ADVANCES IN ONCOLOGY CREATE SCIENCE OF HOPE



Advances in oncology create science of hope

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Carteret Health Care provides a range of oncology services to meet the needs of cancer patients and their

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Imagine intravenous chemotherapy being replaced by a pill. Or a fluid injection that envelops a tumor's exact boundaries to guide the surgeon.

Imagine a laser so precise that its targeting beam captures tiny cancer cells and zaps them to oblivion.

Imagine oncologists using the word "cure."

Across North Carolina, scientific processes for detection coupled with treatment utilizing high-tech equipment are allowing physicians to mount stronger forces toward destroying existing cancers and predict the disease's demise. Armed with cyber radiation, nuclear medicine, strategically developed antibodies, immunotherapy, targeted therapy and oral-dose alternatives, oncologists are increasingly optimistic. And hospitals' outreach projects to screen and treat residents in rural areas who may not have access to major medical centers are assuring more people have knowledge about cancer's causes and venues for care.

"We really do have the opportunity to cure a patient of cancer. We're pretty far ahead in some specific cancers; in some cases, we are there, and for others, we have a ways to go," says Emmanuel Zervos, executive director of Greenville-based Vidant Cancer Care. "Certainly today as compared to years past, we have a far better understanding of what technology can do in that regard. We're seeing advances that we could never have imagined five years ago."

Jay Manikkam, a medical oncologist at UNC Cancer Care at Nash's Danny Talbott Cancer Center in Rocky Mount, points out that physicians used to say stage 4 cancer was incurable.

"Patients only had six months or so. Now, they are lasting five years. And some have actually stopped their treatment after five years," he says

At the Sandra Levine Young Women's Breast Cancer Program, part of Atrium Health's Levine Cancer Institute in Charlotte, co-directors Julie Fisher, a medical oncologist, and Lejla Hadzikadic Gusic, a breast surgical oncologist, specialize in treating women 40 and younger. They say five-year survival rates for patients with early-stage breast cancer exceed 90%.

"These numbers have improved steadily over the past decades thanks to improved screening technology. improved education about the importance of screening, and improvements in the treatments we offer," Fisher

Vidant, with a coverage area of 1.4 million people in 29 eastern N.C. counties, opened its 96-bed Vidant Cancer Care at the Eddie and Jo Allison Smith Tower in Greenville in 2018. "I think that this building and the hope that it offers for rising the entire tide of cancer care in the east is long overdue. We now have a facility and technology resources that allow us to compete across the state and across the country," Zervos says.

Zervos' arsenal includes the CyberKnife System, acquired in March 2018, and Gamma Knife, upgraded and installed for use in December. The radiosurgery equipment transmits highly concentrated doses of radiation to a small area without irritating normal, surrounding tissue. "We were the second center in the country to have the $latest\ Cyber Knife\ operating\ software,\ but\ l'm\ sure\ others\ have\ caught\ up,"says\ Zervos,\ who\ says\ the\ method\ has$ excellent feedback in treating prostate cancer. "It offers a tremendous advantage for patients who have isolated cancer but are not candidates for surgery."

The Gamma Knife, which is not actually a knife, emits more than 200 precise beams of radiation to control malignant and nonmalignant brain tumors without harming surrounding tissue. "The patient used to have a frame literally screwed into their skull to direct the radiation, but with this new, multimillion-dollar software, we are able to treat some patients without the frames," Zervos says.

In the trial stage, Zervos says, is the CivaSheet, a business-card-size implantable unit that delivers increased doses of radiation directly to a tumor site. "It allows the treatment to be delivered in a very focused way," he



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"The blue light defines the tumor a lot better. The real benefit is small tumors or early cancer that you may not have seen," Walsh says. "The other thing is the margins — the outside areas of the cancer. It shows that better, so we're not overtreating."

The American Cancer Society estimates 72,570 cases of bladder cancer are diagnosed annually in the U.S., and that 50% to 80% of patients will have their cancer reappear, making it the highest recurrence rate among all cancer forms.

Without a strong, visual outline of the cancer, its removal prior to blue light technology was not always complete. "We normally would take [the patient] to the operating room and cut out anything we saw that looked abnormal. Without this, you could miss as much as 30% of the cancer," Walsh says. "We're pretty aggressive at looking back three months after treatment, and now the cancer is gone that would have been there if you hadn't used this treatment."

The use of oral-dose medications for chemo treatments also is increasing, says John Krahnert, chief medical officer and senior vice president of FirstHealth of the Carolinas Inc. in Pinehurst.

"The direction now is oral medications rather than putting [the patients] in the chair and giving them an IV," Krahnert says. "And genetic therapy: how to gene-map to see if patients are more susceptible to cancer. If a patient does develop cancer, you can home in on a more specific approach — what I call the sniper approach rather than the shotgun approach."

He calls advanced diagnostics the other soldier in the fight.

"With more blood work, more screening, you can identify cancers before they even show up on X-rays," he says.
"The other thing that's coming is artificial intelligence to take pictures of lesions and have computer protocols to predict if they're cancerous prior to biopsies, particularly with skin lesions. You can have mega-data at your fingertips. This is going to be huge."

In Rocky Mount, Manikkam works with three classes of immunotherapy, recent breakthroughs of biological therapy that use living organisms to attack cancer. His weapons include checkpoint inhibitors, which are drugs that keep cancer cells from avoiding an attack by the immune system. In adoptive cell transfer, or CAR T-cell therapy, T-cells, a type of white-blood cell that is active in fighting the cancer, are removed from the body and multiplied in a lab before being injected back in. Finally, cancer vaccines boost the immune system's reaction to cancer cells

"Immunotherapy has revolutionized the landscape of cancer management, particularly stage 4 cancer that had a dismal prognosis just a few years ago," Manikkam says. "Lung cancer is a great example. Patients with stage 4 non-small cell lung cancer used to live less than 12 months. Now with immunotherapy, one in six are alive after five years, which was unheard of a decade ago."

In December, two researchers from the UNC Lineberger Comprehensive Cancer Center at UNC Chapel Hill presented findings at the 60th American Society of Hematology annual meeting in San Diego concerning immunotherapy studies of CAR T-cells targeting a type of acute myeloid leukemia. Drs. Eben Lichtman and Gianpietro Dotti forecast being able to genetically engineer normal white blood cells to create CAR T-cells to target and kill AML cells via a substance called B7-H3 on the cells' surface.

 ${\tt Dotti\ says\ the\ B7-H3\ marker\ may\ eventually\ help\ with\ combating\ ovarian\ and\ pancreatic\ cancer.}$

CAR-T cell therapy, Manikkam says, usually is done in a bone marrow transplant center. "We collect a type of immune cells and modify them in a protein that can detect the cancer cells," he says. "It's like gene editing, so your cells can detect the cancer cells. Then we introduce them back into the body."

Targeted therapy blocks cancer cells' growth by targeting the molecules needed for tumor growth. "What this tells us is we're moving more and more away from the sites and to the molecular, what drives it, what targets it. That has made a dramatic impact on the outcome," Manikkam says. "In five years, we won't care where it came from — breast, lung, and so on — we can give it targeted therapy."

Wake Forest Baptist Medical Center's Comprehensive Cancer Center in Winston-Salem opened a theranostics clinic in September when it first used an FDA-approved theranostics compound on a patient. A scientific form of precision medicine, theranostics combines targeted therapy and targeted diagnostic tests. "The completion of the sequencing of the human genome in the early 2000s, along with the dramatic progress in molecular biology techniques, now enables us to identify specific targets, or receptors, at the surface of cancer cells," says Jean-Luc Urbain, a professor of diagnostic radiology. "Using these techniques, we can also synthesize small molecules that bind effectively and specifically to these targets, like a key to a door lock."

Urbain says the United States is five to 10 years behind Europe in theranostics use, but not for long. Research companies, he says, estimate the global theranostics market at \$5 billion. "The current projections are looking at a market of about \$50 billion by 2025," he says. "Hundreds of new theranostics molecules are currently being tested for various types of cancers and diseases."

Wake Forest is the only U.S. site offering a clinical trial for Bispecific T-cell engager therapy, or BiTE, using the AMG 424 antibody for the treatment of myeloma, a malignant tumor in bone marrow. Seven patients are envalled

Trial vaccine used to wipe out melanoma, cancer of the pigment-producing cells in skin, has been successful at Mission Health in Asheville, according to oncologist Martin Palmeri.

Melanoma was expected to have 91,000 new U.S. diagnoses in 2018, resulting in 10,000 deaths. It affects one in 34 women and one in 53 men. Newer research has led to the approval of additional treatments for recurrent or metastatic melanoma. Examples of these treatments include injections that target specific markers on melanoma cells and, more recently, a vaccine that can be injected directly into a melanoma tumor, Palmeri says.

Patients receiving the vaccine in clinical trials showed a 26% overall response, with 11% "having complete resolution of the melanoma tumor injected."

The malice of cancer is not selective in its victims. Children and young women are not beyond its reach.

Mission Children's Hospital has a pediatric hematology/oncology division, with certified pediatric oncology nurses, a pediatric oncology pharmacist, a certified child-life specialist, speech and occupational therapists, a chaplain, and pediatric palliative care staff.

"We are the only pediatric oncology program in western North Carolina. We treat children, adolescents and young adults with any oncologic diagnosis and continue to care for them throughout their diagnosis for many years following," says hematologist/oncologist Ginna Priola.

The Sandra Levine program's Hadzikadic Gusic and Fisher know a cancer diagnosis goes well beyond the patient.

"Receiving a breast cancer diagnosis is life-altering for anyone, but young women face different challenges," Fisher says. "They may be raising children or working outside the home.

They may have concerns about how treatment will affect their fertility, their sexuality and their relationships with their partners or future partners. Women under 40 account for fewer than 10% of breast-cancer diagnoses each year. It can feel incredibly isolating to find yourself in that minority."

Levine offers a support group and counseling and is working to explore how the disease may be biologically different from its occurrence in older patients.

"Our current panel of trials includes immunotherapy, targeted therapies in conjunction with endocrine therapy, Phase I trials that examine new agents, and surgical trials that allow us to continue fine-tuning the optimal approach to removing breast cancers," Fisher says. "Many patients can live with the disease for some time, even for years, but a definitive cure has been elusive."

Levine's Edward S. Kim is chairman of the Department of Solid Tumor Oncology. With an emphasis on early detection, he says oral dental exams are essential for tobacco smokers.

"The beauty of it is they can be detected if you're looking for them. You don't need a PET scan or CAT scan," he says. "There are UV light cameras that can detect abnormal patches in the mouth. If you stumble on it, it's probably too late, but we have to be vigilant in making sure we check."

Kim, who traveled to Korea in December to speak about precision medicine at a medical symposium, agrees immunotherapy is a "tremendous area" in fighting cancer, along with gene profiling. He also is a proponent of prevention, particularly with smoke-related disorders.

His practice conducts a cancer screening program for first responders and firefighters. "It's because of the smoke they inhale," he says. "Anything that's smoky or burned cannot be a good thing."

The treatment of cancer is undergoing a renaissance, Kim says.

"The number of drugs and the number of new targets that we're identifying just continues to grow, and I would anticipate that this would continue," he says.

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