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# Development of a new tumor tissue necrotizing technology using nano-sized droplets requiring approximately one-tenth conventional ultrasonic Intensity

*-- Controlling the sustainability of microbubbles formed from droplets using ultrasonic waves --*

**Tokyo, October 12, 2010** --- Hitachi, Ltd. (NYSE : HIT/TSE : 6501, hereafter Hitachi) today announced the development of a new tumor tissue necrotizing technology using a contrast agent[*1], nano sized droplets (nano-droplets[*2]), targeted for tumor tissue. This technology reduces the intensity of the ultrasonic pulse required to cause necrosis to about one-tenth of conventional technologies.

In 2006, Hitachi developed the nano-droplets which maintain nanometer-size until they reach inside the target tumor tissue, and expand to micron-size bubbles (microbubbles[*3]) when ultrasonic pulses are applied.
This time, Hitachi has succeeded in controlling the sustainability of the microbubbles state which ordinarily barely lasts for 0.001 seconds before disappearing after being generated from the nano-droplets. As a result, it is now possible to confirm that the microbubbles have dispersed throughout the tumor tissue. Further, as the microbubbles enhance the ultrasonically-induced temperature rise, it is now possible to necrotize the tumor tissue with an ultrasonic intensity of approximately one-tenth the level applied in methods which do not use microbubbles. This development is a fundamental achievement towards establishing medical technology which enables contrast agents in ultrasonic diagnostics to be used from diagnosis through to treatment.
Part of this research was conducted under the medical and welfare equipment research and development scheme of the New Energy and Industrial Technology Development Organization (NEDO), Japan.

Today, microbubbles are widely used as a conventional ultrasonic contrast agent in the field of echography. Microbubbles circulate throughout the body through the blood vessels and are used to image tumor vascularity. However due to their large size, they are unable to exit the blood vessles and therefore it is difficult to reach inside the actual tumor tissue. Therefore, in 2006, a research team from Hitachi and the University of Tokyo co-developed the nano-droplet method to penetrate the walls of blood vessels lining tumor tissue. When the nano-droplets reach the target site, ultrasonic pulses are applied which transform the nano-droplets into microbubbles enabling the actual tumor itself to be imaged.

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On the other hands, in recent years, the technology which destroys tumor tissue by convering the ultrasonic pulse and thermally coagulating the tissue is becoming increasingly common in clinical settings. In previous research, Hitachi confirmed that the ultrasonically-induced thermal effect is enhanced by the presence of microbubbles generated locally from nano-droplets within the tumor tissue, and necrosis of tumor tissue could be achieved with one-tenth the ultrasonic pulse intensity of conventional methods which do not use nano-droplets. As the microbubble state ordinarily lasts for only 0.001 seconds, in order to inflict enough damage on the tumor tissue it was necessary to repetitively generate microbubbles and apply focused ultrasonic pulses, resulting in longer treatment time.

In response to this need, Hitachi has developed technology to control the sustainability of the microbubble state. This technology was achieved by the discovery that the microbubble state could be maintained for over 10 seconds by the application of a low-intensity ultrasonic pulse. From live tissue simulation experiments to determine the optimal ultrasonic conditions, it was confirmed that the microbubbles state could be sustained over a wide range. An experiment using a mouse intravenously injected with nano-droplets also confirmed the sustainability of the microbubble state.
In the future, when this technology is applied to ultrasonic therapy, it is expected to contribute to a significant reduction in treatment time and patient burden.

These results will be presented at the 2010 IEEE International Ultrasonics Symposium (IUS) which will be held from October 11 to 14, 2010 in San Diego, California, U.S.

## ■Notes

*1 Contrast agent: A pharmaceutical agent used to increase the contrast between different tissue types in imaging diagnostics.

*2 Nano-droplet: A nano-droplet formed from phospholipid film containing superheated perfluorocarbon. The super-heated state is the opposite of the super-cooled state. Even when a temperature at which phase change occurs is reached, it maintains its current phase, and in the case of the nano-droplet, even above boiling point, the droplet remains in its liquid state. When an ultrasonic pulse is applied as a physical stimulus, the nano-droplet changes from a liquid state to a gaseous state and become a microbubble. Blood vessels lining tumor tissue are irregular structure and known to allow larger substances to penetrate its walls into adjacent tissue compared to vessels lining healthy tissue. The size of nano-droplet developed is large enough not to penetrate the lining of blood vessels lining healthy tissue but small enough to penetrate the tumor tissue, thus having a selectivity for tumor tissue.

*3 Microbubble: A bubble of a few micrometers formed from a gas such as air or fluorocarbon and stabilized with a surfactant. As the characteristic response to sound is different from living tissue, it is used as a contrast agent in ultrasonic.

## ■ About Hitachi, Ltd.

Hitachi, Ltd., (NYSE:HIT / TSE:6501), headquartered in Tokyo, Japan, is a leading global electronics company with approximately 360,000 employees worldwide. Fiscal 2009 (ended March 31, 2010) consolidated revenues totaled 8,968 billion yen ($96.4 billion). Hitachi will focus more than ever on the Social Innovation Business, which includes information and telecommunication systems, power systems, environmental, industrial and transportation systems, and social and urban systems, as well as the sophisticated materials and key devices that support them. For more information on Hitachi, please visit the company's website at http://www.hitachi.com.

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