

NIH News in Health

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Technologies Enhance Tumor Surgery Helping Surgeons Spot and Remove Cancer

For surgeons, removing a tumor is a balancing act. Cut out too much and you risk removing healthy tissues that have important functions. Remove too little and you may leave behind cancer cells that could grow back into a tumor over time.

NIH-funded researchers are developing new technologies to help surgeons determine exactly where tumors end and healthy tissue begins. Their ultimate goal is to make surgery for cancer patients safer and more effective.

“Currently, surgeons view MRI and CT scans taken prior to an operation to establish where a tumor is located and to plan a surgical approach that will minimize damage to healthy tissues,” says Dr. Steven Krosnick, an NIH expert in image-guided surgery. “But once the operation has begun, surgeons generally rely only on their eyes and sense of touch to distinguish tumor from healthy tissue.”

Surgeons go through many years of training to understand the subtle cues that can distinguish tumor from normal surroundings. Sometimes the tumor is a slightly different color than healthy tissue, or it feels different. It might also bleed more readily or could contain calcium deposits. Even with these cues, however, surgeons don't always get it right.

“In a lot of cases, we leave tumor behind that could be safely removed

if only we were able to better visualize it,” says Dr. Daniel Orringer, a neurosurgeon at the University of Michigan.

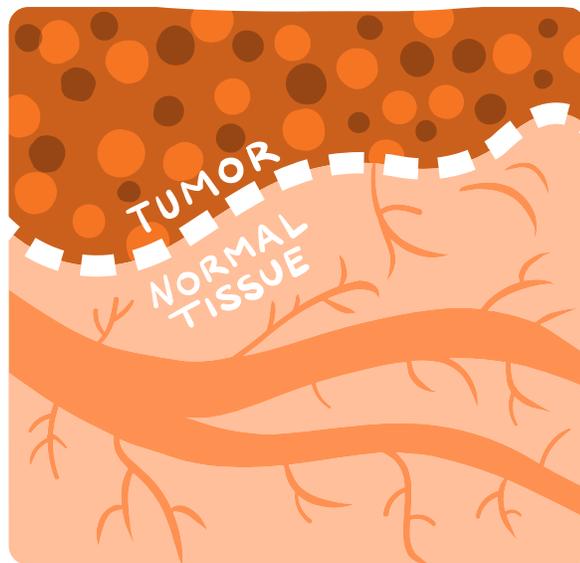
In today's operating rooms, **pathologists** can often help surgeons determine if all of a tumor has been taken out.

A pathologist may view the edges of the tissue under a microscope and look for cancer cells. If they're found, the surgeon will remove more tissue from the patient and send these again to the pathologist for review. This process can occur repeatedly while the patient remains on the operating table and continue until no cancer cells are detected.

“Each time a pathologist analyzes tissue during an operation, it can take up to 30 minutes because the tissue has to be frozen, thinly sliced, and stained so it can be viewed under the microscope,” Krosnick says. “If multiple rounds of tissue are taken, it can greatly increase the length of the surgery.”

In the days following an operation, the pathologist conducts a more thorough review of the tissue. If cancer cells are found at the margins, the patient may undergo a second surgery to remove cancer that was left behind.

Orringer is part of a research team that's testing a new technology that could help surgeons tell the difference between a tumor and healthy brain tissue during surgery. The team developed a special microscope with NIH support that shoots a pair of low-energy lasers at the tissue. That causes the chemical



bonds in the tissue's molecules to vibrate. The vibrations are then analyzed by a computer and used to create detailed images of the tissue.

From a molecular point of view, the components of a tumor differ from those in healthy tissue. This specialized microscope can reveal differences between the tissues that can't be seen with the naked eye.

“Our technology enables us to get a microscopic view of human tissues without taking them out of the body,” Orringer says. “We can see cells, blood vessels, the connections between brain cells...all of the microscopic components that make up the brain.”

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Definitions

Pathologists

Doctors who identify diseases by studying cells and tissues under a microscope.

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Orringer and colleagues developed a computer program that can quickly analyze the images and assess whether or not cancer cells are present. This type of analysis could



Wise Choices Questions To Ask Your Doctor

If you've been diagnosed with cancer, consider asking your doctor some of these questions before choosing a treatment plan:

- What are the ways to treat my type and stage of cancer?
- What are the benefits and risks of each of these treatments?
- What treatment do you recommend? Why do you think it is best for me?
- When will I need to start treatment?
- Will I need to be in the hospital for treatment? If so, for how long?
- What is my chance of recovery with this treatment?
- How will we know if the treatment is working?
- Would a clinical trial (research study) be right for me?
- How do I find out about studies for my type and stage of cancer?

For more questions to ask your doctor about cancer, see www.cancer.gov/about-cancer/treatment/questions.

help surgeons decide whether all of a tumor has been cut out. To date, Orringer has used the specialized microscope to help remove cancer tissue in nearly 100 patients with brain tumors.

Other researchers are taking different approaches. For example, Dr. Quyen Nguyen—a head and neck surgeon at the University of California, San Diego—has developed a fluorescent molecule that's currently being tested in clinical trials. The patient receives an injection of the molecules before surgery. When exposed to certain types of light, these molecules cause cancer cells to glow, making them easier to spot and remove. The surgeon then uses a near-infrared camera to visualize the glowing tumor cells while operating.

Nguyen is also developing a fluorescent molecule to light up nerves. Accidental nerve injury during surgery can leave patients with loss of movement or feeling. In some cases, sexual function may be impaired.

"Nerves are really, really small, and they're often buried in soft tissue or encased within bone. When we have to do cancer surgery, they can be encased in the cancer itself," Nguyen says. The fluorescent molecule could help surgeons detect hard-to-spot nerves, so they can be protected. The nerve-tagging molecule is now being tested in animal studies.

Other NIH-funded researchers are focusing on ways to speed up cancer surgeries. Dr. Milind Rajadhyaksha, a researcher at Memorial Sloan Ketter-



Web Links

For more on cancer surgery technologies, click the "Links" tab at: <http://newsinhealth.nih.gov/issue/Feb2016/Feature1>

ing Cancer Center, has developed a microscope technique to reduce the amount of time it takes to perform a common surgery for removing non-melanoma skin cancers.

Each year about 2 million people in the U.S. undergo Mohs surgery, in which a doctor successively removes suspicious areas until the surrounding skin tissue is free of cancer. The procedure can take several hours, because each time more tissue is removed, it has to be prepared and reviewed under a microscope to determine if cancer cells remain. This step can take up to 30 minutes.

The technique developed by Rajadhyaksha shortens the time for assessing removed tissue to less than 5 minutes, which greatly reduces the overall length of the procedure. Tissue is mounted in a specialized microscope that uses a focused laser line to do multiple scans of the tissue. The resulting image "strips" are then combined, like a mosaic, into a complete microscopic image of the tissue.

About 1,000 specialized skin surgeries have already been performed guided by this technique. Rajadhyaksha is currently developing an approach that would allow doctors to use the technology directly on a patient's skin, before any tissue has been removed. This would allow doctors to identify the edges of tumors before the start of surgery and reduce the need for several pre-surgical "margin-mapping" biopsies.

There are many types of cancer surgeries, and researchers continue to work hard to develop better techniques. If you're considering surgery to treat your cancer, you can learn more at www.cancer.gov/about-cancer/treatment/types/surgery. ■

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Focusing on Fibromyalgia

A Puzzling and Painful Condition

You've probably heard of fibromyalgia, but you may not know what it is. Fibromyalgia is a long-term (chronic) pain condition that affects 5 million or more Americans ages 18 and older. For unknown reasons, most people diagnosed with fibromyalgia are women, although men and children also can be affected. People with certain disorders, such as rheumatoid arthritis or lupus, may also have fibromyalgia, which can affect their disease course and treatment.

Fibromyalgia can take a powerful toll on health, well-being, and quality of life. "People with fibromyalgia suffer from severe, daily pain that is widespread throughout the body," says Dr. Leslie J. Crofford, an NIH-supported researcher at Vanderbilt University. "Their pain is typically accompanied by debilitating fatigue, sleep that does not refresh them, and problems with thinking and memory."

People with fibromyalgia often see many doctors before finally receiving a diagnosis. The main symptoms—pain and fatigue—overlap with those of many other conditions, which can

complicate the diagnosis.

"To make things more challenging, there are no blood tests or X-rays that are abnormal in people with the disorder," says Crofford. With no specific diagnostic test, some doctors may question whether a patient's pain is real. "Even friends, family, and coworkers may have a difficult time understanding the person's symptoms," Crofford says.

A doctor familiar with fibromyalgia can make a diagnosis based on the criteria established by the American College of Rheumatology. Diagnostic symptoms include a history of widespread pain lasting more than 3 months and other symptoms such as fatigue. In making the diagnosis, doctors consider the number of areas throughout the body where the patient had pain in the past week, and they rule out other causes of disease.

What causes fibromyalgia isn't fully understood. Many factors likely contribute. "We know that people with fibromyalgia have changes in the communication between the body and the brain," Crofford says. These changes may lead the brain to interpret certain sensations as painful that might not be bothersome to people without the disorder.

Researchers have found several genes that may affect a person's risk of developing fibromyalgia. Stressful life events may also play a role.

Fibromyalgia isn't a progressive disease, so it doesn't get worse over time and may even improve. It's never fatal, and it won't harm the joints, muscles, or internal organs.

Medications may help relieve some—but not all—symptoms of fibromyalgia. "Drug treatments by themselves don't result in remission or cure of fibromyalgia," says Crofford. "We've learned that exercise may work as well as or better than medications. In addition, therapies such as tai chi, yoga, and cognitive behavior therapy can also help to reduce symptoms."



People with fibromyalgia often have the best results when treated with multiple therapies. "It's critically important for health care providers to help patients develop an understanding of fibromyalgia, and to provide realistic information about treatments, with an emphasis on using exercise and other physical therapies in conjunction with medications," Crofford says.

Crofford and her colleagues are exploring whether a treatment called TENS (transcutaneous electrical nerve stimulation) can help people with fibromyalgia exercise more comfortably and reduce pain. She and other NIH-funded teams are also seeking markers of fibromyalgia in the blood that might ultimately lead to more targeted and effective treatments.

If you or someone you know has fibromyalgia, see the "Wise Choices" box for tips on reducing its impact. ■



Wise Choices Feeling Better with Fibromyalgia

- **Get enough sleep.** Getting the right kind of sleep can help ease pain and fatigue. Discuss any sleep problems with your doctor.
- **Exercise.** Research has shown that regular exercise is one of the most effective treatments for fibromyalgia.
- **Try a complementary health approach.** Practices such as tai chi, qi gong, yoga, massage therapy, and acupuncture may help relieve some symptoms.
- **Consider medicines.** Talk to your health care provider about an approved medication for treating fibromyalgia.



Web Links

For more information about fibromyalgia, click the "Links" tab at: <http://newsinhealth.nih.gov/issue/Feb2016/Feature2>

Health Capsules

For links to more information, see these stories online:
<http://newsinhealth.nih.gov/issue/Feb2016/Capsule1>

Infertility Treatments and Children's Development

A growing number of would-be parents are turning to infertility treatments to help them have a baby. A new study found no evidence that these treatments cause any developmental delays. The findings may offer some relief to parents concerned about the long-term health risks of infertility therapies.

Infertility can be treated in many ways. Some complex treatments are called assisted reproductive technologies (ART). ART approaches include in vitro fertilization (in which an egg is fertilized in a lab dish) and frozen embryo transfer (in which a previously frozen embryo is implanted in the uterus).

NIH researchers and their colleagues investigated the effects of ART on children's development. They studied more than 5,800 newborns.

Over 1,800 were conceived using infertility treatment, and more than 2,000 were twins.

Parents completed a series of questionnaires until their children were 3 years old. The questions covered 5 developmental areas: fine movement skills, large movement skills, communication, personal and social functioning, and problem-solving ability.

Overall, kids conceived through ART were more likely to fail one of the areas. But twins were more likely to fail than kids born singly, regardless of the conception approach. When the researchers accounted for the higher percentage of twins in the ART group, they found no effect from ART on kids' development.

Similarly, ART didn't affect whether children were referred for evaluation by developmental specialists.

"When we began our study, there was little research on the potential effects of conception via fertility treatments on U.S. children," says lead author Dr. Edwina Yeung of NIH. "Our results provide reassurance to the thousands of couples who have relied on these treatments to establish their families." The researchers will continue to evaluate the children until they reach 8 years of age. ■

Help for Rare and Undiagnosed Conditions

Trying to get a diagnosis for a perplexing medical condition can be a long and frustrating process. For rare diseases, a diagnosis may take years. NIH's Genetic and Rare Diseases (GARD) Information Center (<https://ncats.nih.gov/gard>) features information about thousands of rare diseases as well as resources to help with diagnoses and finding appropriate care.

GARD includes tips and resources for dealing with undiagnosed conditions at <https://rarediseases.info.nih.gov/resources/pages/24/tips-for-the-undiagnosed>. You can learn how to cope with disorders that have no definitive diag-

nosis, and locate research programs and helpful organizations.

When a condition is rare, it can be hard to find a health care provider who has experience with many similar cases. Learn more at <https://rarediseases.info.nih.gov/resources/pages/25/how-to-find-a-disease-specialist>.

If you can't find the information you need on the GARD website, call toll-free to 1-888-205-2311, or write to GARD at PO Box 8126, Gaithersburg, MD 20898-8126, and an experienced information specialist will help answer your questions. ■

Featured Website NIH Office of Dietary Supplements

<https://ods.od.nih.gov>

Dietary supplements include vitamins, minerals, botanicals, and more. In the U.S., they're used by half of all adults and a third of all children. This site offers reliable, evidence-based information about dietary supplements for health professionals and consumers in both English and Spanish.

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