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TECHNOLOGY UPDATE

Jun 16, 2009

Nanotubes reveal breast cancer spread

An early sign that a breast tumour has turned metastatic is the detection of cancer cells in nearby lymph nodes. This can be achieved by locating the first nodes that escaping cells will drain into and then biopsying a few of these sentinel lymph nodes. If the results are positive, all lymph nodes under the arm will be removed. If negative, then patients are spared the extra surgery.

Sentinel lymph-node biopsy is certainly less drastic than no-questions-asked underarm lymph-node dissection, but it is not without its disadvantages. Node identification typically involves injection of a gamma ray-emitting radiotracer and/or blue dye into the breast. There is no guarantee that all sentinel lymph nodes will be found and the procedure can lead to complications. Patients – and possibly practitioners – will also be exposed to ionizing radiation.

Photoacoustic imaging with a carbon single-walled nanotube (SWNT) contrast agent could provide a non-invasive alternative to sentinel lymph-node biopsy, according to researchers at Washington University in St. Louis, MO, and the State University of New York (Stony Brook, NY). *In vivo* tests have shown that SWNT-enhanced photoacoustic imaging can identify sentinel lymph nodes. Adding functional groups to these SWNTs may make it possible to see signs of cancer on imaging too (*Phys. Med. Biol.* **54** 3291 (<http://www.iop.org/EJ/abstract/0031-9155/54/11/001>)).

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Photoacoustic imaging relies on the conversion of light energy to heat when biological tissues are bombarded with laser pulses. Localized tissue heating leads to thermoelastic expansion and the generation of pressure waves. Ultrasound images may be formed if there is sufficient difference

in photoacoustic signal between target structures and other tissue components.

"The strong optical absorption property of SWNTs is the key to their use as photoacoustic contrast agents," said co-author Lihong Wang, professor of biomedical engineering and director of Washington University's Optical Imaging Laboratory. "They have a wide absorption spectrum, making them good contrast agents in the visible and near-infrared spectral region. These nanotubes can also potentially be functionalized easily to target biomarkers for molecular photoacoustic imaging."

Optimal particles

The mean distance between sentinel lymph nodes and the breast surface is approximately 12 mm. Imaging at this depth requires near-infrared light, so any contrast agent must absorb strongly at this frequency band, Wang said. The size of particles used as contrast is also important. Transit time to the sentinel lymph node should be relatively short, but the clearance rate must not be too rapid.

Phantom experiments, using chicken tissue to simulate the human breast and a light source tuned to a wavelength of 793 nm, showed that SWNTs enhanced the photoacoustic signal at depths of over 20 mm. A SWNT-filled tube buried beneath the tissue was seen clearly on ultrasound images.

The technique was also trialled *in vivo* on rats. Images of sentinel lymph nodes acquired at 25–30 minute intervals after injection of the SWNTs showed high contrast-to-noise ratio and good resolution. The photoacoustic signal from the SWNTs also remained strong when the laser was tuned to different near-infrared wavelengths (740–820 nm).

"The uptake time for SWNT accumulation in the lymph node was quick," Wang said. "Within minutes of SWNT injection, we were able to see the node in the photoacoustic image. The SWNTs stayed in the node for several hours, so we could see it for a long time."

The *in vivo* biocompatibility of the SWNTs needs to be examined thoroughly before the system can be used clinically, Wang told *medicalphysicsweb*. Real-time imaging may also be required for clinical applications.

"Currently, this imaging system is limited by its slow scanning speed. Employing a higher pulse-repetition-frequency laser and an ultrasound array system could accelerate data acquisition, potentially allowing real-time photoacoustic imaging," he said.

About the author

Paula Gould is a contributing editor on *medicalphysicsweb* (<http://www.medicalphysicswebs.org>).