

# New Products and Processes

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## **MEDICAL ‘LIGHTSABERS’: LASER SCALPELS GET ULTRAFAST, ULTRA-ACCURATE AND ULTRA-COMPACT MAKEOVER**

Whether surgeons slice with a traditional scalpel or cut away with a surgical laser, most medical operations end up removing some healthy tissue, along with the bad. This means that for delicate areas, like the brain, throat and digestive tract, physicians and patients have to balance the benefits of treatment against possible collateral damage.

To help shift this balance in the patient’s favor, a team of researchers from the University of Texas at Austin has developed a small, flexible endoscopic medical device which fitted with a femtosecond laser ‘scalpel’ that can remove diseased or damaged tissue while leaving healthy cells untouched. The researchers will present their work at this year’s Conference on Lasers and Electro-Optics (CLEO: 2012) in San Jose, California, taking place May 6 to 11.

The device, which was engineered with off-the-shelf parts, includes a laser capable of generating pulses of light a mere 200 quadrillionths of a second in duration. These bursts are powerful, but are so fleeting that they spare surrounding tissue. The laser is coupled with a mini microscope that provides the precise control necessary for highly delicate surgery. Using an imaging technique known as ‘two-photon fluorescence,’ this specialized microscope relies on infrared light that penetrates up to 1 mm into living tissue, which allows surgeons to target individual cells or even smaller parts, such as cell nuclei.

The entire endoscope probe package, which is thinner than a pencil and less than an inch long (9.6 mm in circumference and 23 mm long), can fit into large endoscopes, such as those used for colonoscopies.

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An image taken with the probe’s two-photon fluorescence microscope shows cells in a 70  $\mu\text{m}$  thick piece of vocal cord from a pig. The scale bar is 10  $\mu\text{m}$  (Credit: Ben-Yakar Group, University of Texas at Austin).

## **NANOPARTICLES HOME IN ON BRAIN TUMORS, BOOST ACCURACY OF SURGICAL REMOVAL**

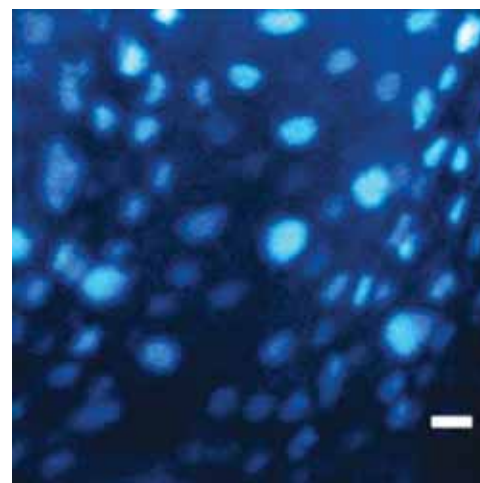
Like special-force troops laser-tagging targets for a bomber pilot, tiny particles that can be imaged in three different ways at once have enabled Stanford University School of Medicine scientists to remove brain tumors from mice with unprecedented accuracy.

In a study, published online April 15 in *Nature Medicine*, a team led by Sam Gambhir, MD, PhD, Professor and Chair of Radiology, showed that the minuscule nanoparticles engineered in his laboratory homed in on and highlighted brain tumors, precisely delineating their boundaries and greatly easing their complete removal. The new technique could someday help to improve the prognosis of patients with deadly brain cancers.

About 14,000 people are diagnosed annually with brain cancer in the United States. Of those cases, about 3,000 are glioblastomas the most aggressive form of brain tumor. The prognosis for glioblastoma is bleak: the median survival time without treatment is 3 months. Surgical removal of such tumors—a virtual imperative whenever possible—prolongs the typical patient’s survival by less than a year. One big reason for this is that it is almost impossible for even the most skilled neurosurgeon to remove the entire tumor while sparing normal brain.

The nanoparticles used in the study are essentially tiny gold balls coated with imaging reagents. Each nanoparticle measures less than five one millionth of an inch in diameter—about one-sixtieth that of a human red blood cell.

‘We hypothesized that these particles, injected intravenously, would preferentially home in on tumors but not healthy brain tissue,’ said Gambhir, who is also a member of the Stanford Cancer Institute (Fig. 1).



**Fig. 1:** Nanoparticles (bright) enhancing the tumor cells

The tiny blood vessels that feed a brain tumor are leaky, so we hoped that the spheres would bleed out of these vessels and lodge in nearby tumor material. The particles' gold cores, enhanced as they are by specialized coatings, would then render the particles simultaneously visible to three distinct methods of imaging, each contributing uniquely to an improved surgical outcome.

One of those methods, magnetic resonance imaging (MRI) is already frequently used to give surgeons an idea of where in the brain the tumor resides before they operate. MRI is well-equipped to determine a tumor's boundaries but, when used preoperatively, it cannot perfectly describe an aggressively growing tumor's position within a subtly dynamic brain at the time the operation itself takes place.

The Gambhir team's nanoparticles are coated with gadolinium, an MRI contrast agent, in a way that keeps them stably attached to the relatively inert spheres in a blood-like environment (in a 2011 study, published in *Science Translational Medicine*, Gambhir and his colleagues showed in small animal models that nanoparticles similar to those used in this new study, but not containing gadolinium, were nontoxic).

A second, newer method is photoacoustic imaging, in which pulses of light are absorbed by materials, such as the nanoparticles' gold cores. The particles heat up slightly, producing detectable ultrasound signals from which a three-dimensional image of the tumor can be computed. Because this mode of imaging has high depth penetration and is highly sensitive to the presence of the gold particles, it can be useful in guiding removal of the bulk of a tumor during surgery.

The third method, called Raman imaging, leverages the capacity of certain materials (included in a layer coating the gold spheres) to give off almost undetectable amounts of light in a signature pattern consisting of several distinct wavelengths. The gold cores' surfaces amplify the feeble Raman signals so they can be captured by a special microscope.

The study was funded by the National Institutes of Health, the National Cancer Institute's Center for Cancer Nanotechnology Excellence, the Ben and Catherine Ivy Foundation, the Canary Foundation and the Leon Levy Foundation. Available at: <http://www.sciencedaily.com/releases/2012/04/120415151334.htm>129.