'SpectroPen' could aid surgeons in detecting edges of tumors

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This hand-held device called a SpectroPen could help surgeons see the edges of tumors in human patients in real time during surgery.

Biomedical engineers are developing a hand-held device called a SpectroPen that could help surgeons see the edges of tumors in human patients in real time during surgery.

Scientists at Emory University School of Medicine, the Georgia Institute of Technology, and the University of Pennsylvania describe the device in an article published this week in the journal Analytical Chemistry.

What a patient with a tumor wants to know after surgery can be expressed succinctly: “Did you get everything?” Statistics indicate that complete removal, or resection, is the single most important predictor of

patient survival for most solid tumors.

“This technology could allow a surgeon to directly visualize where the tumors are, in real time. In addition, a post-surgery scan could check tumor margins,” said Shuming Nie, a professor in the Wallace H. Coulter Department of Biomedical Engineering at Georgia Tech and Emory University. “A major challenge is to completely remove the tumor as well as identify lymph nodes that may be involved.”

The SpectroPen can be used to detect fluorescent dyes, and also scattered light from tiny gold particles, a technology that Nie and his colleagues have been refining.

The particles consist of polymer-coated gold, coupled to a reporter dye and an antibody that sticks to molecules on the outsides of tumor cells more than it sticks to normal cells. Through an effect called surface-enhanced Raman scattering, the gold in the particle greatly amplifies the signal from the reporter dye. Nie and his team have been able to show that the particles can detect tumors smaller than one millimeter grafted into rodents.

The SpectroPen combines a near-infrared laser and a detector for fluorescence or scattered light. It is connected by a fiber optic cable to a spectrometer that can record fluorescence and Raman signals.

In the *Analytical Chemistry* paper, the researchers used the pen to detect the dye indocyanine green, infused intravenously into mice with implanted human breast cancer cells. The dye accumulates at a higher rate in tumor cells because of the leaky blood vessels and membranes surrounding tumors. The SpectroPen’s signal from the tumor is ten times higher than from normal tissue. Indocyanine green has been approved by the FDA for purposes such as measuring cardiac output and liver function.

The cancer cells had a gene from fireflies added, so that tumors glow after the mice are given a “luciferin” solution. This allowed the scientists to check that the outline of the tumor seen through the SpectroPen matched the glow.

“Our in vivo studies demonstrate that the tumor borders can be precisely detected preoperatively and intraoperatively, and that the contrast signals are strongly correlated with tumor bioluminescence,” Nie said.

In the laboratory, the fluorescence and Raman signals are resolvable when the nanoparticles are buried 5-10 mm deep in fresh animal tissues. However, the gold nanoparticles are 40 to 50 times more sensitive than fluorescent dyes.

Future plans include in vivo tests of the nanoparticle contrast agents, along with the SpectroPen.

The research was carried out by an interdisciplinary team of senior investigators including May Wang, Coulter Department at Georgia Tech and Emory University; Sunil Singhal, University of Pennsylvania; and James Provenzale and Brian Leyland-Jones, Emory University. They are developing an integrated spectroscopic and wide-field color imaging system for image-guided surgery and cancer detection during surgery using animal models.

Provenzale and surgeons at the University of Georgia College of Veterinary Medicine are currently using this device to operate on dogs with naturally occurring tumors. Singhal, who is director of the Thoracic Surgery Research Laboratory at the University of Pennsylvania School of Medicine, is applying to conduct clinical trials involving patients with lung cancer.

More information: Research paper: dx.doi.org/10.1021/ac102058k