INNOVATION ARTICLES
THE IDEA SUBMISSION PORTAL FROM MEDTRONIC

HANDHELD NANOPARTICLE SCANNER

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For many types of cancer, surgical removal of the tumor is the main treatment strategy. But tumors aren't always easy to tell from healthy cells, meaning that sometimes cancerous cells get left behind. Many recurring tumors grow around the margins of the original tumor - meaning that they probably came from leftover cancer cells. Surgeons have tried numerous methods to visualize the tumor edges such as MRI and ultrasound, but no one method has stood out. Until now that is.

A New York based research group is using Raman spectroscopy to image cancer, in particular brain tumors called glioblastoma. These tumors are notoriously hard-to-see because they have a ragged diffuse shape rather than forming well-defined tumors. The team's aim? To combine this method with a handheld scanner that surgeons can use during surgery to check that no cell has been left behind.

Raman spectroscopy had previously been used to distinguish healthy cells from cancer cells, but the team wanted to do better. Imaging cells on a metal base hugely boosts the Raman signal in an effect called surface enhanced raman scattering (SERS). Plus the scientific community already knew that nanoparticles tend to accumulate more in tumors than in healthy tissue, a phenomenon called the enhanced permeability and retention (EPR) effect. Putting these two effects together, the team developed a gold-based nanoparticle to flag up, or “tag” brain tumors. The nanoparticles were injected into the tail of mice with glioblastoma, and after letting the solution circulate in the blood for up to a day, they scanned the brains of the living mice with a Raman spectrometer. The tumors lit up with Raman scanning, showing that the nanoparticles and the SERS Raman scanning were working as hoped for (1).

Next the team tried the technique during surgery to remove glioblastoma from the brains of mice. The mice were injected with a new version of nanoparticle the day before surgery. During the operation the mice were scanned with a static Raman scanner, a handheld Raman scanner or normal white light. Both the static and handheld Raman scanners picked up the cancer cells, allowing the surgeons to better see the tumor edges than with white light. The handheld scanner, which looks like a laser pointer, was better at picking up cancer cells than the static scanner, since the surgeon could check for errant cancer cells from different angles, leaving cancer cells nowhere to hide. The handheld scanner even detected a cancer signal in the heart of one of the mice, which was confirmed by standard testing to be a cluster of cancer cells. The handheld scanner used is commercially available (3), and was previously used by a UK group to detect cancer in the axially lymph nodes of breast cancer patients (4).

> “The new generation of nanoparticles could detect different types and stages of cancer, even pre-cancerous cells”

Last year, the team reported that they improved detection of nanoparticles about 400-fold, by re-engineering the nanoparticle to have a star-shaped core, a silica shell and by tweaking resonance (5). In mouse models of cancer, the team showed that the new generation of nanoparticles, termed nanostars, could detect different types and stages of cancer, even pre-cancerous cells. In a paper published in May this year, Kircher and his colleagues describe how they increased the sensitivity of the method for detecting glioblastoma cells in the brain tissue of mice, by engineering the nanostars to specifically target a protein called integrin that appears on the outside of cancer cells (6).

The team hope that steady improvements of the nanoparticles, in pace with the evolution in commercially available Raman detectors means that the technology can be quickly taken from the lab to the clinic. Innovation doesn't just mean developing a new machine or technology - it is equally about finding intelligent ways to use an existing technology to fill an unmet need. As new technologies come online in coming years, a key challenge is to figure out how to apply them in the clinic to treat, test or diagnose disease. Kircher's nanoparticles are bringing Raman out of the lab and into the clinic with work that is at the interface of medical technology, pharma and medicine; three worlds that are clearly no longer mutually exclusive.

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