

## Ultrasound-enhanced drug delivery for efficacy

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One of the barriers to drug delivery is the presence of a prominent stromal matrix that separates blood vessels from tumor cells. In order for the chemotherapeutic agent to be effective in solid tumors, the agent must be able to penetrate into the tumor in sufficient quantities without causing significant toxicity to normal tissues. Researchers at Nanyang Technological University (NTU), Singapore, have designed a novel approach to enhance the penetration of small molecules into ex vivo tissue.

The hypothesis of researchers at the NTU is that the mechanical effect of ultrasound energy, radiation force of ultrasound pulse and microstreaming resulting from bubble cavitation are the major mechanisms of pulse high-intensity focused ultrasound (pHIFU)-enhanced drug penetration.

The Ultrasound Science and Application Research Laboratory of the NTU has developed an image-guided ultrasound-enhanced drug delivery system to be applied to a transgenic mouse model. The feasibility of enhancing penetration of a small-molecule drug through the connective structure using high-intensity focused ultrasound (HIFU) pulses has been proven and it has been demonstrated that utilizing the mechanical effect, instead of thermal effect of the HIFU pulses, brings greater efficacy and decreases toxicity.

"This approach is cost-effective, compelling and can be extended to more novel chemotherapy agents (highly-diffusive carriers and nanoparticles). This technology can be easily realized in a commercial system, and it has a great opportunity of

translating into human trials soon, since several clinical HIFU devices exist, and additional new devices are currently under development," shares Dr Yufeng Zhou, assistant professor, School of Mechanical & Aerospace Engineering, NTU, Singapore.

Once confirmed in the transgenic mouse model, HIFU pulse-enhanced drug delivery can be tested in clinics using the existing HIFU system in an appropriate protocol. Dr Yufeng Zhou believes that at this stage, close collaborations between oncologist, radiologist, gastroenterologist, ultrasound physicist and medical administration are of importance for the multiple-center randomized clinical trial.