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Organ-Sparing Therapy for Esophageal Cancer

Endoscopic surgery, ablation treat early-stage cancer, dysplasia while avoiding esophagectomy

By Sarah Bronson

Until recently, patients with esophageal cancer were treated with esophagectomy, or removal of the affected part of the esophagus and surrounding lymph nodes, followed by reconstruction. Barrett esophagus with high-grade dysplasia, which carries a substantial risk of progressing to cancer, was treated the same way. However, esophagectomy leads to significant lifestyle changes, including diet limitations and an inability to sleep horizontally; and the operation itself can be dangerous for some older patients. Now, an increasing number of patients with early-stage esophageal cancer or dysplastic Barrett esophagus can be effectively treated with esophagus-sparing surgery and/or ablation.

Physicians at The University of Texas MD Anderson Cancer Center are incorporating new modalities in the diagnosis, treatment, and prevention of esophageal cancer. Among the new treatments is the use of local therapy administered endoscopically to remove early-stage tumors or dysplastic cells while preserving the esophagus.

"Around 2007, we began a program here at MD Anderson of performing local therapy for early esophageal disease," said Wayne Hofstetter, M.D., a professor and the director of the esophageal surgery program in the Department of Thoracic and Cardiovascular Surgery. "We perform ablation for precancerous conditions and endoscopic mucosal resection followed by ablation for early-stage cancers."

Staging workup

To determine the appropriate course of treatment, patients with suspected esophageal cancer or dysplastic Barrett esophagus are given a thorough staging

Left: An endoscopic image shows a lesion with malignant and dysplastic features (arrow). Center: During endoscopic mucosal resection, lesions are marked with cautery (white areas). Right: The esophagus is seen after removal of the lesions. Images courtesy of Dr. Wayne Hofstetter.

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[Continued from **page 1**]

workup. This workup usually includes endoscopic ultrasonography to identify tumor tissue, determine how deep the tumor extends into the esophageal wall, and determine whether the disease involves the lymph nodes.

If needed, advanced endoscopic imaging techniques are used to identify areas of dysplasia within an esophageal segment affected by Barrett esophagus, a precancerous lining that develops owing to exposure to acid or bile. One such method is confocal endomicroscopy. "Confocal endomicroscopy is like doing a live pathological exam; you insert a probe through the endoscope, and you can see the actual cells," said Marta Davila, M.D., a professor in the Department of Gastroenterology, Hepatology, and Nutrition. Another such method is volumetric laser endomicroscopy, which visualizes metaplastic glands (i.e., Barrett glands) buried under normal mucosa in the esophagus.

A section of Barrett esophagus is treated with a radiofrequency ablation catheter (top of image) mounted on the endoscope. Image courtesy of Dr. Marta Davila.

Endoscopic mucosal resection

Patients with esophageal tumors that appear superficial on workup can undergo endoscopic mucosal resection (EMR), a definitive resection in which the esophagus is accessed via the mouth and pharynx.

EMR avoids a full-thickness injury to the esophagus and is easier for patients to withstand than open surgery. Whereas open esophagectomy is a 6-hour operation that requires a significant amount of physiological reserve and several days of postoperative recovery in the hospital, EMR is an outpatient procedure that requires patients to tolerate only 45 minutes of anesthesia and is associated with a better quality of life.

To be effective, EMR must be performed at a level of care that is not widely available. "EMR requires expertise with a scope," Dr. Hofstetter said. "It requires a lot of experience with esophageal cancer, knowing where to cut and where not to cut, how deeply to cut, and how aggressive to be."

Whether EMR is therapeutic, i.e., does not need to be followed by esophagectomy, is determined by pathological interpretation of the resected tissue. If pathological analysis shows that the tumor is limited to the mucosa or very superficial submucosa, is less than 2 cm wide, does not invade any blood vessels, and has been removed with negative margins, then the patient has a good chance of a complete cure without surgery. But if pathological analysis shows otherwise, the patient will likely need to undergo esophagectomy.

The experience of the esophageal surgery program led Dr. Hofstetter and his colleagues to rewrite the Society of Thoracic Surgeons' guidelines for treating early-stage esophageal cancer in 2013; the former gold standard of esophagectomy has been replaced by EMR combined with ablation. The National Comprehensive Cancer Network guidelines also now designate EMR as a standard therapy for early-stage disease.

"We perform ablation for precancerous conditions and endoscopic mucosal resection followed by ablation for early-stage cancers."

– Dr. Wayne Hofstetter

Ablation

Endoscopic ablation is used as an adjuvant to EMR for patients with superficial tumors or as the sole treatment for patients with dysplastic Barrett esophagus whose disease is not nodular. One of two ablation modalities may be used. The first, radiofrequency ablation, delivers heat energy to the lining of the esophagus, leading to tissue destruction. Radiofrequency ablation can be administered by a balloon catheter, by a metal plate mounted at the tip of an endoscope, or by other devices. The second modality, cryoablation, uses cold gases, such as liquid nitrogen or carbon dioxide, dispensed from the end of a probe to freeze and kill abnormal cells.

The ablation modality chosen for a specific patient depends on the anatomy and the characteristics of the Barrett segment. "If we are dealing with a flat area of Barrett esophagus, we prefer radiofrequency ablation," Dr. Davila said. "If there is mild nodularity to the area and cancer has been excluded by previous EMR, we may prefer cryoablation, which can go slightly deeper than the mucosa and into the submucosa." Cryoablation is also used in patients in whom radiofrequency ablation failed.

Patients who have undergone EMR and do not need esophagectomy typically undergo three or four ablation sessions spaced 2–3 months apart. These ablations completely eradicate remaining dysplasia and Barrett esophagus, resulting in a new growth of healthy squamous epithelium, in 92%–93% of patients treated at MD Anderson.

Patients with Barrett esophagus with low- or high-grade dysplasia but no tumor nodule usually forgo EMR and proceed directly to endoscopic ab-

lation. Dr. Davila noted that 10 years ago, many such patients—those with high-grade disease, and hence a high risk of progression to cancer—would have been advised to undergo esophagectomy. "Ablation has completely changed the way we manage this disease," she said. "It's been revolutionary."

Next steps

In the future, esophagus-preserving therapy could be extended to more types of patients with esophageal cancer. For example, patients with regional extension of cancer to the lymph nodes, which is currently treated with esophagectomy, could receive local therapy with EMR plus ablation within the esophagus and surgery or chemoradiation for the affected nodes.

Also on the horizon are systemic therapies in new combinations. Dr. Hofstetter said, "We're trying to find ways of pushing patients' response to medical therapy or chemoradiation to the point where they don't need surgery."

Technological advances also are refining best practices. Dr. Davila described a new cryoballoon ablation tool recently adopted at MD Anderson and a few other centers. The device is a through-the-scope balloon catheter that is simultaneously inflated and cooled by nitrous oxide delivered from a disposable handheld unit. The balloon can be particularly useful in narrow areas that are difficult to navigate with other ablation devices.

Overall, the esophageal surgery program at MD Anderson has brought focus to first-line strategies in managing esophageal cancer and continues to seek better up-front choices for patients with early disease. "We always say that our first shot at cancer is our best shot," Dr. Hofstetter said. ■

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IN BRIEF

Surgeons Perform Unique Allogeneic Soft Tissue Transplant Between Identical Twins

Surgeons at The University of Texas MD Anderson Cancer Center recently performed a unique, extensive soft tissue transplant between identical twins to repair a large wound resulting from a rare, recurrent cancer in one of the twins.

One of the 65-year-old twin sisters presented to MD Anderson in early 2017 with a large recurrent tumor on her back and an open wound from previous surgeries and radiation treatments. This tumor was so extensive that it had been deemed unresectable at other institutions because the wound would be too big for reconstruction using standard techniques. MD Anderson pathologists diagnosed the tumor as plexiform fibrohistiocytic sarcoma, a rare, aggressive skin cancer that often recurs and invades surrounding tissue but does not spread to distant parts of the body.

A patient with a rare plexiform fibrohistiocytic sarcoma is shown before tumor resection (left) and after reconstructive surgery (right) using an allogeneic tissue transplant from her identical twin. Images courtesy of Dr. Jesse Selber.

The tumor resection and reconstruction were planned by a multidisciplinary team led by Keila Torres, M.D., Ph.D., an associate professor in the Department of Surgical Oncology, and Jesse Selber, M.D., an associate professor in the Department of Plastic Surgery. Dr. Selber said that the reconstruction was challenging because the patient herself did not have adequate donor tissue to provide coverage for the surgical wound (22 x 55 cm, extending down to the spine and ribs). The patient's sister, however, was substantially larger because she had once had a pituitary tumor that led to gigantism; the sister therefore had enough abdominal tissue to donate for the procedure.

Dr. Selber said that reconstructive allogeneic transplants are seldom performed following cancer surgery because the immunosuppressive regimens necessary to prevent tissue rejection also impair the immune system's ability to fight cancer cells. But having a donor who is both genetically identical and histocompatible could theoretically allow the transplant to be done without postoperative immunosuppression therapy. However, without a perfect match, immunosuppression would be necessary to prevent graft rejection, and the risk of cancer recurrence would become too great. For this reason, Dr. Selber asked the transplant team from Houston's Methodist Hospital to perform a living related donor workup, which confirmed that the twins were 100% histocompatible as well as genetically identical.

Four days after Dr. Torres performed the tumor resection, once pathological analysis of the resected specimen had confirmed negative margins, Dr. Selber and a team of five reconstructive plastic surgeons performed the tissue harvest from one sister and transplant to the other in two adjacent operating rooms. The surgeons removed a 54.6 × 21.6 × 5.1 cm flap of abdominal skin, muscle, and blood vessels from the donor sister and repaired the donor site using a procedure similar to a combination of a tummy tuck and a hernia repair. The flap was so large that eight separate microvascular anastomoses were required to restore and maintain circulation to the entire volume of transplanted tissue.

The patient and donor recovered without complications. "They're now at home and doing well," Dr. Selber said. ■

Advances in Breast Reconstruction

New reconstruction techniques increase breast cancer surgical options, improve cosmetic outcomes

By Bryan Tutt

As systemic, surgical, and radiation treatments continue to evolve and to improve survival outcomes for patients with breast cancer, new techniques for partial and total breast reconstruction also have emerged. Some of these techniques improve functional or cosmetic outcomes; others expand breast cancer treatment options by making satisfactory reconstruction available.

As part of a multidisciplinary care team, plastic surgeons at The University of Texas MD Anderson Cancer Center have employed several new techniques for partial or total breast reconstruction in response to the evolving nature of breast cancer treatment. These techniques include the use of nontraditional donor sites and new harvest methods for vascularized tissue transfer flaps and improvements to implant-based reconstruction. "As plastic surgeons," said Jesse Selber, M.D., an associate professor in the Department of Plastic Surgery, "we have to be able to adapt different techniques to fit in with the overall breast cancer treatment."

Advanced pedicled chest wall perforator flap options for partial breast reconstruction are shown. Flaps from the anterior chest wall (highlighted in orange), such as anterior intercostal artery and medial intercostal artery perforator flaps, are used to repair medial (A) or inferior (B) breast defects. Flaps from the lateral chest wall (highlighted in blue), including lateral intercostal artery and lateral thoracic artery perforator flaps, are used to repair lateral breast defects (C). Image courtesy of Dr. Mark Schaverien.

Reconstruction after lumpectomy

Breast-conserving therapy, in which patients undergo lumpectomy followed by radiation therapy, has been shown in several large studies to be oncologically equivalent to mastectomy for many types of breast tumors; as a result, an increasing number of patients are considering lumpectomy. "Relative to the number of mastectomies, we've seen an increase in the number of breast-conserving surgeries with immediate reconstruction," said Mark Schaverien, M.D., an assistant professor in the Department of Plastic Surgery.

Reconstruction as part of breast-conserving surgery most commonly involves breast tissue rearrangement using modified breast reduction or mastopexy techniques, which do not restore the breast to its former volume and therefore usually necessitate symmetrizing reduction surgery on the contralateral breast. These techniques are indicated for patients with large, ptotic breasts in whom bilateral breast reduction is viewed as a positive outcome or reduction is necessary to facilitate radiation therapy.

For patients with small or moderate breasts, minimal ptosis, and a large tumor-to-breast volume ratio, pedicled perforator soft tissue flaps are sometimes the best option for partial breast reconstruction. The lumpectomy and reconstruction are performed in a single outpatient operation, and symmetrizing surgery to the contralateral breast is not required.

The latissimus dorsi muscle and thoracodorsal artery perforator flaps are well established for partial breast reconstruction; however, more advanced flaps are indicated for some defects. For instance, lateral breast defects can be repaired using pedicled flaps from the lateral chest wall, such as the lateral intercostal artery or lateral thoracic artery perforator flaps. And inferior or medial breast defects can be repaired using flaps from the anterior chest, such as the anterior intercostal artery or medial intercostal artery perforator flaps. The scars from these advanced flaps lie in the inframammary or lateral breast folds and are well concealed by a bra or swimsuit strap.

"These flaps are commonly used outside of the United States and are a valuable addition to the armamentarium of plastic surgeons performing oncoplastic breast reconstruction," said Dr. Schaverien, who was among the first surgeons in the United States to introduce advanced pedicled chest wall perforator flaps for immediate partial breast reconstruction. "These chest wall flaps do not involve or include muscle, so there is very low donor site morbidity. Most importantly, the latissimus dorsi muscle and its blood supply are preserved in case they are needed for

total breast reconstruction in the future."

After partial breast reconstruction using breast tissue or a perforator flap, radiation therapy sometimes causes contracture or scar tissue in the reconstructed breast. "Deformities that develop during radiation therapy can be repaired by an injection of fat, or what we call autologous fat grafting," said Matthew Hanasono, M.D., a professor in the Department of Plastic Surgery who pioneered the technique (see "New Fat Grafting Technique Improves Aesthetic Outcomes Following Head and Neck Reconstructive Surgery," *OncoLog*, April 2014).

Reconstruction after mastectomy

For patients who require mastectomy, total breast reconstruction may be performed using implants, vascularized tissue flaps, or both. Dr. Selber said that new techniques for both implant- and flap-based breast reconstruction are improving aesthetic and functional outcomes for patients at MD Anderson.

Implant-based total reconstruction

Implant-based reconstruction, the most common type of total breast reconstruction, was introduced in the 1970s and is traditionally performed by detaching the pectoral muscle, placing a tissue expander underneath, and suturing the muscle back together to hold the implant in place; the tissue expander is later replaced by the permanent implant.

The first major innovation in implant-based reconstruction came in 2005 with the use of acellular dermal matrix to hold the tissue expander (and later the implant) in place. Typically, the top of the implant is held in place by the pectoral muscle, and the bottom is supported by acellular dermal matrix so that the implant can sit lower for a more natural appearance. But when acellular dermal matrix is used in this manner, the pectoral muscle is still dissected and reattached, which causes temporary pain and creates an animation deformity such that the breasts move when the pectoral muscle moves.

Several surgeons, including Dr. Selber, decided to experiment with a different way to use acellular dermal matrix. "About a year and a half ago, some of us in the global plastic surgery community started to think that if we were using acellular dermal matrix in this fashion to sort of create an internal bra for the implant, then perhaps we didn't need to use the pectoral muscle at all," he said.

The resulting technique, prepectoral implant-based breast reconstruction, may be the next evolutionary step in implant-based breast reconstruction, according to Dr. Selber. In such a reconstruction, the tissue expander/implant is placed on the pectoral muscle, and the acellular dermal matrix supports the implant from beneath and on its front surface, holding it securely against the chest wall to provide stability.

Dr. Selber now uses the prepectoral technique for almost all his implant-based breast reconstructions. "Patients are very happy with the results," he said. He added that, compared with the traditional method of covering the implant with the pectoral muscle, "The pain and recovery time are dramatically reduced, and the early aesthetic results are better. Also, it's a faster and simpler technique. There are a lot of advantages to both the patient and the surgeon. I would say this technique is revolutionizing implant-based breast reconstruction."

Flap-based total reconstruction

Other recent advances in total breast reconstruction have been in the use of tissue flaps. Some of these advances reduce scarring; others increase options for donor sites or improve function.

A major functional impairment for many breast cancer survivors is lymphedema of the upper extremity, a condition caused by removal or damage to the limb's draining lymph nodes. To relieve this condition, MD Anderson surgeons often perform a vascularized lymph node transfer, in which lymphatics are moved and anastomosed along with a free deep inferior epigastric perforator (DIEP) flap for simultaneous total breast reconstruction (see "Advances in Surgical Management of Lymphedema," *OncoLog*, April 2017).

When a patient's anatomy is not

Dr. Jesse Selber *pioneered the use of the da Vinci surgical robot (pictured) to harvest the latissimus dorsi muscle for breast reconstruction. The robotic harvest procedure results in less donor site scarring than an open procedure.*

[Continued from **page 5**]

suited for a DIEP, transverse rectus abdominis myocutaneous, or other free abdominal flap for total breast reconstruction, plastic surgeons have other options. Profunda artery perforator or transverse upper gracilis flaps harvested from the upper thigh and gluteal artery perforator flaps harvested from the buttock result in well-concealed scars with minimal donor site morbidity. Along with these flaps, advanced techniques such as stacked or bipedicled flap configurations can be used to increase the tissue volume available for breast reconstruction. "These free flaps and techniques are expanding the options for patients who have insufficient abdominal tissue for breast reconstruction or have previously had multiple abdominal surgeries," Dr. Schaverien said.

A more common donor site for tissue flaps for total breast reconstruction is the latissimus dorsi muscle, which can be used with or without the overlying skin to cover an implant. For patients who do not need a skin flap, Dr. Selber devised a minimally invasive technique for harvesting the latissimus dorsi muscle (see "Robotic Surgery Makes Tissue Harvest for Breast Reconstruction Less Invasive," *OncoLog*, May 2013).

In the minimally invasive procedure, the surgeon uses robotic instruments to separate the latissimus dorsi muscle from the surrounding tissue. The pedicled flap is then transferred under the skin to the breast. "If you don't need to transfer skin, you don't need to make a skin incision," Dr. Selber said.

The robotic procedure has a specific place in MD Anderson's algorithm for "delayed immediate" breast reconstruction, which is when a patient gets a tissue expander in the same operation as her mastectomy and then undergoes radiation therapy followed by final reconstruction. During the final reconstruction, the expander may be replaced by a permanent implant; in such a case, a vascularized tissue flap is often needed to cover the implant.

Dr. Selber has taught the robotic tissue harvest technique to several colleagues and trainees at MD Anderson, some of whom have since moved to other institutions. However, the procedure is routinely done only at MD Anderson.

Visible Light Spectroscopy Improves Postoperative Tissue Flap Monitoring

A recent study by MD Anderson surgeons showed that a new postoperative tissue monitoring technique, visible light spectroscopy, offers greater sensitivity and specificity in detecting thrombosis in vascularized free tissue transfer flaps than does the standard of care.

Vascularized free flaps are commonly used in reconstructive surgery after oncological resection of breast and other cancers, but nationwide up to 9% of free flaps fail because of thrombosis. If thrombosis is detected early, compromised flaps can usually be salvaged. However, the standard techniques for flap monitoring, which are visual inspection and Doppler ultrasonography, have significant limitations. Both techniques are performed intermittently rather than continuously, visual inspection is done by staff with varying experience levels, and Doppler ultrasonography detects only arterial—not venous—compromise.

Visible light spectroscopy is a noninvasive technique that continuously monitors hemoglobin saturation of tissue at the capillary level and total hemoglobin concentration. Decreased hemoglobin saturation indicates arterial compromise, and increased total hemoglobin concentration indicates venous compromise.

In the recent study, Dr. Selber and his colleagues used both visible light spectroscopy and standard postoperative monitoring in 68 patients with 81 flaps. In three patients, flap compromise was detected by visible light spectroscopy but not by visual inspection or Doppler ultrasonography. All three patients returned to surgery, and the compromised flaps were salvaged.

"Visible light spectroscopy is a technology we've introduced here recently that can be used with any free tissue transfer that has a skin pad on the outside," Dr. Selber said. "It's the next generation of flap monitoring that goes beyond human observation."

The study's report was published in *Plastic and Reconstructive Surgery* (Mericli AF, et al. *Plast Reconstr Surg.* 2017;140:604–613). ■

Multidisciplinary care

Drs. Selber, Hanasono, and Schaverien emphasized the importance of plastic surgeons' involvement with the multidisciplinary care team. The type of oncological surgery and the need for radiation therapy affect the options for reconstructive surgery. Conversely, the type of reconstructive surgery (e.g., prepectoral versus standard placement of tissue expanders) can affect radiation therapy planning.

"There are many options in breast cancer treatment and breast reconstruction," Dr. Selber said. "So it's important to have deep and ongoing communication between the medical, surgical, and radiation oncologists and plastic surgeons—not just at the initiation of therapy but throughout therapy because the patient's condition and the treatment needed evolve throughout the course of care." ■

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Facing the Financial Burden of Cancer Treatment

Talking to care team, seeking out resources are important steps in managing cancer-related financial stress

Cancer treatment can be expensive, and even patients with good medical insurance can face a large financial burden. Factors like missing work and traveling to receive treatment can add to this burden and the stress that comes with it. Although help often is available for patients who face financial stress, many do not know whom to ask or where to look.

"Financial stress decreases patients' quality of life and can make it difficult for them to adhere to treatment," said Grace Smith, M.D., Ph.D., M.P.H., an assistant professor in the Departments of Radiation Oncology and Health Services Research at The University of Texas MD Anderson Cancer Center. "Some studies suggest that up to half of cancer patients have financial stress with their treatment."

Dr. Smith said that treatment-related financial stress is sometimes referred to as "financial toxicity" because it can be as disruptive as the physical toxic effects—such as nausea and hair loss—of some cancer treatments. Thus, cancer patients need information and resources to help deal with their financial stress.

Starting the conversation

Although doctors, nurses, and other cancer care specialists can help patients deal with financial stress, many patients find it difficult to discuss finances with their care team. However, this discussion is an important one to have.

"Research shows that most cancer patients want to talk to their care team about treatment costs, but few actually do," Dr. Smith said. She noted that patients may be too overwhelmed with new information about their disease and treatment options to do so. She suggested that patients write down their questions—including those about prescription costs, missed work, and travel and lodging—before their appointment and bring a friend or caregiver to the appointment to help ask questions and take notes.

"It's important that patients know they can discuss their concerns with a variety of members of their care team," Dr. Smith said. This team includes not only doctors and nurses but also the hospital's pharmacists, social workers, chaplains, patient advocates, and business office personnel. These experts often can help patients directly or point patients to agencies that can help.

Where to get help

Sources of financial assistance may include nonprofit groups, pharmaceutical companies, professional organizations, and government agencies.

Nonprofit groups can provide information, assistance, and support directly to patients. The American Cancer Society, for example, has a help line (800-227-2345) for cancer-related questions, including questions about financial issues. Also, the organization's Web site (http://bit.ly/2vYanZZ) has tips for navigating health insurance and other financial concerns. And the Leukemia & Lymphoma Society offers co-pay and travel assistance programs (http://bit.ly/2fagBTt) to patients with these cancers.

Other nonprofit groups help patients deal with the cost of medicine. The Patient Assistance Program Center (www.rxassist.org) and the Partnership for Prescription Assistance (www.pparx.org) match patients who cannot afford medicine with pharmaceutical companies' patient assistance programs.

Patients can also look to some oncology professional organizations for helpful information. For example, the American Society of Clinical Oncology offers a detailed pamphlet about dealing with the financial burden of cancer care (http://bit.ly/1mEZSCZ).

In addition, patients can contact the federal government to see if they qualify for benefits that could help cover costs related to their care. The Centers for Medicare & Medicaid Services (www.cms.gov; 800-633-4227), Social Security Administration (www.ssa.gov; 800-772-1213), and Department of Health & Human Services (www.hhs.gov; 800-677-1116) are good places to start.

Cancer support groups—especially those that offer peer mentoring, like MD Anderson's myCancerConnection (www.mdanderson.org/mycancerconnection)—can also provide information about financial assistance. Peer mentors are cancer survivors who offer patients support and can often direct them toward financial assistance resources.

Finally, patients who may miss time from work should talk to their employers about their leave benefits and whether a flexible schedule or telecommuting is an option during treatment. Patients should also contact their insurance companies with questions about coverage. Some insurance plans will cover items such as nutritional supplements and medical supplies if those items are prescribed as part of cancer treatment.

Cancer patients can seek out a variety of resources to help relieve the financial stress that accompanies cancer treatment. "The most important thing cancer patients who have financial stress should know is that they are not alone," Dr. Smith said. ■

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IN BRIEF

Proton Therapy plus Chemotherapy Shows Promise in Lung Cancer Trial

For patients with unresectable stage III non–small cell lung cancer (NSCLC), concurrent proton therapy and chemotherapy may offer better survival outcomes and less toxicity than the standard of care, according to a recent clinical trial from The University of Texas MD Anderson Cancer Center.

The single-institution phase II trial enrolled 64 patients with unresectable stage IIIA or IIIB NSCLC who had not undergone previous radiation therapy to the chest. All patients received carboplatin and paclitaxel with concurrent passively scattered proton beam therapy.

"We hypothesized that proton therapy would offer a survival benefit to patients and reduce treatment-associated toxic effects, which can be very serious," said Joe Chang, M.D., a professor in the Department of Radiation Oncology and the trial's principal investigator.

"We hypothesized that proton therapy would offer a survival benefit to patients and reduce treatment-associated toxic effects."

– Dr. Joe Chang

The 26.5-month median overall survival duration for patients in the trial was substantially longer than the historical median overall survival duration of 16.0 months (at the time of the trial's design) for similar patients treated with chemotherapy and concurrent photon-based radiation therapy.

The toxic effects experienced by patients in the trial included grade 2, 3, and 4 esophagitis and grade 2 and 3 pneumonitis. The rates of these effects were lower than those in previous studies of chemotherapy and concurrent photon-based radiation therapy. Unlike patients in some previous studies of the standard treatment, none of the patients in the trial died of toxic effects.

These results, which represent the longest follow-up to date of stage III lung cancer patients who received proton therapy, were recently published in *JAMA Oncology*.

Dr. Chang noted that since the trial began, the delivery of both photon-based radiation therapy and proton therapy have improved, thereby reducing the rate and severity of both treatment modalities' adverse effects. To determine how these improvements will affect survival, MD Anderson researchers are now enrolling patients with stage II or III NSCLC in a randomized phase II trial (No. 2011-1058) of chemotherapy with concurrent photon-based or proton-based intensity-modulated radiation therapy (see "Proton Therapy for Non–Small Cell Lung Cancer," *OncoLog*, June 2016). ■

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