.855495

Discourse

Introduction of the speaker of discourse

Ko Ichihashi, MD, PhD
Director, IMSJ

Pianist and music producer Hiroo Hadame will give us a lecture titled "Music is a Flower that Blooms with Time". Mr. Hadame’s broad-ranging and unique activities include the planning and producing of Italian operas, classical concerts, and others in Noh theaters, shrines, temples, and

rural settings, as well as the teaching of posture and glottal movements through scientific analysis inside and outside Japan. He is going to introduce some of his activities, and also going to use his own piano performance and beautiful voice to make his lecture easy-to-understand for us. Please look forward to his lecture.

Discourse: Music is a Flower that Blooms with Time

Hiroo Hadame
Pianist, Music producer

I cannot thank you enough for giving me this wonderful opportunity!
I feel as if my long-standing science complex has been lifted.

Now, as a musician myself, I would like to talk a little about music and language, and the necessity of music in a liberal arts context.

In recent days, the word “diversity” has become a key word in our society. In Japanese, this word is translated as 多様性 (groups with widely differing properties co-existing). But in the case of Italy, for example, the word "different" is not used very often in everyday life, but rather use the word "Diverso" (noun form Diversità). In other words, “A” and “B” are different.
If I had been able to substitute numbers so that A=B, I would have gone into the science field.

When talking about vocal music education, unlike piano and violin, the instrument is inside the body and is difficult to visualize, so numbers do not intervene in instruction but rather emotion and experience becomes the key in instruction throughout history.
The reality is that medical and scientific guidance on the differences in skeletal structure between A and B, muscle strength, posture, vocal cord mechanisms, diaphragm function, angles, language frequencies and sound movement is not mainstreamed in the teaching field.

Focusing on the voice, during vocalization, we close the vocal folds and place them on the exhaled breath, but when singing, the amount and timing of the inhaled breath can affect the following expression.
When adding language to this mix, the modulation of consonants and vowels when singing in a language other than one's native tongue is quite impregnable and requires technique. Therefore, leads to cultivating the perception and acting ability to instantly bloom, from conscious to the unconscious.

At the School of Liberal Arts, to which I belong to, although Liberal Arts is the foundation, few students have a deep understanding of the seven liberal arts (astronomy, arithmetic, geometry, rhetoric, grammar, music, and philosophy) that have been advocated since Plato's Academia, and many simply think that it is enough to have a broad or shallow knowledge or have in-depth knowledge. The understanding of why music (perception) was needed from that time period has become an out of interest for many.

When talking about music, it can be said that music cannot be spoken or sung unless all of the following are in place: phenomenological sound = astronomy, harmonic arrangement = arithmetic, graphic interpretation of musical notation = geometry, rhetoric as its underlying grammar, how it is sung and its expression as rhetoric.
In addition, when performing, the probability of being moved by the performance depends on the instantaneous perception of space (environment, score), time (notes, beats, measures, or shared performance time), force (emotional and physical coefficient of diversity between oneself and the composer), and direction (the entire space or an audience in a particular direction), as initial settings before any esoteric philosophy.
In other words, it is necessary to think thoroughly about one's own stature, position, and location from a cultural fixed point, and have the knowledge and education to quickly derive the center (solution to the problem), and music is to be done after covering all of these bases.
For example, in my field, opera singers were

originally known as the well-rounded, cultured, and educated that even the presidents would bow down to them.

I have interacted with opera singers, conductors, and others in the field, mainly in Italy, and while I enjoy the excitement of star singers in costume, performing traditional operas, the more I meet the masters of this art form, the more I feel the importance of "Human being as a collective art" in the sense that Opera = Opus (Latin) = work.

Therefore, for a musician, in order to become an expressive person who can attract not only a limited audience but also people from other genres, one must consciously and physically manipulate the body, become "empty" and receive the energy of the subject (in classical music, the musical score). Once getting the sense of "emptiness", then "color" should be added and transmitted to the space and the object. Because of this, I have struggled with my spine flexing and receiving too much.
But now that I have been involved in both poles of Japanese "nodding culture" and Western "horizontal culture," I think I finally understand how to transmit in my way.

Now that my mother, who used to love Gymnaster (miyakowasure), is in need of nursing care and is now like Edelweiss, every day is full of surprises.
Whether it be water lilies or daffodils, violets or dandelions, even if we encounter each other in different environments, sometimes under extremely different circumstances, I would like to see a development where we can better each other, understanding the stature and thoughts of the counterpart.

Maintaining status quo is decline!

Grazie!