In Memoriam – Hiroshi Furuhashi, M.D., Ph.D. (1944–2012)

When Hiroshi Furuhashi, M.D., Ph.D., passed away peacefully on August 11, 2012, just before his 68th birthday, the world lost one of its great pioneers in the field of sonothrombolysis for stroke treatment. Hiroshi Furuhashi was born on September 6, 1944 in Nagano-shi, Japan. In 1977, he received a doctoral degree from the department of Engineering at Keio University for his work on ultrasonic Doppler blood flow meters. He then attended the Jikei University School of Medicine, receiving his medical degree in 1982. He became an associate professor at the Medical Engineering Laboratory at Jikei in 1983. In 2002, he was appointed as professor and director of this institute until his retirement in 2010. Professor Furuhashi was an advisory board member at the Neurosonology Research Group of the World Federation of Neurology, an honorary member of the Japan Academy of Neurosonology and of the European Society of Neurosonology and Cerebral Hemodynamics and the president of the Japan Society of Embolus Detection and Treatment.

Hiroshi Furuhashi was the first to describe the ability of ultrasound to accelerate thrombolysis through the skull, thus paving the way for future clinical trials of treating stroke with sonothrombolysis. This finding was made upon the foundation of decades of dedicated research on the quantitative measurement of blood flow with Doppler ultrasound. Furuhashi's shift to therapeutic ultrasound resulted in numerous important contributions to the field of sonothrombolysis, including the development of novel dual frequency equipment for combined ultrasound therapy and monitoring. Much of what

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we know about the safety of sonothrombolysis stems from his elegant work which elucidates the biological effects of ultrasound upon the brain. Following the unexpected occurrence of hemorrhages in the TRUMBI (The Transcranial Low-Frequency Ultrasound-Mediated Thrombolysis in Brain Ischemia) trial, Furuhashi strove to understand how low frequency ultrasound might be able to promote bleeding in conjunction with recombinant tissue plasminogen activator therapy. He hypothesized that the parameters used in the TRUMBI trial could

cause an overlap of the ultrasound wave as it runs its course back and forth across the brain, reflecting off the skull. Thus, he argued, the instantaneous intensity of ultrasound in the brain tissue may multiply constructively at some localized sites of brain tissue, resulting in mechanical indexes that are larger than the maximum limit set by the FDA. Indeed, recent simulations support his view and show that even small increases in the applied pressure could lead to such phenomena. In further studies, he demonstrated safe parameters for low frequency ultrasound in vivo and showed that this therapy could be administered safely in hypertensive rodents. Furuhashi also discovered other beneficial effects of ultrasound upon brain tissue. For example, he showed that ultrasound treatment increases the level of nitric oxide, which he postulated could have an effect upon angiogenesis following stroke. His last studies evaluated the safety and efficacy of sonothrombolysis in primates, a last step before the translation to clinical studies with his new dual mode system.

Those who knew Furuhashi admired his strong passion for research, his broad knowledge of medical engineering and his determination for the clinical translation of his

discoveries. 'Meticulousness of a devil and boldness of an angel' described his attitude as a researcher. Workers in his laboratory were familiar with his motto 'Polish it 100 times'. Furuhashi enjoyed celebrations and held events to encourage work in his laboratory or to show appreciation for a member of his research group who had received an award. His family recalled that he often enjoyed family trips to hot springs and always had a radiant smile. In contrast, if he was made to stay at home for more than three days, he became restless. Even shortly before his death following a long illness, he was determined to travel to the International Symposium on Therapeutic Ultrasound in Heidelberg for a discussion of new avenues for sonothrombolysis research. He was forced to cancel this trip, leaving us sadly without further opportunities to learn from this great scientist.

We will remember the spirit of Hiroshi Furuhashi and we will do our best to continue in his footsteps by developing treatments for stroke with the utmost care for patient safety.

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