

# How to enhance non-thermal effects of ultrasound

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In recent years HIFU has been widely used for the treatment of solid tumors, such as liver tumor, bone tumor, and breast cancer. The mechanism for therapeutic actions of HIFU includes thermal effects and non-thermal effects with the latter dominated by cavitation effects. Adjusting acoustic parameters of pulsed high intensity focused ultrasound (PHIFU) can control thermal effects and non-thermal effects; short duty cycle and high intensity favors the occurrence of cavitation. Ultrasound contrast agent (UCA) can enhance cavitation effects. Lesions caused by non-thermal effects have characteristic pathological changes quite different from those of thermal lesions.

A research article to be published on November 21, 2008 in the *World Journal of Gastroenterology* addresses this question. The research group led by Professor Zhi-Biao Wang from Department of Biomedical Engineering of Chongqing Medical University used PHIFU with short duty cycle and high intensity combined with UCA to damage rabbit liver VX2 tumour by non-thermal effect, and the non-thermal damage was evaluated by histopathology.

Liver VX2 tumor model were established in 20 rabbits, which were then divided randomly into PHIFU combined with UCA group (PHIFU+UCA group) and sham group, with 10 rabbits in each group. In the PHIFU+UCA group, 0.2 mL of SonoVue was injected intravenously, followed by rapid injection of 1 mL normal saline. Fifteen seconds after the injection, the tumours were exposed to HIFU with ISP 5900W/cm<sup>2</sup> for 90 seconds. Rabbits were sacrificed one day after HIFU exposure.

Specimens of the exposed tumor tissues were obtained and observed pathologically under light microscope and transmission electron microscope.

The remaining exposed tumor tissues were sent for TTC staining. Before TTC staining, tumor tissues in both the sham and the PHIFU+UCA group resembled gray fish meat; after TTC staining, the tumour tissues were uniformly stained red, with a clear boundary between tumor tissue and normal tissue. For PHIFU + UCA group, light microscopy displayed abundant vacuoles of various sizes in the cytoplasm and in some cells, chromatin margination and karyopyknosis were present. Electron microscopic examination revealed presence of karyopyknosis and chromatin margination in some cells, intercellular space widening, the presence of high electron-density apoptotic bodies and many vacuoles of various sizes in the cytoplasm.

This study found that PHIFU combination with UCA can enhance non-thermal effects of ultrasound, and the pathological characteristics of the non-thermal damage is different from those of thermal damage. Immunohistochemical detection found that PHIFU combined with UCA can promote tumor cell apoptosis and inhibit tumor cell proliferation, which will be reported in another article.

Source: World Journal of Gastroenterology

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