Enhanced antitumor efficiency by thermosensitive liposome with high-intensity focused ultrasound

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Purpose: In recent years, thermosensitive liposomes (TSLs) have been extensively used in combination with high-intensity focused ultrasound (HIFU) for cancer therapy. However, a conventional immediate heating approach (IHA) leads poor penetration of liposome, limiting the efficient antitumor activity. In an attempt to maximize the accumulation of doxorubicin (DOX), a delayed heating approach (DHA) has been developed.

Methods: DOX was encapsulated into a fatty acid-conjugated elastin-like polypeptide (FELP)-bearing TSLs (FTSLs) by the ammonium sulfate gradient method. DOX-FTSLs were characterized by using size exclusion chromatography (SEC) with a Sephadex (G-25M) column, UV-VIS spectrometer, and FPAR-1000 fiber optics particle analyzer. Fluorescence spectrometer was used to detect DOX at the wavelength of 470nm. With two different heating approaches, IHA and DHA, in vivo biodistribution of DOX-FTSLs was investigated using Optix MX3 optical molecular imaging system.

Results: As shown in Figure 1, the real-time images of DOX accumulation in tumor tissue were obtained from the live animal model. Although Cy5.5-DOX-FTSLs were detected at tumor site by both approaches, the signal intensity was noticeably strong over time with DHA as compared to IHA. This indicates that the DHA increased the vascular permeability of DOX-FTSLs and enhanced DOX accumulation in tumor. In Figure 2, tumor growth was successfully suppressed with DOX-FTSL when DHA was applied.

Conclusions: Despite of the large attention to the TSLs in cancer therapy, their inefficient penetration into tumor tissue hinders the clinical application. In this study, we developed the DHA as a novel approach of HIFU to enhance the tumor accumulation of TSLs. Tumor tissue was pre-treated with HIFU to increase the permeability of tumor blood vessel and re-treated with HIFU to induce release of the DOX from DOX-FTSLs at their maximum accumulation time point. In contrast to IHA, this new approach can be applied to various cancer treatments using TSLs.

References: