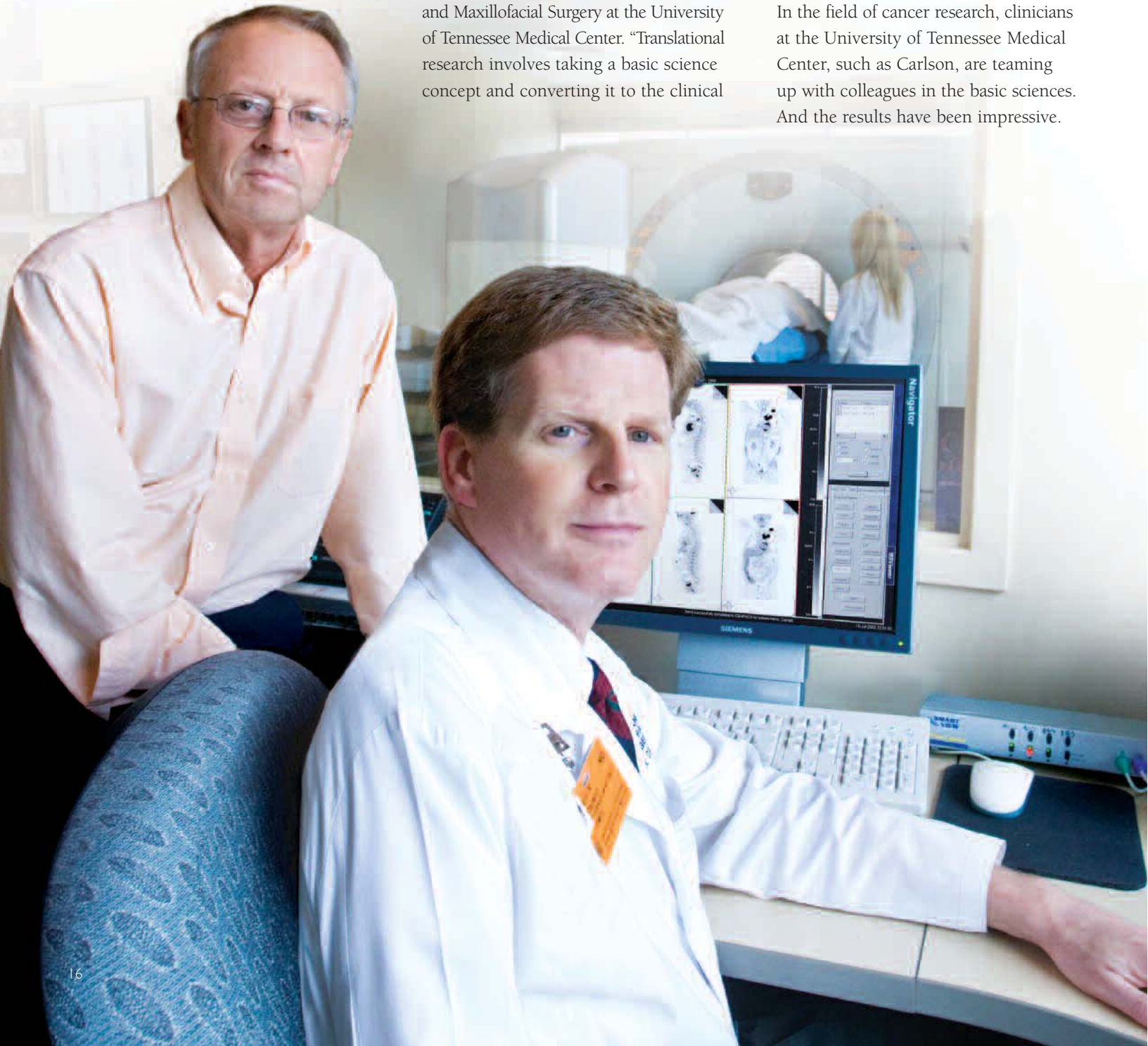
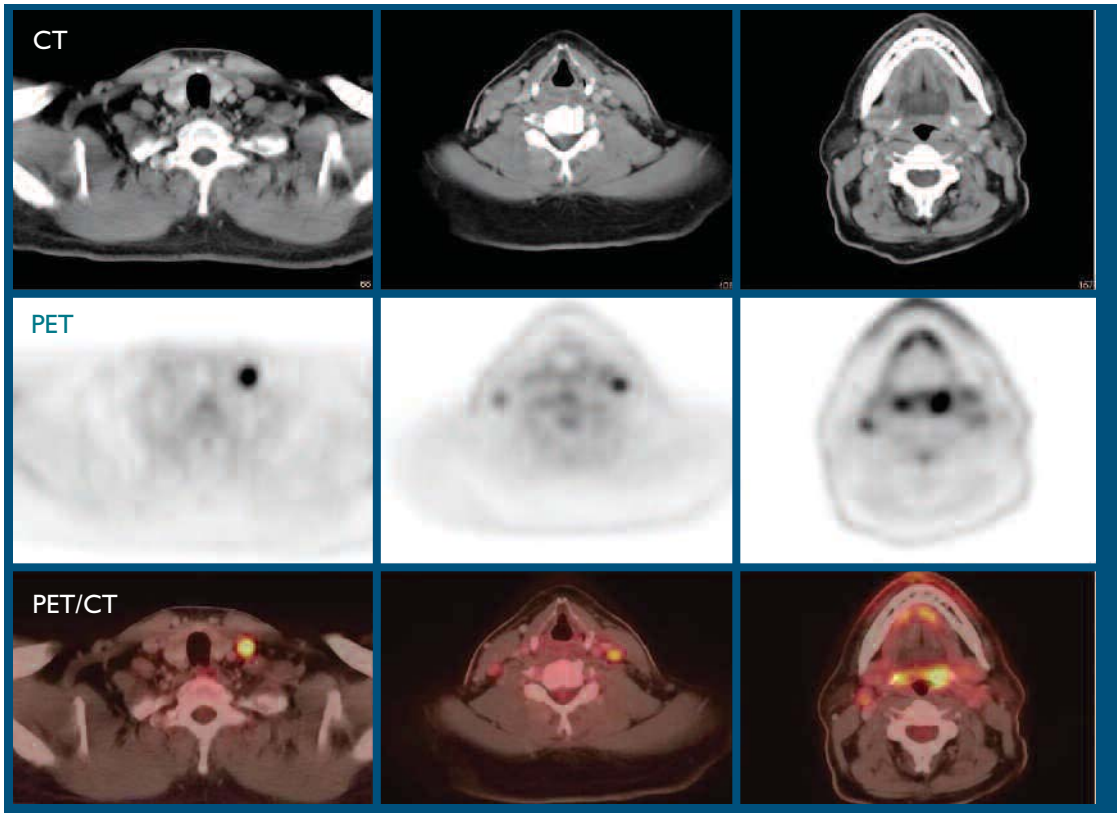
Translation Please...

Translational Research Benefits Cancer Patients

"There's an innovative concept in medicine known as translational research," says Eric Carlson, DMD, MD, chairman of the Department of Oral and Maxillofacial Surgery at the University of Tennessee Medical Center. "Translational research involves taking a basic science concept and converting it to the clinical level, so something that's discovered in the lab can translate into a benefit for patient care."

In the field of cancer research, clinicians at the University of Tennessee Medical Center, such as Carlson, are teaming up with colleagues in the basic sciences. And the results have been impressive.





PET, CT, and PET/CT images show metastatic nodes from a primary tumor in the right tonsil.

Carlson says he works with "a world-class team in molecular imaging and translational research. When I came here six years ago, one of my expressed intentions was to collaborate with as many basic science researchers in the Medical Center as possible. I'll develop a clinical idea, and they put it into scientific language. This represents a perfect collaboration between a clinician and a researcher. That's one of the elements of my career that I thoroughly enjoy."

These translational collaborations have generated several fruitful lines of research. With physicist David Townsend, PhD, director of the UT Molecular Imaging and Translational Research Program, Carlson is studying the use of PET/CT imaging in staging oral and head-and-neck cancers.

In cancers of the oral cavity, metastasis usually occurs first in the lymph nodes on the side of the neck closest to the primary cancer. The dilemma for physicians, says Carlson, is that in many of these cases, the cancer metastasizes to the nodes in the neck that can't be detected by clinical exams or imaging studies.

PET/CT, a pairing of positron emission tomography (PET) and computed tomography (CT), has rapidly become the imaging tool of choice in such cases. It was devised 10 years ago by Townsend and Ron Nutt, PhD, then CEO of CPS Innovations, a PET company based in Knoxville that is now part of Siemens Molecular Imaging.

The combination of CT, which images the anatomy and location of suspicious growths or enlarged lymph nodes, and PET, which identifies abnormal or suspicious metabolic activity that can be characteristic of cancer, helps clinicians identify and localize cancerous tissues. Carlson and other clinicians rely on PET/CT imaging because of the images' quality and their usefulness to clinicians in determining the best way to fight cancer.

This continued research increases the likelihood that the PET/CT device and molecular markers will continue to be improved. Because surgeons routinely remove lymph nodes in the neck, the ongoing study allows comparison of the lymph nodes removed during surgery with the preoperative images as a check on those images' accuracy. While PET/CT is important for effective

David W. Townsend, PhD, and Eric Carlson, DMD, MD

diagnosis and treatment ("I'm at the point where I don't feel comfortable treating a patient with head and neck cancer without PET/CT," Carlson says), recent research led by Carlson, Townsend, and co-workers found that PET/CT alone detected only about 30% of metastases in those patients. These data reveal an opportunity to improve the PET/CT procedure—one that Carlson and Townsend are actively pursuing in their research.

Carlson is also collaborating in other translational research endeavors, including work with David Gerard, PhD, in studying the connections between the genetic makeup of specific cancer cells and the way they behave biologically. "The underlying fact," says Carlson, "is that cancer is a genetic disease and the genome creates a certain behavior." Using a procedure called complimentary DNA (or cDNA) microarray analysis, he says, "we're going to take the last 100 or 200 cancers I've removed and examine the genetics of those cancers. Dr. Gerard will try to predict the biologic behavior, which I will know (the biologic behavior) based on the follow-up of these patients. Results of this study may lead to examining the genome of a cancer at the time of the initial biopsy, resulting in the ability to predict the behavior of that cancer. Therapy may be adjusted accordingly in a proactive fashion."

Eric Carlson, DMD, MD, (third from left) with the surgical team.

Wahid Hanna, MD

Townsend has partnered with other clinicians too, including recent work with Wahid Hanna, MD, chief of the Medical Center's oncology division, on the use of PET/CT to assess response to chemotherapy as early as possible in patients with non-small-cell lung cancer.

"Traditionally," says Hanna, "we give three cycles of chemotherapy—the cycles would each be about three weeks long. Then we would wait two weeks and evaluate the response. Unfortunately, if we do that and we discover the patient has not responded, we've wasted valuable time." If the patient doesn't respond to one chemotherapy regimen, another may be tried, but as the cancer progresses the patient's condition may weaken. "Sometimes it's a race between us and the cancer," Hanna says.

In a study of 18 patients, Hanna reports that PET/CT imaging was able to accurately predict responses to chemotherapy as early as just three weeks into treatment. He's now testing a larger group of 50 patients to confirm those results. If the results hold, PET/CT might be used to fine-tune chemotherapy early in the treatment.

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>
> John L. Bell, MD

Because this kind of research improves patient outcomes, it has long been part of what the Medical Center is all about. "We do the most research of any medical facility in town," says Barbara Munsey, the center's clinical trials manager. "In an academic medical center like ours, it's a major part of our mission. It's understood that we're doing research for the greater good."

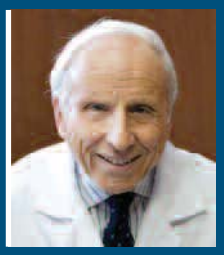
"Basic science, clinical and translational research allows us to identify ways to diagnose cancers earlier and to treat people with less toxicity and fewer side effects," says John L. Bell, MD, director of the University of Tennessee Medical Center's Cancer Institute. "There are now approximately 15 million people living in this country who have survived cancer. They're survivors because of the research that occurred over the past 50 years."

John Yates

New Discovery

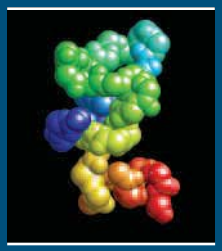
The discovery of a structurally unique protein in jaw tumors by scientists at the University of Tennessee Graduate School of Medicine's Human Immunology and Cancer Program could have important implications for the diagnosis and treatment of certain diseases.

An article published in the May/June 2008 issue of Molecular Medicine by a team headed by Alan Solomon, MD, reported the discovery of odontogenic ameloblast-associated protein (ODAM). The team found that amyloid associated with a rare jaw tumor was composed of ODAM fragments, the first evidence of expression of the unusual protein.



Alan Solomon, MD

Subsequently the team made antibodies to ODAM, as well as recombinant ODAM, and serendipitously found the molecule was expressed not only in jaw tumors but also by other epithelial cancers, including breast, gastrointestinal, and lung. Patients with these malignancies were also found to have significant titers of anti-ODAM antibodies in their blood.



ODAM Protein

Follow-up efforts, says Daniel Kestler, PhD, a lead researcher in the study, "are directed toward delineating why ODAM is expressed in these cancers, as well as the function of this protein, its role in tumorigenesis, and especially whether it can serve as a novel tumor biomarker."

Daniel Kestler, PhD