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NEWS

RSNA Press Release

Pulsating Ultrasound Enhances Gene Therapy for Tumors

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At A Glance

- Pulsed-high intensity focused ultrasound (HIFU) uses sound waves to increase the permeability of tissues and enhance gene delivery.
- Tumors exposed to pulsed-HIFU exhibited signs of a reporter gene injected into a mouse immediately after ultrasound treatment; non-treated tumors showed virtually no signs of the gene.
- Pulsed-HIFU is non-invasive, leaves cells undamaged and can be used in all areas except the lungs and bone.

OAK BROOK, Ill. - High-intensity focused ultrasound emitted in short pulses is a promising, non-invasive procedure for enhancing gene delivery to cancerous cells without destroying healthy tissue, according to a study in the May issue of the journal *Radiology*.

High-intensity focused ultrasound (HIFU) is more powerful than standard ultrasound. HIFU can destroy tumors through long and continuous exposures that raise the temperature inside cancerous cells, effectively "cooking" them. Under a technique introduced by King C.P. Li, M.D., M.B.A., from the National Institutes of Health (NIH), short pulses of HIFU can be used to prevent exposed tissue from becoming too hot and damaged. Pulsed-HIFU instead renders tissues permeable and helps target them for taking up genes and other therapeutic substances injected into the body.

"Basically, we're using sound waves to open up the tissue by producing gaps between the cells, making it leakier and more prone to taking up various genes, agents and compounds," said Victor Frenkel, Ph.D., a staff scientist for the diagnostic radiology department at the NIH Clinical Center in Bethesda, Md.

Working with lead authors Kristin M. Dittmar, M.D., and Jianwu Xie, M.D., the researchers used pulsed-HIFU on tumors in mice, then immediately injected an easily measurable reporter gene into the vein in their tails. The reporter gene in this study—a fluorescent-green protein found in deep-sea invertebrates—was visible in all sections of the tumors exposed to pulsed-HIFU. Tumors not targeted with pulsed-HIFU showed negligible signs of the gene.

An analysis showed reporter gene levels to be nine times higher in tumors treated with pulsed-HIFU compared with tumors left unexposed.

Researchers were especially encouraged by the results because the type of cancer treated in

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the study—squamous cell carcinoma, found in head and neck tumors—is one of the least permeable cancers and does not respond well to chemotherapy or radiation. However, these types of tumors have responded to certain types of therapeutic genes.

"This procedure is hypothetically generic for enhancing delivery to all tissues," Dr. Frenkel said. "Previous studies by Dr. Li have shown that pulsed-HIFU increases the uptake of drugs. Now we've shown that it works for genes and we're making the case that there's a connection between the two."

Other methods currently being investigated for enhancing gene delivery, such as lasers and electric current, are limited to surface lesions or require needles to be inserted in the body. Pulsed-HIFU is non-invasive and can treat any area of the body accessible by ultrasound, the exceptions being the lungs and bones. Additional advantages of pulsed-HIFU include no scarring, limited blood loss and infections, reduced risk of other complications, shortened recovery time, significant reduction in costs and the potential for many procedures to be done on an outpatient basis.

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The Radiological Society of North America (RSNA) is an association of more than 37,000 radiologists, radiation oncologists and related scientists committed to promoting excellence in radiology through education and by fostering research, with the ultimate goal of improving patient care. The Society is based in Oak Brook, Ill. (RSNA.org)

"Pulsed High-Intensity Focused Ultrasound Enhances Systemic Administration of Naked DNA in Squamous Cell Carcinoma Model: Initial Experience." Collaborating with Drs. Frenkel, Dittmar and Xie on this paper were Finie Hunter, B.S., Cameron Trimble, B.S., and Monica Bur, B.S.

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