

HeadWay

NEWS FOR PHYSICIANS FROM JOHNS HOPKINS
 OTOLARYNGOLOGY-HEAD AND NECK SURGERY

More than an ED drug

Most people associate the drug tadalafil (Cialis) with advertisements depicting middle-aged and older couples, all wine and intimate dinners, romance and seduction.

Outside of The Johns Hopkins Hospital, however, few people connect the erectile dysfunction (ED) drug with one of its lesser-known benefits: the potential to help patients who have head and neck cancer. Now, with a just-opened clinical trial and a growing battery of evidence showing the drug's tumor-fighting benefits, head and neck surgeon Joseph Califano hopes he can change the narrow view of tadalafil from a purely ED-related medication to a drug that could possibly save lives. "From what we know and have seen so far," Califano explains,

"WE THINK THAT, FOR A LOT OF PATIENTS, IMMUNE SUPPRESSION MAY BE WHY THEIR TUMORS ARE SO AGGRESSIVE."

"this drug weakens the tumor's ability to evade immune system responses. We think that, for a lot of patients, immune suppression may be why their tumors are so aggressive."

It makes sense that, in the fight against cancer, a strong

immune system is crucial. But over time, Califano says, tumors have developed strategies for evading the body's natural immune responses. By exploiting the nitric oxide produced by immune cells, tumors create a sort of fog that keeps them hidden from the lymphocytes (T-cells) that normally attack and rid the body of germs and disease. Impotence drugs, however, prevent the immune system from generating nitric oxide, allowing T-cells to detect and attack the tumor.

The link between ED drugs and cancer treatment was first discovered by Califano's colleague, Hopkins oncology researcher Ivan Borrello. Together, the two have conducted studies in mice and human blood samples, all showing a marked improvement in the immune responses of subjects who received tadalafil. Some of that research also involved another popular ED drug, sildenafil (Viagra), which, though initially successful, had too short a half-life to offer the same benefits as tadalafil, with a half-life twice as long. Despite being a drug commonly thought of as specific to men, when it comes to cancer, tadalafil is a viable option for women too.

Califano and Borrello recently enrolled the first patient into the clinical trial, which is funded with a National Cancer Institute grant. The study protocol is simple and straightforward. Patients are given a once-daily dose of tadalafil for 10 to

14 days. At the end of the test period, their blood samples are examined to determine the drug's success in boosting the immune system. Then patients proceed with traditional treatments such as surgery, chemotherapy or radiation therapy. "We're able to evaluate this drug within the normal clinical treatment schedule," Califano says. "Patients can enroll and still undergo standard therapies without delay. It's a nice thing for patients, because they can participate in a clinical trial without sacrificing or delaying other treatment options."

Right now, Califano is considering tadalafil primarily as a complement to other standard treatments. But, he says, with further investigation there exists the potential that the drug could eventually lessen or eliminate the need for chemo or radiation. "This is a great treatment option," Califano says, "because it's an incredibly safe drug, one of the

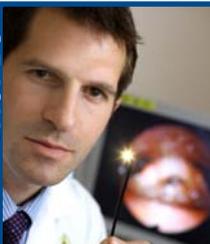


Joseph Califano believes one cancer cure could lie in the erectile dysfunction drug Cialis.

safest drugs around, and, to be honest, some patients really like the idea of being on tadalafil." ■

The Cialis cancer trial began enrolling patients in April 2009 and is expected to continue for the next year or longer. Both men and women with head and neck cancers are eligible to participate. Patients who have had a recent heart attack or who are taking nitrates are not eligible for this trial. **To find out more or to enroll, please call Zubair Khan at 410-955-3157.**

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We're in good shape

In times of economic hardship, alarm quickly rises over the state of our nation's health care system, which can be one of the first entities to suffer. When that happens, patients often pay the price.



So when I tell you that our Department of Otolaryngology–Head and Neck Surgery remains on solid ground, it is with no lack of relief or pride.

During the past five years—before words like *recession* and *downturn* became part of our daily vocabulary—our department has worked to grow to meet our increasing clinical demands. We've been steadily hiring new professionals, increasing our full-time faculty from 34 members to 48. We've actively sought and received funding for multiple research endeavors. And we've branched out into the community around us by improving access and making our services available to patients whether they're coming from the Baltimore suburbs or Dubai. The result?

Today, we are stronger than ever. We've been able to support ever-increasing clinical volumes and to maintain our primary missions of patient care, cutting-edge research and teaching. In fact, we've seen a 35 percent increase in our patient volumes and have multiple clinical trials available to patients seeking the most advanced option in care. Research support for our faculty has increased by 50 percent. Whether their specialty is robotics, skull-base surgery, cancer screening or cochlear implants, our physicians are constantly working to extend the forefront of their fields by advancing knowledge and translating their findings to treatments for the patients who rely on us.

Of course, despite any success, we must remain grounded. In such a strained economy, opportunities to grow and improve are increasingly precious. Even so, we are confident that our efforts during the past few years will allow us to remain strong and persevere through the economic difficulties that pose challenges to health care as a whole. More importantly, though, we are proud that our patients will be able to reap the benefits. ■

Lloyd Minor, M.D.

Andelot Professor and Director
Otolaryngology–Head and Neck Surgery

Adapting robotic technology for the head and neck

When the da Vinci surgical robot first entered the minimally invasive surgery scene in the late 1990s, it quickly became the preferred tool for operating on patients with prostate conditions. Over time, it's made its way into other fields, including bariatric, gynecological and cardiovascular surgery, to name a few. But for the minimally invasive procedures performed by head and neck surgeons, robotic surgery has proven tricky.

That, says head and neck surgeon Jeremy Richmon, could soon change.

The problem with using the robot for head and neck tumors is that the “arms” of the machine—used to navigate surgical instruments—are too large to maneuver through the mouth, which is the preferred minimally invasive method for treating tumors of the upper aerodigestive tract. “The robot wasn't designed for this,” Richmon explains. “It was designed for surgeries of the prostate and abdomen,” which are usually performed by fitting the robotic arms through multiple openings in the body at once. So far, he says, a handful of other centers across the country have successfully pioneered methods of using the robot for trans-oral surgeries. Now Hopkins hopes to take the lead.

Minimally invasive procedures are especially beneficial in treating head and neck conditions, which have often required large incisions to perform surgeries that, using a robot, could be done through the mouth or nose. Meanwhile, the deeper and less accessible a tumor or lesion, the more invasive the treatment might need to be. “The goal is to develop surgical approaches for the head and neck that are less invasive than traditional ones,” Richmon says, “and

“WHAT WE'RE DOING IS
A NEW APPLICATION OF
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to decrease the morbidity of going through other areas of the head and neck and making large incisions.”

Richmon and his colleagues have already successfully tested robotic techniques in cadaver and other models, and are awaiting approval to perform the procedures in clinical practice. “Because we're trying to fit



Head and neck surgeon Jeremy Richmon hopes to adapt current robotic technology to suit his patients.

everything in through the mouth,” Richmon says, “what we're doing is a new application of existing technology.” But, he continues, there is a potentially superior option that he and his colleagues, along with researchers in the Johns Hopkins University Whiting School of Engineering, are developing. Together, the team is devising new technology that will be more appropriate for head and neck surgeries than the robot available today.

The greatest challenge with the current robot, Richmon explains, is the rigidity of its arms, which makes it difficult to maneuver around the corners and narrow passages between the mouth and the tumor site. To overcome that obstacle, Richmon and his collaborators are developing bendable, snakelike arms as an alternative.

Even without yet having perfected such modifications, Richmon says, “we've been able to use the existing robot to reach tumors that otherwise would have required large incisions. Our goal is to come up with even better approaches, and we would like to be one of the first centers that really pushes this to the forefront in the United States.” ■

Seeking precision in the most delicate spaces

In the field of otolaryngology—head and neck surgery, precision is everything. But with so many delicate organs and systems standing between surgeons and their target, precision has often proven elusive and difficult to gauge.

Now, hoping to obtain more accurate measurements and exact locations of the structures on which they operate, physicians in the Johns Hopkins Department of Otolaryngology—Head and Neck Surgery are examining a new concept in robotic surgery called quantitative endoscopy. The department recently received a grant for a clinical trial testing the use of robotics in measuring and treating pediatric airway obstructions, and researchers are examining the possibility of incorporating the technique into skull-base surgery as well.

“Right now, all the information we’re able to get from endoscopes comes from looking with our eyes, and we’re not really able to analyze that information at all,” says head and neck surgeon Masaru Ishii, a lead investigator on the grant and research. “But, by using a camera attached to an endoscope, we can take pictures that allow us to derive quantitative information, including exact measurements.”

Such precision is important to all surgeons, but especially those operating on delicate places like the base of the skull or a child’s obstructed airway. Until the emergence of quantitative endoscopy, Ishii says, physicians have possessed few clinical methods for determining whether airways are too narrow and require surgical intervention. “Being able to get a good understanding of



Masaru Ishii believes endoscopy is the solution to offering better head and neck surgery.

airway size allows us to develop systems for better repairing these defects and for determining whether we’re successful,” Ishii says.

The benefits of quantitative endoscopy apply also to skull base surgery. “The base of the skull is a difficult place to reach,” he says, “because a lot of structures come out of the brain or run through it.” In the past, surgeons were forced to operate on skull-base tumors by performing a craniotomy—a procedure that requires a portion of the skull to be removed and the brain to literally be lifted up so that the surgeon can reach the

tumor. Now, developments in minimally invasive robotic surgery and endoscopy allow surgeons to approach skull-base tumors through the nose, subsequently avoiding the dangers of a highly invasive cranial procedure.

“Quantitative endoscopy allows you to understand the position of objects to a very high level of precision,” Ishii says. “It allows you to drill precisely through bone to find structures and make openings in a very accurate fashion. It’s more accurate than any other system we’ve had for doing this.” ■

VESTIBULAR RESEARCH

Achieving prosthetic balance

Few people ever think about the tiny structures at work inside their ears, keeping balance in check. But when those organs are corrupted, and a person’s equilibrium is thrown out of whack, balance becomes as important as any of the traditional senses like sight, hearing or smell. And, like deafness or blindness, a loss of balance can be devastating.

With such patients in mind, ear surgeon Charley Della Santina has spent the past seven years developing a vestibular prosthesis. Much like the cochlear implants used to restore hearing, the device he’s inventing would restore balance by sending electric pulses into the inner ear. “When someone loses his sense of balance, it’s a real problem,” Della Santina explains. “The parts of your inner ear that control balance also keep you from falling down and keep your eyes on target. Without that, you’re unstable, and it’s hard for you to walk. And if your head is moving at all, you can’t

see clearly.”

A person’s balance is determined primarily in the ear’s labyrinth. When damage occurs—whether through infection, antibiotics, chemotherapy, radiation or trauma—the ability to effectively sense and communicate directional motion is lost, crippling the labyrinth and destroying balance.

Della Santina has seen formerly active patients—many of them skiers, tennis players or swimmers, for instance—whose lives have been turned upside down because of damage to the inner ear. One of his most severe cases involves a man who suffered vestibular damage to his ear and



Charley Della Santina

today can no longer walk straight. When he takes a stroll down the beach, mothers cling to their children, thinking he’s drunk. The patient is first in line for a vestibular implant, as soon as the device is approved for trial and use in humans. That time, however, is a few years off.

For now, Della Santina explains, the implant is being tested in animals, but he hopes to make it available to patients within about five years. His team recently finished a new version of the prosthesis that is smaller and uses less energy than previous models. “This device is a lot like a cochlear implant, but instead of a microphone that takes in sound and stimulates the auditory nerve to help people hear,” he says, “this uses sensors of head movement and orientation to stimulate the vestibular nerve to help people maintain their balance.” ■

A proactive and preemptive strike against cancer

During The Johns Hopkins Hospital's first head and neck cancer screening in 2008, Chris Gourin and her colleagues noticed a troubling similarity among the participants asking to be examined: They weren't the patients who most needed to be there.

The small crowd, made up mostly of young professionals and college graduates, contained only a very few who fit the description of high-risk patients. This year's screening, held the last week of April, drew a similar group.

"They just didn't fit the typical profile of head and neck cancer patients," says Gourin, a head and neck surgeon who's made a medical mission of educating and spreading awareness about the risks of head and neck cancer. Now, hoping to improve their reach for next year's event, Gourin and her colleagues are searching for the best means of educating not only the medical community, but the patients who may benefit from the free screenings. The challenge, she says, is getting those patients out of their homes and neighborhoods and into the Johns Hopkins Outpatient Center.

Typically, high-risk patients include people who use illicit drugs, alcohol or tobacco, or practice unsafe sex. Socioeconomic factors—such as poverty or a low education level—also predispose people to head and neck cancers, Gourin says, though the reason remains unclear. One hypothesis is that such patients are more likely to contract human papilloma virus (HPV), which can lead to head and neck cancer.

Screening for head and neck cancer is simple and noninvasive. Physicians take

a brief medical history, conduct a physical exam, and ask questions about any possible symptoms, like ear pain, throat pain or trouble swallowing. The process takes only a few minutes but allows enough time for physicians to assess a patient's risk or detect the possibility of an already-present tumor early, before it has a chance to spread.

Unfortunately, Gourin says, awareness about the risk factors for head and neck cancers remains low, particularly among patients who are most likely to have them. "People don't think about head and neck cancer when they think about malignant disease," she says. "They think of the most common cancers like breast, colon or lung cancer, which get a lot of media attention." In a recent study published this year in the *Laryngoscope*, Gourin polled a large group of people and found that the majority were unfamiliar with the signs and symptoms of head and neck cancer.



Head and neck surgeon Chris Gourin examines a patient with cancer. A screening, she says, could have offered prevention.

For that reason, the highest-risk patients seem to have remained oblivious to screening initiatives. "We have found that people who do come to a screening were most likely to have learned about the screenings through television or newspaper stories," rather than hospital publicity efforts, word of mouth or doctor referrals, Gourin says. "If we want to target high-risk patients and educate the larger community, we need to find better ways to get the word out about head and neck cancer." ■

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