



HeadWay

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

Johns Hopkins Launches Center for HPV-Related Head and Neck Cancer

New center brings together experts that focus on these unique tumors.

More than a decade ago, physician-researchers at Johns Hopkins began noticing and documenting a wave of head and neck cancers that differed from traditional presentations. Patients with these tumors were often missing the usual factors that doctors had been taught to expect, such as smoking and alcohol use, and they tended to be significantly younger than those usually diagnosed with these cancers — in their forties and fifties, rather than their sixties and beyond. The malignant cells even looked different under the microscope. Doctors here were among the first in the world to link these tumors with human papilloma virus (HPV), the virus that also causes genital warts and the overwhelming majority of cervical cancers.

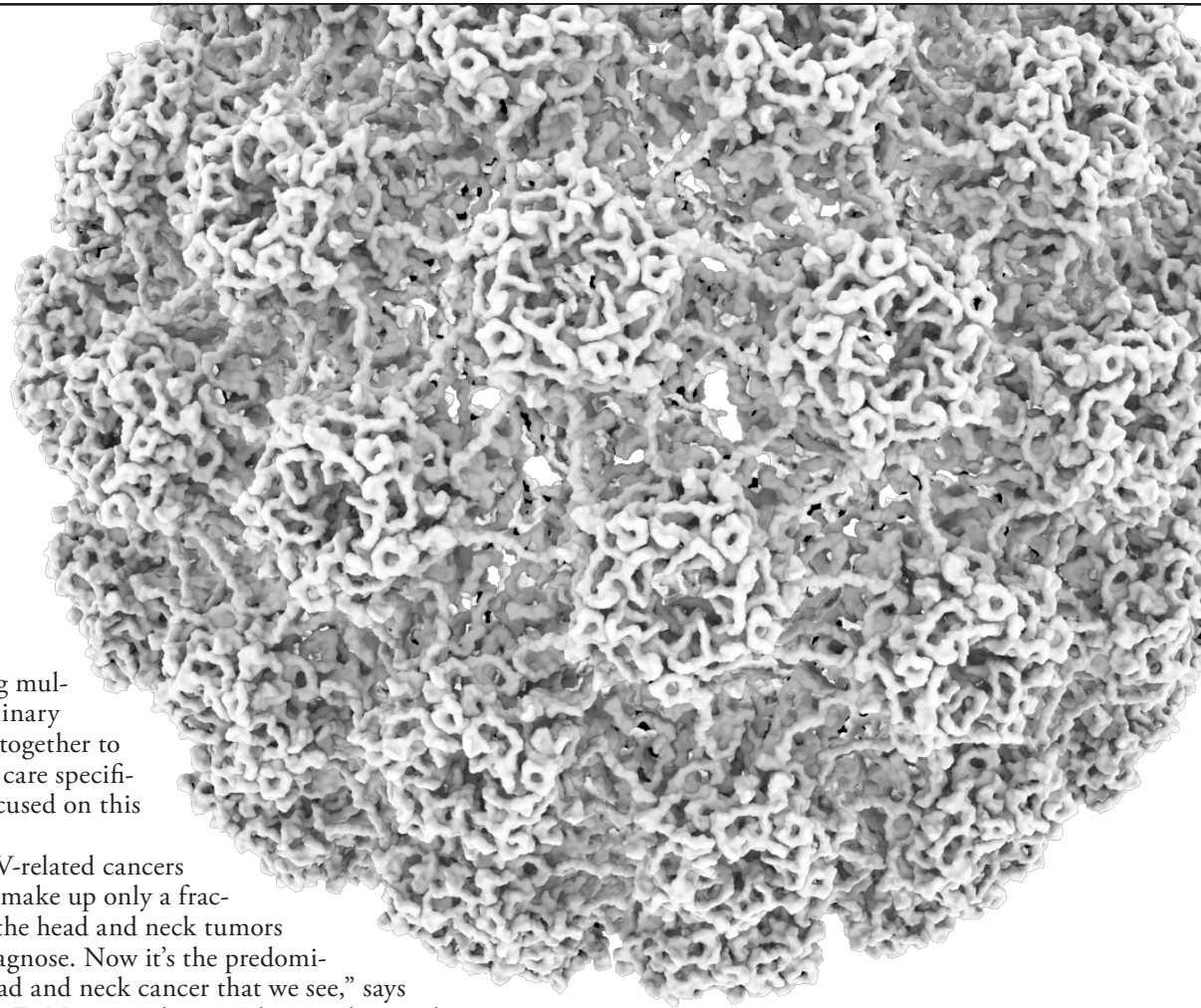
Since then, Johns Hopkins has continued to be a pioneer in learning the unique features of HPV-associated head and neck cancers and finding new ways to treat them. Recently, physicians here decided to pool their expertise to launch the Center for HPV-Related Head and Neck

Cancer, bringing multidisciplinary experts together to provide care specifically focused on this disease.

“HPV-related cancers used to make up only a fraction of the head and neck tumors we’d diagnose. Now it’s the predominant head and neck cancer that we see,” says **Carole Fakhry**, a Johns Hopkins otolaryngologist-head and neck surgeon who specializes in this condition. “Recognition of this shift led to many questions regarding diagnosis, treatment and support of this unique patient population.”

Fakhry says that unlike traditional head and neck cancers, HPV-related tumors respond more readily to treatment, including surgery, radiation and chemotherapy. As a result of this, the question of whether or not patients can achieve similar outcomes with greatly reduced treatment intensity has emerged as a question of great interest. Johns Hopkins will soon launch a treatment deescalation trial in which eligible patients are offered immunotherapy followed by surgery and nearly half the doses of chemotherapy and radiation delivered to those with traditional disease. With careful monitoring, she says, these patients may be able to avoid lifelong side effects caused by collateral damage from these treatments.

Other clinical trials run through the center focus on the trigger for the disease itself, adds **Tanguy Seiwert**, a Johns Hopkins head and neck medical oncologist who specializes in immunotherapy and HPV-related head and neck cancer. The center’s team will soon be monitoring patients who have finished their treatment protocols for residual traces of HPV in their saliva and blood. Those who test posi-



Johns Hopkins will soon launch a treatment deescalation trial in which eligible patients are offered immunotherapy followed by surgery and nearly half the doses of chemotherapy and radiation. Image shows 3D rendering of HPV.

tive will receive immunotherapy aimed at fighting the virus to potentially prevent cancer recurrence. Similarly, another clinical trial will use immunotherapy as a first-line treatment — a milder therapy that could help patients avoid high doses of harsher treatments.

Patients cared for through the center will have access to a host of experts in this condition, including medical, surgical, and radiation oncologists, physical therapists, and social workers. A patient navigator will help assemble each patient’s care team based on their unique needs, maximizing efficiency so patients can be seen and treated quickly.

“We are at an unprecedented point where we can really change outcomes for HPV-associated cancer patients,” says Seiwert. “For these cancers, Johns Hopkins will continue to lead the way.” ■



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—CAROLE FAKHRY

To refer a patient, call 443-997-6467.

Johns Hopkins Head and Neck Surgeons First in U.S. to Use Radiofrequency Ablation to Treat Thyroid Nodules

Thyroid nodules are ubiquitous — an estimated 80 percent of Americans have these typically benign growths, says Johns Hopkins otolaryngologist–head and neck surgeon **Jonathon Russell**. But in a fraction of individuals, thyroid nodules expand to a size that becomes problematic, leading to troubles with swallowing, breathing or changes in appearance that patients find unsightly.

“Several years ago, the choice on how to respond to benign thyroid nodules was binary: either perform surgery or not,” Russell says. “Because these growths typically aren’t life-threatening, many patients chose to live with them rather than deal with the recovery and scars of surgery.”

But recently, says Russell and his colleague thyroid surgeon **Ralph Tufano**, Johns Hopkins began offering a third option: radiofrequency ablation (RFA), a technique that destroys unwanted tissue using heat generated from medium frequency alternating current and is offered at just a handful of centers in the U.S. for this indication.

RFA has been used for decades to treat conditions affecting the heart, liver, and other areas. But its use in the neck has been limited due to the close proximity of vulnerable anatomical structures, such as nerves critical for swallowing and speaking, explains Tufano. With better technology and more

refined techniques, he adds, RFA has become a popular way to treat benign thyroid nodules elsewhere in the world. Johns Hopkins’ leadership in “scarless” techniques to treat thyroid and parathyroid nodules and cancers made it a fit to be a pioneer for RFA in the U.S.

Currently performed under twilight anesthesia, Russell, Tufano, and their colleagues use ultrasound guidance to insert the RFA probe into a nodule, creating a pattern of damage that’s visible under imaging. Depending on the size of the nodule, this procedure takes as little as 30 minutes to complete, Russell says. Over the next several weeks and months, the damaged tissue shrinks and disappears, leaving patients with markedly reduced nodule size and related symptoms.

Because RFA is minimally invasive and extremely targeted, says Tufano, there are no scars and patients can avoid the long-term consequences of surgery, such as the need to take thyroid hormones for life.

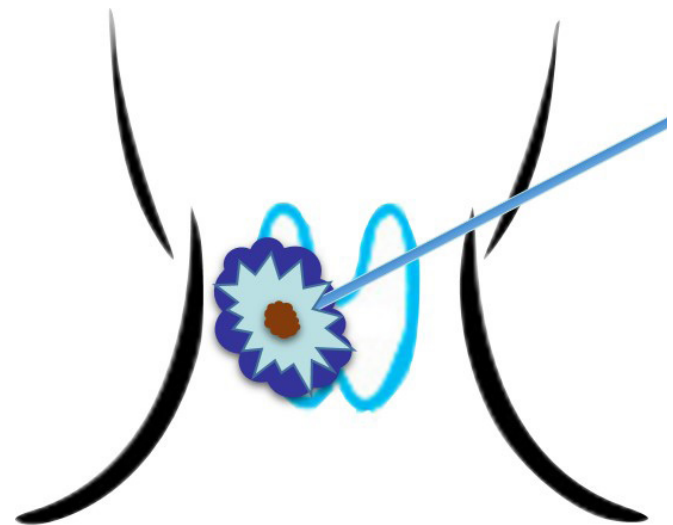
Right now, he adds, the procedure is limited to benign nodules, in which patients have at least two confirmed biopsies showing no malignancy. But eventually, RFA may be an option for patients with small cancerous tumors. In time, Russell says,



Ralph Tufano



Jonathon Russell



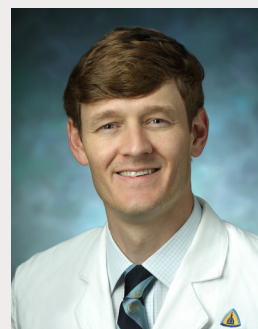
Represented in illustration: Johns Hopkins experts use ultrasound guidance to insert a radiofrequency ablation probe into benign thyroid nodule, creating a pattern of damage that’s visible under imaging. Depending on the size of the nodule, this procedure takes as little as 30 minutes to complete.

he and Tufano plan to also offer this procedure under local anesthesia, performing it right in the clinic.

“Patients whom we’ve already treated with RFA tell us that it’s a relief to avoid surgery and avoid the need for thyroid hormone while still being able to reduce their thyroid nodules’ size and relieve their symptoms,” Tufano says. “We’re pleased to offer them another option.” ■

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3 New Faculty Members Join Department of Otolaryngology—Head and Neck Surgery



Francis “Pete” Creighton, M.D.

Pete Creighton is a fellowship trained neurotologist and lateral skull base surgeon. His clinical practice specializes in surgical and medical treatment of middle ear, inner ear, skull base and facial nerve disorders. These include skull base tumors, vestibular schwannomas (acoustic neuromas), hearing loss, cholesteatoma, cerebrospinal fluid leaks and eardrum perforations. Treatment specializations include cochlear implantation, stapedectomy, mastoidectomy, and middle fossa and translabyrinthine craniotomies.

His research focuses on the integration of robotic and augmented reality platforms to improve surgical safety and efficiency.

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Predicting Who Will Respond to Cancer Immunotherapy

A new Johns Hopkins study suggests that genetic sequencing could hold key to identifying patients who would benefit from treatments.

Immunotherapy drugs have made remarkable headway in many types of cancers, including melanoma, lung, colorectal, and head and neck. However, only a subset of patients benefit from these treatments. To improve the chances for success, researchers have searched for biomarkers that could signal which patients might benefit the most. One such marker, mutations in mismatch repair genes — which affect how well DNA repairs itself when it makes a mistake during replication — boost the odds that immunotherapy will work. However, only 50% of patients with these mutations respond to immunotherapy drugs.

A new study led by Johns Hopkins otolaryngologist–head and neck surgeon **Rajarsi Mandal** suggests that it's not the mutation itself that makes immunotherapy more likely to work — it's the number of resulting DNA mismatches that build up in cancer cells over time.

Mandal and colleagues performed several experiments to tease out immunotherapy response in mismatch repair deficient tumors in mice and humans. The researchers purposely created mismatch repair deficient mouse cell lines. They found that those grown for longer developed more mismatch-related mutations. When these cells were injected into

mice, the animals were more likely to respond to immunotherapy drugs to eradicate these cells.

Furthermore, when the researchers extracted the resulting tumors and dissected them, those with a higher mutational burden had a greater infiltration of immune cells, suggesting that the immune system was mounting a stronger attack. After sequencing the DNA of animals treated with immunotherapy, researchers found a lower mutational burden, suggesting that the immune system was specifically targeting cells that carried more mutations.

Building on these findings, the team looked at clinical data drawn from three independent cohorts of cancer patients to see what the relationship might be between mutational intensity and response to immunotherapy in people. The researchers saw a general relationship between patients with a high mutational burden and more immune activity. In a group of 15 patients from Hopkins with mismatch repair deficient tumors, this translated into a better response to immunotherapy among patients with more mutations. This finding held true in a group of 33 patients from Memorial Sloan Kettering.

Mandal notes that these results could lead to better ways to stratify which patients might benefit from immunotherapy or help researchers develop

ways to universally improve survival with these drugs.

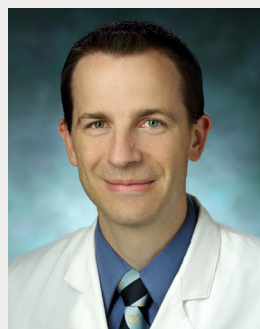
“This could open up a whole new avenue for precision medicine,” he says, “using science to change people’s clinical care and boost outcomes.” ■



"THIS COULD OPEN UP A WHOLE NEW AVENUE FOR PRECISION MEDICINE, USING SCIENCE TO CHANGE PEOPLE'S CLINICAL CARE AND BOOST OUTCOMES."

—RAJARSI MANDAL

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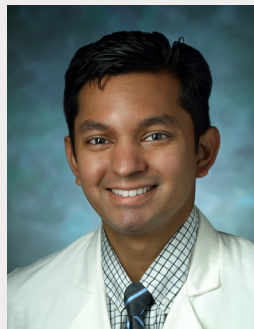


Nyall London, M.D., Ph.D.

Nyall London's clinical practice focuses on inflammatory sinonasal disease, skull base disorders, and malignancies of the skull base and sinonasal cavity. This includes chronic rhinosinusitis, skull base defects such as encephalocele or cerebrospinal fluid leak, as well as malignancies such as squamous cell carcinoma, olfactory neuroblastoma (esthesioneuroblastoma) and nasopharyngeal carcinoma. He recently completed fellowship training focused on sinonasal tumors and endoscopic and open approaches to the skull base.

London has published more than 40 peer-reviewed research articles, reviews and book chapters in publications such as *Nature*, *Nature Medicine*, *Science Translational Medicine* and *Nature Cell Biology*. He also directs a laboratory at the National Institutes of Health/National Institute on Deafness and Other Communication Disorders focused on clinical trials and mechanisms of olfactory neuroblastoma (esthesioneuroblastoma) tumorigenesis.

For referrals or patient appointments, call 301-896-3330.



Shumon Dhar, M.D.

Shumon Dhar has expertise in the comprehensive management of voice, upper airway and swallowing disorders. Dhar has unique training in bronchoesophagology, which positions him to treat patients with profound swallowing, reflux and motility problems from a holistic perspective. He uses the latest in diagnostic modalities within a multidisciplinary care model. He also offers minimally invasive endoscopic options for the treatment of GERD and Barrett's esophagus. Advanced interventions performed by Dr. Dhar include endoscopic and open treatment of cricopharyngeus muscle dysfunction and

Zenker's diverticulum, complete pharyngoesophageal stenosis, vocal fold paralysis, and severe dysphagia in head and neck cancer survivors and patients with neuromuscular disease-related swallowing dysfunction.

Dhar's research focuses on risk factors, prevention and management of patients with profound swallowing disorders. In addition to dysphagia, he is interested in neurolaryngology, specifically laryngeal dystonia and using implantable medical devices to improve patient outcomes and quality of life.

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Please include the following patient information:

- Name
- Date of birth
- Medical problem
- Patient's contact information
- Physician office contact information

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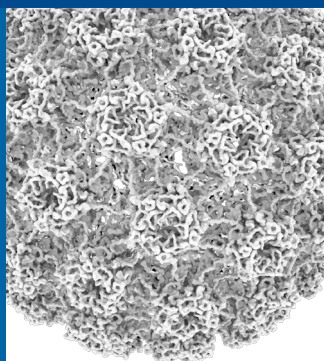
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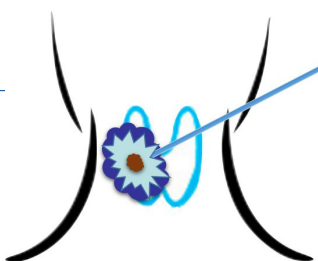
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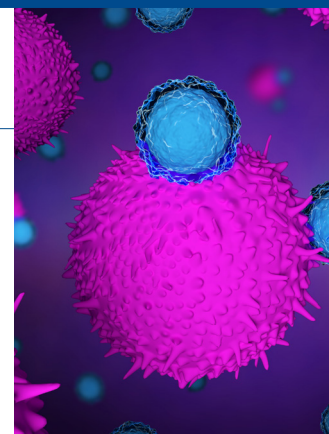
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Johns Hopkins
Launches
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Hopkins Head
and Neck
Surgeons First
in U.S. to Use
Radiofrequency
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Thyroid Nodules



3

Predicting Who
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Immunotherapy