

## Medical Engineering Laboratory

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### General Summary

The Medical Engineering Laboratory has developed new ultrasound (US) therapeutic technologies. This year, with the support of a research grant from the Ministry of Health, Labour and Welfare, we focused on the development of new thrombolytic treatments for patients with acute ischemic stroke. Basic research studies in molecular medical engineering have also been continued to develop ultrasonic drug delivery system. In particular, the safety of phase-change nanodroplets from fluid to gas by ultrasonication has been evaluated histopathologically, and the increase in nitric oxide (NO) generation by ultrasonication has been analyzed by means of immunochemical real-time monitoring. We have contributed to the development of a national database on less-invasive medical devices that includes information on less-invasive technology from around the world and gathers the needs of clinicians. We have also improved previously developed diagnostic techniques for measuring cerebral circulation and hemodynamic variables by the means of noninvasive transcranial ultrasonography.

### Research Activities

#### *An integrated US system for the diagnosis, analysis, and treatment of acute stroke*

This system uses transcranial ultrasonication to enhance the thrombolytic effects of recombinant tissue plasminogen activator (rt-PA) in the treatment of acute ischemic stroke according to navigation with US performed with a single probe. For the clinical application of this system, we have developed a new device for holding the US probe near the patient's head. Because many Japanese patients have an insufficient temporal bone window, we developed a brain virtual ultrasonography method for the use of this sonothrombolysis system in these patients. This new technology can display as a US image in real time the same cross-sectional image obtained with magnetic resonance imaging or computed tomography.

#### *Ultrasonic thrombolysis*

The accelerating effect on thrombolysis of combined use of low-frequency (500-kHz) US, rt-PA, and bubble liposomes was verified *in vitro*. Bubble liposomes have a great potential for accelerating the thrombolytic effect of rt-PA with continuous-wave US.

#### *Verification of the safety of an ultrasonic drug delivery system for cancer therapy*

We have been developing an ultrasonic drug delivery system that is integrated with an ultrasonic diagnostic and therapeutic system with phase-change nanodroplets to provide US images of tumors and to simultaneously kill tumor cells with US heating effects for the selective treatment of tumors. We established a method to verify damage to normal

tissue surrounding tumors by means of histopathological evaluation with hematoxyline/eosin and Masson's stain.

#### *NO generation by US stimulation*

We have reported that the NO concentration in the thigh adductor muscle of rabbits increased with the intensity of applied US. Moreover, we have also demonstrated that US stimulation enhances NO generation in tumors.

#### *Development of database for less-invasive medical devices*

On the basis of an existing database of nanomedicine, we have developed a new database to provide a "knowledge infrastructure for minimally invasive medical technology." This database can be accessed via the Internet and includes a special forum for discussions of various less-invasive technologies. This development was supported by a research grant from the Ministry of Health, Labour and Welfare.

#### **Publications**

**Nakagawa K (Dept Anesthesiol), Ishibashi T (Dept Neurosurg), Matsushima M (Div Clin Res Dev), Tanifuji Y<sup>1</sup>, Amaki Y<sup>1</sup> (Dept Anesthesiol), Furuhashi H.** Doppler monitoring require a pause for safer use? *Cerebrovasc Dis* 2007; **24**: 27-34.

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**Sugita Y, Mizuno S, Nakayama N, Iwaki T, Murakami E, Wang Z, Endoh R, Furuhashi H.** Nitric oxide generation directly responds to ultrasound exposure. *Ultrasound Med Biol* 2007; **34**: 487-93.

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