# Medical Engineering Laboratory

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## General Summary

Medical engineering is an essential base for developments in medicine. In our laboratory, there are 2 key technologies: ultrasound and polymeric biomaterials. We have developed ultrasound technology for a new thrombolytic treatment for acute ischemic stroke. Our ultrasound research uses medium-frequency ultrasound and close collaboration with clinical departments and basic science departments both in our university and in other universities and hospitals. For the other key technology, polymeric biomaterials, we have been researching their applications to drug delivery systems. We have also recently applied polymeric biomaterials to diagnostic imaging through the synthesis of new polymeric contrast agents. In particular, we are studying polymeric micelle systems that can deliver both drugs and contrast agents. Therefore, these systems are called "theranostic" systems because they have functions in both therapy and diagnostics. Additionally, we have research topics combining the ultrasound and polymeric-biomaterials technologies. One example is ultrasound-assisted targeting of polymeric drug carrier systems.

## Research Activities

*Medical application of ultrasound*

We have applied ultrasound to transcranial therapy for ischemic stroke. Although injection of tissue plasminogen activator has been the only effective therapy, an even more effective therapy is urgently required. The transcranial ultrasound can enhance thrombolytic activity of tissue plasminogen activator. Our technology features the use of medium-frequency ultrasound, which possesses greater thrombolytic enhancement than does ordinary ultrasound. However, the medium-frequency ultrasound is believed to be associated with a high risk of brain hemorrhage. To decrease this risk, we control both the period and interval of irradiation and have successfully proven the safety of ultrasound irradiation in models of hypertensive brain ischemia. We have been developing this new therapy through the Super Special Consortium for Supporting the Development of Cutting-Edge Medical Care program supported by the Ministry of Health, Labour and Welfare of Japan.

*Polymeric micelle drug carrier systems*

Polymeric micelles are assemblies of synthetic polymers that have been applied to drug targeting. Associate Professor Yokoyama, director of this laboratory, is an international pioneer in the development of polymeric micelle targeting systems. Currently, 4 formu-

lations of polymeric micelle anticancer drugs are undergoing clinical trials in Japan, Europe, and the United States. We are trying to establish next-generation science technology in the polymeric micelle systems. We are studying the immunological properties of polymeric micelles. Curiously, the polymeric micelle carriers differ greatly from liposome systems. Although both carrier systems possess poly(ethylene glycol) on their surfaces, only liposomes exhibit an immunological response called the accelerated blood clearance phenomenon. This difference is a great advantage of the polymeric micelle systems. We also study basic chemistry to analyze the drug-incorporated inner core through the use of the Super Photon Ring 8 GeV (SPring 8) Large-Scale Synchrotron Radiation Facility and to prepare polymeric micelles with cross-linked inner cores through photochemistry. These cross-linked micelles are extremely useful for clarifying the in vivo fates of polymeric micelles.

*Polymer-based contrast agents for image diagnosis*

We have developed new polymeric micelle contrast agents for magnetic resonance (MR) imaging. These agents were shown to target solid tumor sites and to exhibit clear MR images of extremely small tumors. Therefore, the polymeric micelles can be used for tumor theranostics because they can direct both drugs and contrast agents towards solid tumors. Furthermore, we are studying a novel application of the polymeric carrier system for diagnosis of ischemic stroke. We observed that the polymeric micelle MR contrast agent successfully targets a specific site in the ischemic hemisphere and provides high-contrast images that were not obtained with a conventional low-molecular-weight MR contrast agent. Therefore, the polymeric micelle carrier system may be extremely useful for both the diagnosis and treatment of ischemic stroke.

## Publications


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## Reviews and Books


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***Yokoyama M.*** Molecular imaging for evaluation of drug targeting (in Japanese). *Idenshi Igaku Mook* 2010; **18:** 127–32.