“Hunger Training” Helps Manage Weight, May Reduce Cancer Risk

Clinical trial tests weight loss strategy to reduce cancer risk in obese participants

By Joe Munch

Obesity, already associated with a litany of other diseases, is now the number one cause of cancer among non-smokers. However, strategies aimed at avoiding obesity are often undermined by people’s lifelong eating habits. To help people break these habits and avoid obesity—and the cancer risk that accompanies it—researchers at The University of Texas MD Anderson Cancer Center are investigating a new weight management approach that helps people rethink their relationship with food.

The weight management approach uses glucose monitoring to help people manage their food intake. A clinical trial is under way to see if this approach can improve weight losses achieved during a 16-week lifestyle intervention for obese postmenopausal women at high risk of developing breast cancer.

A major risk factor

Obesity is known to increase the risk of colorectal, endometrial, and postmenopausal breast cancers; cancers of the pancreas, kidneys, liver, thyroid, stomach, gallbladder, esophagus, and ovaries; and meningioma and multiple myeloma. Whether losing weight decreases this risk is less clear, however. “Epidemiological data show that being obese is associated with increased cancer risk, but we don’t yet have a lot of data about how weight loss affects cancer risk,” said Karen Basen-Engquist, Ph.D., a professor in the Department of Behavioral Science. “We do have some...
Hunger Training

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data showing that weight loss is associated with a decreased risk of developing endometrial cancer, and we’re starting to see data showing that a large amount of weight loss after bariatric surgery is associated with decreased cancer risk.”

Although the exact mechanisms are unclear, obesity is believed to increase the risk of cancer primarily through the accumulation of adipose tissue. Adipose tissue—fat—is very active metabolically and secretes numerous growth factors and hormones associated with cancer development and progression. For example, adipose tissue secretes estrogen, which drives many breast cancers, as well as vascular endothelial growth factor, which enables malignant transformation by promoting angiogenesis. Because obesity often goes hand in hand with a poor diet, diet-related factors may also contribute to the development of cancer. Genetics, too, may play a role in the relationship between obesity and cancer.

“It’s probably not just one thing we can point to, but a number of characteristics that are linked with obesity that help drive increased cancer risk,” Dr. Basen-Engquist said, “and the driving characteristics might be different for different types of cancer.”

Importance of achieving balance

Energy balance—the state in which the number of calories a person expends is equal to the number of calories that person consumes—is key to staying at a healthy weight, said Susan Schembre, Ph.D., an assistant professor and registered dietitian in the Department of Behavioral Science.

“Food is fuel and nutrients; it’s not anything other than that physiologically,” Dr. Schembre said. “But we eat for other reasons. We eat to celebrate, or reward ourselves, or comfort ourselves.”

In other words, a desire to eat may not be connected to a physiological cue for the need for fuel. This disconnect is encouraged by intensive weight-loss interventions that focus on strictly scheduling eating times to offset the tendency to eat outside those periods. And once these interventions end, patients drift back to the poor eating habits they had beforehand.

“People’s relationship with food and their disconnect from physiological cues can interfere with their ability to control their weight,” Dr. Schembre said. “We need to provide people with the skills to understand their relationship with food and learn how to self-regulate.”

**Hunger Training**

To help people sever their unhealthy connections with food and better manage their weight, Dr. Schembre and other researchers are turning to an intervention called “Hunger Training.” The aim of Hunger Training is to teach people to recognize when they are truly hungry—i.e., when they have a negative energy balance and their bodies need fuel.

Patients who practice Hunger Training use glucose monitors to assess their need for food. (Glucose is used as a biomarker of short-term energy status; it serves as a proxy for a physiological

### Outreach Programs Help Communities Overcome Obstacles to Healthy Living

Preventing obesity requires more than individual motivation. People’s environments also shape their opportunities for a healthy lifestyle, said Lorna McNeill, Ph.D., M.P.H., an associate professor in and chair of the Department of Health Disparities Research.

“We have to realize that people are affected by their family and culture and upbringing,” Dr. McNeill said. “We can’t just focus on the individual and think that we’re going to make lasting changes. We have to consider the context in which that person lives.”

Dr. McNeill develops interventions that work within the context of people’s social environment to help them overcome obstacles to a healthy lifestyle. Her projects are largely directed at minority populations in underserved communities, whose risk for obesity is higher than that of the general population. These projects, which focus on social support, particularly among women, have included recruiting participants for a yoga-based intervention through churches and setting up a healthy food co-op in a church in a food desert (an area with limited access to nutritious food).

One of Dr. McNeill’s main goals is to understand the relationship between environment and physical activity—specifically, how environment affects people as they adopt physical activity and how it affects them after they have adopted and maintained the behavior.

Overcoming environmental barriers to activity requires placing innovative, evidence-based programs in the community so that more people have access to them, Dr. McNeill said. She added that the main challenge in these programs is finding ways to sufficiently engage people to ensure their long-term adherence to the behaviors the interventions foster.

“Some interventions can get people to change their behavior to lose weight over 3 months, but then they regress, and we don’t yet know how to get people to maintain what they’ve started,” Dr. McNeill said. “As researchers, that’s the hardest obstacle we still haven’t been able to crack.”

need for food.) The glucose monitor—typically a small patch-like apparatus placed on the upper arm and secured with adhesive—connects wirelessly to a reader that allows patients to check their glucose levels in real time. A blood glucose level at or near a person’s fasting level is the threshold that signals “true hunger,” or an energy deficit and a need to eat.

“With Hunger Training, there are no other dietary recommendations; it’s just, don’t eat if your glucose is above your threshold,” Dr. Schembre said.

Hunger Training typically lasts 3–4 weeks. Once patients learn to associate feelings of true hunger with the number on the glucometer—i.e., they’ve learned to sense what true hunger is and eat accordingly—they stop Hunger Training.

Recent trials of Hunger Training have been promising, Dr. Schembre said. “People using this intervention have lost up to 7% of their initial body weight within 5 months. These results are as good as if not better than other more intensive interventions, which typically achieve an average of 5% weight loss,” Dr. Schembre said.

Whether such results are enduring has not yet been tested, and Dr. Schembre said that she expects a “booster” program might be necessary to reorient participants to the training in the long term.

Dr. Schembre and her colleagues have opened a clinical trial (No. 2017-0507) to determine the effects of Hunger Training on weight loss in obese postmenopausal women with a high risk of developing breast cancer. The trial is enrolling women who have a body mass index of 30 kg/m² or higher and are identified as being at high risk for cancer based on their background and medical history. Future studies of Hunger Training may look at the relationship between obesity and cancer in different populations.

“We’ll have opportunities to investigate this intervention in other populations, such as cancer patients receiving treatment and cancer survivors, but we’re taking it one step at a time,” Dr. Schembre said.

Re-Irradiation for Recurrent Head and Neck Cancer

By Bryan Tutt

Patients with recurrent or second primary head and neck cancer who previously received radiation therapy to the head and neck region—especially those with unresectable tumors—have typically had a dismal prognosis and limited treatment options. Although radiation therapy offers high rates of local disease control, re-irradiating the region is usually avoided for fear of damaging previously irradiated healthy tissue, including vital structures such as the carotid arteries and neural structures. But advanced imaging and radiation therapy techniques are now being used to re-irradiate recurrent tumors while sparing nearby critical structures in patients with head and neck cancer.

For previously irradiated patients with recurrent head and neck cancer, surgery is historically considered the only potentially curative option. When these recurrent tumors are unresectable, chemotherapy provides a median survival of only 9–11 months—just a few months longer than with supportive care.

“These patients with unresectable tumors don’t have many options, and they die of very morbid disease,” said Jack Phan, M.D., Ph.D., an assistant professor in the Department of Radiation Oncology at The University of Texas MD Anderson Cancer Center.

But Dr. Phan and colleagues have shown that re-irradiating recurrent tumors, if done safely, can provide local tumor control and relieve symptoms.

For information about the Hunger Training trial for postmenopausal women at high risk of breast cancer, visit www.clinicaltrials.org, call 713-794-5494, or email takecharge@mdanderson.org.
Re-Irradiation for Recurrent Head and Neck Cancer

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With the goal of also prolonging patients’ survival, Dr. Phan is now leading a clinical trial that explores re-irradiation in patients with unresectable recurrent head and neck cancer.

Overcoming challenges to re-irradiation

In the 1990s, several clinical trials studied re-irradiating recurrent head and neck tumors with conventional two-dimensional and three-dimensional conformal radiation therapy. “It did improve outcomes in a select group of patients, but the side effects were pretty horrendous,” Dr. Phan said. The practice was restricted to very high risk cases.

In 2013, believing that advances in technology could improve patient safety, MD Anderson physicians began using stereotactic techniques for re-irradiation in patients with unresectable recurrent head and neck cancers. Dr. Phan and colleagues visualize these tumors by creating a composite three-dimensional image from magnetic resonance imaging, computed tomography, and positron emission tomography scans taken with the patient in the treatment position. The composite image is used to plan the delivery of stereotactic body radiation therapy (SBRT) with a linear accelerator or stereotactic radiosurgery with a Gamma Knife.

“We’re at a point now where we can target the tumor with stereotactic precision and avoid the nearby normal, critical tissues,” Dr. Phan said. “We previously couldn’t visualize the tumor very well. Advances in radiation therapy are very closely tied to advances in medical imaging.”

Both stereotactic modalities deliver high doses of radiation to the tumor in very few fractions—typically three to five for SBRT and one to three for radiosurgery—with minimal doses to nearby structures. The patient is re-imaged in the treatment position before each treatment session to ensure precise targeting. SBRT is used for most recurrent head and neck tumors, with stereotactic radiosurgery reserved for small skull base tumors.

Clinical benefits of re-irradiation

Patients who previously received radiation therapy to the head and neck region and receive re-irradiation for recurrent head and neck cancer at MD Anderson are enrolled in an observational study. Data from this study are showing that patients benefit from re-irradiation.

“We currently re-irradiate about 100 patients a year—an increase from about 20 patients a year prior to 2011,” Dr. Phan said. “Many folks we treated 3–5 years ago with SBRT are still alive and doing well.”

In addition to potentially prolonging survival, re-irradiation can provide symptom relief. Dr. Phan and colleagues recently analyzed the outcomes of patients who received stereotactic radiosurgery as a palliative treatment for facial pain from unresectable recurrent skull base tumors. Most patients had significantly lower self-reported pain scores 6 months after treatment. Furthermore, many patients were able to reduce their doses of pain medication, and some patients were able to discontinue their pain medications altogether.

“This was the first study to document a decrease in narcotic use after palliative-intent re-irradiation for patients with pain from recurrent head and neck cancer,” Dr. Phan said. “And in our current clinical trial, re-irradiation with SBRT is being done with the goal of long-term cancer control.”

The current trial (No. 2016-1065) is enrolling patients who have one to three sites of unresectable recurrent or second primary head and neck cancer who previously received at least 30 Gy of radiation therapy for head and neck cancer. Each tumor must be smaller than 60 cm³, and the total tumor volume must be less than 100 cm³.

Patients enrolled in the trial are randomly assigned to one of two treatment groups. One group receives SBRT at a dose of 45 Gy in five fractions over 2 weeks, and the other group receives intensity-modulated radiation therapy (IMRT) or intensity-modulated proton therapy (IMPT) at a dose of 60–70 Gy in 33–35 fractions over 6 or 7 weeks.

The trial’s outcome measures include toxic effects, local tumor control, and patient-reported symptoms. “All three modalities used in the trial are highly conformal,” Dr. Phan said. “The ques-
tion we have is, which modality will give better local tumor control and a better side effect profile?"

So far, patients in both treatment groups are doing well. "We only have 1 year of follow-up, but the local tumor control rate for all patients is 80%–90%," Dr. Phan said, emphasizing that these results are too early for meaningful analysis. "We don’t know how these patients will do 5 years from now, but it’s promising."

In the 1990s, re-irradiation for head and neck cancer was believed to cause carotid artery damage in 8%–13% of patients; however, Dr. Phan and his colleagues have not seen any carotid artery damage in patients in the observational study or the current clinical trial.

**Future directions**

Other clinical trials of stereotactic radiation techniques are expected to begin enrolling previously irradiated patients with head and neck cancer in the near future. Some of these trials will combine radiation therapy with immunotherapy.

A phase I trial will combine SBRT and an immune checkpoint inhibitor for patients with recurrent head and neck cancer and one to three head and neck lesions who have previously undergone radiation therapy to the head and neck region. "Head and neck tumors have a high risk of spreading regionally and distantly," Dr. Phan said. "We hope the immunotherapy will help the body target any stray tumor cells outside the radiation field." The researchers also hope that the radiation therapy will create an abscopal effect, i.e., that antigens released by the irradiated tumors will enhance the effect of immunotherapy on the non-irradiated metastatic lesions.

Dr. Phan and colleagues also want to see if re-irradiation plus immunotherapy can benefit patients with resectable disease. A trial combining re-irradiation and immunotherapy will enroll patients with resectable recurrent head and neck cancer who previously underwent radiation therapy. After resection of the recurrent disease, patients will receive lower-dose SBRT in combination with immunotherapy drugs. One of these drugs is a novel immune checkpoint inhibitor that also has the potential to reduce radiation-related inflammation. "This is exciting because re-irradiated patients have a high risk of severe scarring, and this scarring comes from inflammation," Dr. Phan said.

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**Stereotactic Radiation for Newly Diagnosed Head and Neck Tumors**

While much of Dr. Phan’s research in stereotactic treatments has focused on recurrent disease, he believes such treatments could eventually become standard first-line therapies for some head and neck cancers. His current dose-escalation trial of SBRT as organ-preserving therapy in newly diagnosed patients with laryngeal cancer is a step in that direction.

The phase I trial (No. 2016-1023) is enrolling patients with previously untreated T1, N1, M0 or T2–4a, N0–1, M0 squamous cell carcinoma of the larynx. All patients receive SBRT at a minimum dose of 40 Gy in five fractions. "The goal is to avoid surgery while eliminating the tumor in order to preserve swallowing function, which is very important for quality of life," Dr. Phan said.

The study’s outcome measures are the maximum tolerated dose, toxic effects, and complete response rate. Early results are not yet available, but Dr. Phan is optimistic about the patients’ outcomes.

Another trial, which is still in the planning stages, will enroll patients with newly diagnosed nasopharyngeal cancer. Patients will receive an upfront stereotactic radiation boost followed by induction therapy with an immune checkpoint inhibitor and then standard treatment with chemotherapy plus IMRT or IMPT. The researchers plan to obtain blood and tissue samples as well as imaging scans at baseline, after induction therapy, and after the completion of chemoradiation to search for biomarkers that may predict patients’ outcomes. The imaging biomarker study will be headed by Clifton David Fuller, M.D., Ph.D., an associate professor in the Department of Radiation Oncology and the medical director of the Program for Image-Guided Cancer Therapy.

"I believe we can treat these patients with limited side effects so that we don’t impair their quality of life," Dr. Phan said.
Dermoscopy for Early Detection of Melanoma, Other Skin Cancers

MD Anderson physicians train clinicians in underserved areas to use dermoscopy, which can help avoid unnecessary biopsy

By Sarah Bronson

A low-cost diagnostic technique called dermoscopy can help determine the potential malignancy of skin lesions—especially melanoma, in which early diagnosis is key to survival. However, providers with the specialized knowledge and experience to interpret dermoscopic findings are often limited to large academic dermatology programs and cannot be accessed by patients in underserved areas. To help remedy this disparity, dermatologists at The University of Texas MD Anderson Cancer Center are using telementoring to train dermatology residents in underserved communities to use dermoscopy for skin cancer screening.

“Dermoscopy can substantially improve a physician’s ability to evaluate a skin lesion and make appropriate decisions about whether to biopsy the lesion,” said Kelly Nelson, M.D., an associate professor in the Department of Dermatology. Dr. Nelson uses dermoscopy in her practice at MD Anderson and leads the telementoring program to share her expertise.

Dermoscopy

“Dermoscopy is a relatively low-tech, low-cost tool that can improve providers’ accuracy in diagnosing melanoma and nonmelanoma skin cancer,” Dr. Nelson said.

In dermoscopy, the clinician evaluates skin lesions using a brightly lit, handheld 10× magnifier called a dermatoscope. The dermatoscope reveals detailed patterns of blood vessels and pigmentation, helping the physician recognize not only signs of malignancy, such as asymmetry and disorganization in shape and color, but also features of normal skin lesions. Polarized light rather than regular visible light may be used to illuminate certain structures in the lesion, called chrysalis structures, which are associated with scarring, fibrosis, and inflammation.

Beyond increased clarity, a dermatoscope lets the physician take high-quality photographs for later reference. “The development of true mastery of skin cancer diagnosis requires the ability to take not only regular clinical photographs but also dermoscopic photographs of what you see in the course of your clinical care,” Dr. Nelson said, “so that when something unexpected is seen, you can go back and learn from it.”

Better skill in evaluating skin lesions translates into more appropriate uses of skin biopsy. In particular, dermoscopic proficiency has been shown to result in fewer biopsies of normal skin growths, thus reducing anxiety, scarring, and financial cost to the patient. For lesions that require biopsy, dermoscopy can be used to select the most appropriate biopsy site and technique.

Dr. Nelson noted that the removal of nonmalignant skin growths that are large and inflamed is still appropriate medical care. “The goal of dermoscopy isn’t to totally eliminate the removal of benign skin growths,” she said. “It’s to try to improve diagnostic accuracy overall so that fewer lesions need to be removed due to physician uncertainty.”

Telementoring in dermoscopy

To be successfully applied in the clinic, dermoscopy must be paired with education. MD Anderson’s Melanoma Moon Shot program has taken the lead in sharing expertise in the use of dermoscopy through a telementoring initiative called Project ECHO, or Extension for Community Healthcare Outcomes. Project ECHO began at the University of New Mexico in 2003.
Alcohol-Related Cancers

Drinking alcohol increases risk of several types of cancer

For many people, drinking alcohol—a glass of wine with dinner or cocktails with friends after work—is an enjoyable part of life. But drinking alcohol, especially heavy drinking, can cause health problems, including increased risk of several types of cancer.

“Alcohol is a largely unrecognized risk factor for cancer,” said Abena Brewster, M.D., a professor in the Department of Clinical Cancer Prevention at The University of Texas MD Anderson Cancer Center. “People are very aware of the relationship between smoking and cancer, but they’re not quite as aware of the relationship between alcohol and cancer.” To raise awareness about the link between alcohol and cancer, Dr. Brewster and her colleagues from the American Society of Clinical Oncology published a position paper on the topic in the January 2018 issue of the Journal of Clinical Oncology.

The position paper points out that the World Health Organization classifies alcohol as a carcinogen (cancer-causing agent). This classification was made on the basis of research showing associations between alcohol consumption and several types of cancer. For some of these cancers, even moderate alcohol consumption increases the risk.

Alcohol content and consumption

To discuss how drinking alcohol affects cancer risk, it is first necessary to define how much alcohol is in a drink. According to the Dietary Guidelines for Americans by the U.S. Department of Health and Human Services, a standard alcoholic drink contains 14 grams (g), or 0.6 ounces (oz), of alcohol. This is roughly the amount of alcohol found in 12 oz of beer, 5 oz of wine, or 1.5 oz of 80-proof (40% alcohol) liquor.

“We want people to be aware of serving sizes,” Dr. Brewster said. “Hurricanes and other alcoholic drinks that come in massive glasses are more than one serving.”

The Dietary Guidelines define moderate alcohol consumption as one or fewer drinks per day for women and two or fewer drinks per day for men. Heavy drinking is defined as four or more drinks per day, or more than seven per week, for women and five or more drinks per day, or more than 14 per week, for men.

Binge drinking, which causes half of alcohol-related deaths, is defined as four or more drinks for women and five or more for men within 2 hours. “We don’t know what effect binge drinking has on cancer risk, but we know the effect of binge drinking overall is bad,” Dr. Brewster said.

Types of cancer caused by alcohol

**Head and neck cancers.** Moderate drinkers have double the risk of a particular type of cancer, squamous cell carcinoma of the esophagus, as nondrinkers; and heavy drinkers have four times the risk. Some people have an inherited trait that makes it difficult for their bodies to process alcohol; these people have an even higher risk of esophageal squamous cell carcinoma if they drink.

Compared with nondrinkers, heavy drinkers have nearly three times the risk of cancer of the larynx (voice box) and more than five times the risk of cancers of the oral cavity (mouth) and pharynx (the part of the throat that leads from the mouth to the esophagus).

Tobacco use further increases the risk of head and neck cancers in those who drink alcohol. **Liver cancer.** Moderate drinkers have a slightly higher risk of liver cancer than do nondrinkers, and heavy drinkers have double the risk. Chronic liver diseases such as hepatitis B or C infections can make the effect of alcohol even worse.

**Colorectal cancer.** Heavy drinkers have nearly one and a half times the risk of colorectal cancer as nondrinkers.

**Breast cancer.** Women who drink alcohol moderately have a slightly higher risk of breast cancer than do nondrinkers; and heavy drinkers have more than one and a half times the risk. A large study in the United Kingdom found a 12% increase in breast cancer risk for every 10 g of alcohol consumed daily.

Benefits vs. risks

Understanding the risks of alcohol use can be difficult because moderate alcohol consumption has some health benefits. Some studies have linked alcohol to reduced risks of non-Hodgkin lymphoma and kidney cancer. And red wine consumption is known to increase levels of “good” cholesterol (high-density lipoproteins, or HDL), which promotes heart health. However, the Dietary Guidelines, the American Cancer Society, and the American Heart Association all state that nondrinkers should not start drinking alcohol for its perceived health benefits, and all these groups warn against heavy alcohol consumption.

“If you don’t drink, you shouldn’t start,” Dr. Brewster said, adding that people who already drink should limit their alcohol consumption to moderate levels. “Social drinking is increasing among young adults, and we’re very concerned that alcohol-related cancer will become an issue for them down the line.”

For more information

- Ask your physician
- Visit www.mdanderson.org
- Call MD Anderson’s Cancer Prevention Center at 713-745-8040
Dermoscopy for Early Detection
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and was adopted at MD Anderson in 2014, partnering specialists at MD Anderson with providers in underserved communities for teleconferences regarding various aspects of cancer care (see “Useful Resources: Videoconferences Allow Collaboration in Cancer Prevention, Treatment, Survivorship,” OncoLog, January 2018).

Now Project ECHO is bringing education in early melanoma detection to six dermatology residency programs across Texas—and one in Missouri—in the form of monthly educational lectures held by Dr. Nelson and colleagues. Each lesson focuses on a specific topic related to dermoscopy, and the effectiveness of the lessons is tracked by quizzing participants using a series of dermoscopic images at the beginning and end of each session.

“We go through a lot of pictures because we as dermatologists learn through pattern recognition,” said Dr. Nelson. “We’re trying to give people a lot of internal reference points for specific types of lesions.”

More to come

The Project ECHO initiative at MD Anderson is expected to partner with an increasing number of dermatology residency programs over time, Dr. Nelson said. The initiative also seeks to develop educational content that other programs can teach independently.

Also in the works over the next 2–3 years is an online dermoscopy curriculum for primary care physicians. Dr. Nelson envisions a curriculum that is efficient enough to be useful to busy physicians and effective enough to impart the ability to perform full skin evaluations.

“To impact melanoma mortality across the state of Texas and beyond,” Dr. Nelson said, “we will need to have relationships with primary care physicians to support their skill in screening their patients for melanoma.”

FOR MORE INFORMATION
Dr. Kelly Nelson........................................ 713-792-6800 kcnelson1@mdanderson.org

“Dermoscopy can substantially improve a physician’s ability to evaluate a skin lesion.”

– Dr. Kelly Nelson

For those interested in the application of communications technology in dermatology, MD Anderson will host the 7th World Congress of Teledermatology November 17–18, 2018. For more information, call 713-794-1724 or visit https://teledermatology2018.info.