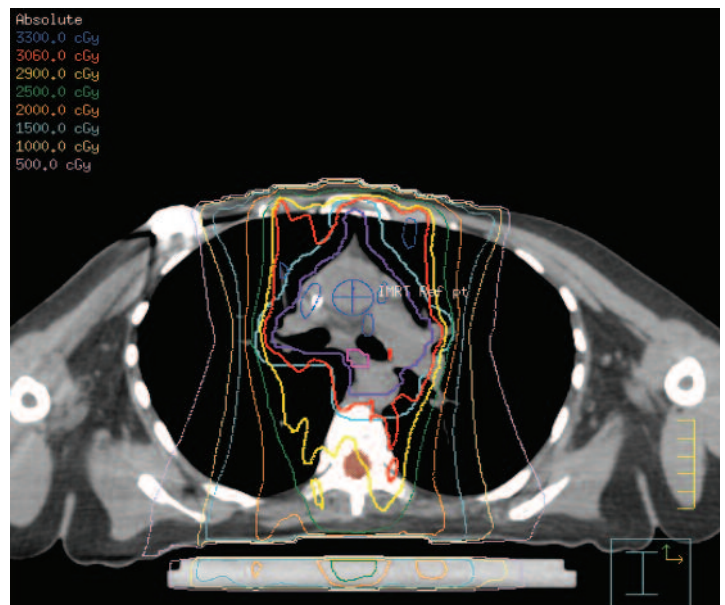


Innovations Decrease Toxic Effects of Radiation Therapy for Mediastinal Tumors from Hematological Malignancies

By Bryan Tutt

Anterior mediastinal masses caused by lymphoma or leukemia can be difficult to treat because sensitive tissues in the area are vulnerable to damage from radiation therapy. To treat these tumors while sparing healthy tissue, radiation oncologists at The University of Texas MD Anderson Cancer Center use a combination of advanced technologies and new techniques.

In addition to standard systemic treatments for their underlying hematological malignancies, patients with anterior mediastinal masses are treated with a radiation dose of 20–30 Gy delivered in daily fractions over 2–3 weeks. Patients with refractory disease may receive a dose as high as 50 Gy over 5 weeks. Historically, treatment plans for these types of tumors delivered the radiation dose using entirely anterior and posterior radiation fields, such that substantial volumes of heart, lung, and/or breast tissue were exposed to an unavoidable radiation dose. Such treatment put patients at risk for cardiotoxicity, radiation pneumonitis, and the development of



A treatment plan for intensity-modulated radiation therapy uses the “butterfly technique” (so called because the radiation fields resemble a butterfly’s wings) to maximize the radiation dose to the anterior mediastinal tumors (dark blue circles) while minimizing the dose to critical structures. Colored lines depict radiation doses ranging from 3,300 cGy (innermost; purple) to 500 cGy (outermost; pink). Image courtesy of Dr. Grace Smith.

secondary tumors in the lungs or breasts.

“Many patients with leukemia or lymphoma are very young with a long lifetime to enjoy the benefits of the most effective treatment or, conversely, to suffer long-term toxic effects associated with treatment,” said Grace Smith, M.D.,

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Radiation Therapy for Mediastinal Tumors

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Ph.D., an assistant professor in the Department of Radiation Oncology. “Other patients may be quite fragile because of the chemotherapy they’ve received. Older patients in particular often are frail at baseline, so they are especially vulnerable to toxicity.”

A symphony of radiation strategies

To avoid the adverse effects from the anterior-posterior delivery of radiation therapy to anterior mediastinal masses in patients with hematological malignancies, Dr. Smith said, “We use a combination of advanced techniques to target the mediastinal tumor with radiation while minimizing toxicity to the neighboring organs.” This combination comprises using the “butterfly technique” for planning and delivering intensity-modulated radiation therapy (IMRT), deep inspiration breath hold to reduce motion, computed tomography (CT) scans before each daily treatment to account for changes in the tumor or patient anatomy, and—for female patients—an inclined board fitted to the couch to reduce the radiation dose to the breasts.

The butterfly technique takes advantage of IMRT’s ability to shape radiation fields. Specifically, a five-beam arrangement creates anterior and posterior radiation fields roughly shaped like a butterfly’s wings. “The key to the butterfly technique is that it ‘squeezes’ the radiation dose anteriorly and posteriorly to optimally target the tumor while avoiding specific critical structures, even individual cardiac chambers and vessels,” Dr. Smith said.

Deep inspiration breath hold, a technique used for radiation therapy to various disease sites, such as the lung or breast (see “Deep Inspiration Breath Hold Protects Against Radiation-Induced Cardiotoxicity in Patients with Left-Sided Breast Cancers,” *OncoLog*, September 2014), requires the patient to take in a deep breath and hold it for about 20 seconds during treatment. In patients with anterior mediastinal tumors, deep inspiration breath hold

reduces the radiation dose to the lungs by minimizing respiration-related movement and to the heart by displacing the heart inferiorly and posteriorly.

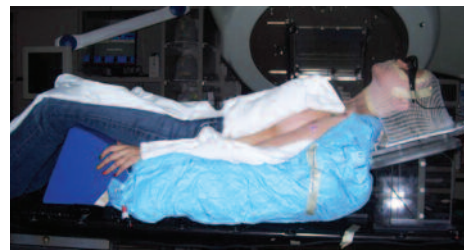
Another standard practice at MD Anderson is for patients with mediastinal tumors to undergo a low-dose CT scan before each treatment session so that the treatment plan can be adjusted to account for changes in the patient’s movement, heartbeat, anatomy, or tumor. For example, Dr. Smith said, “If the tumor is shrinking, then we can further tailor the treatment field.”

The addition of a 15° inclined board to the treatment couch for female patients helps move breast tissue out of the radiation field. “Breast tissue is vulnerable to the effects of radiation, especially in young women,” Dr. Smith said. Studies have shown that, compared with women in the general population, women treated for mediastinal lymphoma with radiation to the chest face a much higher lifetime risk of breast cancer and that this risk is highest for those who underwent radiation therapy at age 30 years or younger.

Some of the techniques used at MD Anderson to treat mediastinal masses have already been widely adopted; others, such as the butterfly technique, are relatively new. “This symphony of radiation techniques has been used for several hundred patients with mediastinal tumors caused by hematological malignancies,” Dr. Smith said. “And we have begun to publish our track record of results.” For example, she said, a study of 150 patients treated at MD Anderson for mediastinal lymphoma showed that the techniques decreased the risk of acute radiation pneumonitis.

Toward broad adoption

Dr. Smith said that she and her colleagues are working on the challenge of disseminating their strategy, which combines new techniques and advanced technologies, to other institutions. But despite the success of the strategy at MD Anderson, Dr. Smith said, several obstacles could delay its wide adoption. “Treatment planning and setup can be



A 15° inclined board displaces breast tissue out of the target field during radiation therapy for anterior mediastinal tumors. © 2014 Voong et al.; licensee BioMed Central Ltd.

very time consuming when these techniques are used,” she said. “Plus, a physician needs to verify the daily CT images to ensure the radiation, which is very conformal and focused, is delivered to the right target in the right way.”

Dr. Smith thinks community oncologists will agree that the benefits of reduced toxic effects for patients with mediastinal tumors from lymphoma or leukemia will outweigh the additional time and cost of the strategy. “Our guiding principle as we develop these techniques is to understand the unique needs of this patient population—they are often curable, but they are vulnerable.” ■

FOR MORE INFORMATION

Dr. Grace Smith.....713-563-2342

FURTHER READING

Pinnix CC, Smith GL, Milgrom S, et al. Predictors of radiation pneumonitis in patients receiving intensity modulated radiation therapy for Hodgkin and non-Hodgkin lymphoma. *Int J Radiat Oncol Biol Phys*. 2015;92:175–182.

Voong KR, McSpadden K, Pinnix CC, et al. Dosimetric advantages of a “butterfly” technique for intensity-modulated radiation therapy for young female patients with mediastinal Hodgkin’s lymphoma. *Radiat Oncol*. 2014;9:94.

Transoral Robotic Surgery Enables Less Toxic Treatment of Early Throat Cancers

By Sarah Bronson

For decades, many patients with hard-to-reach throat cancers received high-dose radiation and chemotherapy, with their often severe toxic effects, because conventional surgery was highly invasive and disfiguring. Now that minimally invasive robotic surgery can be used to resect cancers of the tongue base and tonsils without causing disfigurement, researchers at The University of Texas MD Anderson Cancer Center are learning how this treatment can help minimize the use of radiation and chemotherapy and improve patients' quality of life.

A changing patient population

The typical characteristics of patients with early-stage tongue base or tonsil cancers have changed substantially in recent decades: patients tend to be younger and more likely to survive the cancer, and their cancers are more likely to be related to human papillomavirus (HPV) rather than tobacco use.

“For younger patients with HPV-related early throat cancers, the prognosis is better out of the gate, so their treatment needs are different,” said Neil Gross, M.D., an associate professor in the Department of Head and Neck Surgery. Because more than 90% of patients with this new profile are expected to survive, head and neck specialists are focusing on developing treatments that have less severe long-term toxic effects.

Drawbacks of open surgery or radiation therapy

The standard treatments for early-stage throat cancer have led to good survival rates, but the resulting quality of life has not been ideal. For a long time, open surgery to remove these cancers—which often involves splitting

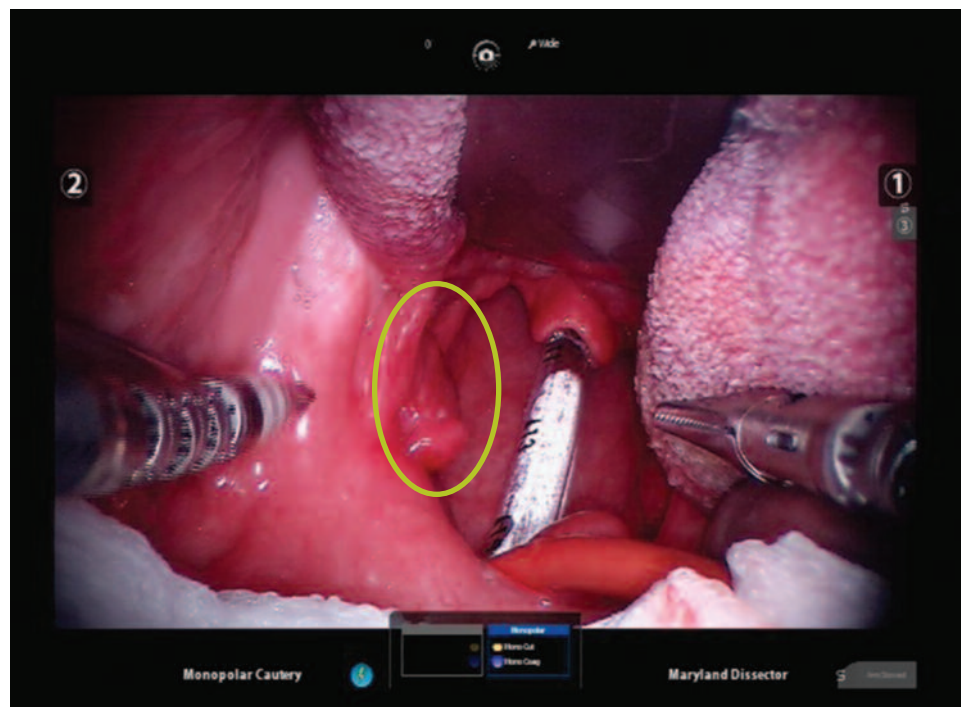
apart the jaw to gain access—has been almost entirely supplanted by intense radiation combined with cytotoxic chemotherapy. This combination avoids the invasive surgery but can lead to serious long-term toxic effects, including

breakdown of the jaw, chronic dry mouth, and dysphagia that can necessitate the placement of a temporary or permanent feeding tube in the stomach. In short, the use of radiation and chemotherapy helps preserve the structures involved but may compromise important speech and swallowing functions and thus diminish quality of life.

“I call this area the ‘kitchen’ of the body because the mouth is where so much happens. It’s involved in social interaction; it’s where you talk, breathe, and eat; it’s where people see you,” Dr. Gross said. “Patients who go through head and neck cancer treatment can have high rates of depression and even suicide because it’s an area that really affects people’s everyday lives.”

Less toxic treatment through surgical technology

The key to minimizing the use of radiation and chemotherapy—and avoiding their toxic effects—in patients with early-stage throat cancers is to increase the use of surgery, but in a minimally



A surgeon prepares to remove a left tonsil tumor (circle) using a minimally invasive transoral robotic technique. Image courtesy of Dr. Neil Gross.

Transoral Robotic Surgery

[Continued from page 3]

invasive form. Today, the da Vinci surgical system for transoral robotic surgery (TORS) allows cancers to be accessed through the mouth rather than through an open approach.

In TORS, head and neck surgeons remotely manipulate flexible robotic arms to control surgical instruments farther back in the throat than is possible with their hands alone. Because surgeons can maneuver the instruments around anatomic structures in the throat, TORS offers an advantage over transoral laser microsurgery, which can be used to perform line-of-sight resections only. In this way, surgeons are able to resect many early-stage tongue base and tonsil tumors with tumor-free margins. For these patients, radiation and/or chemotherapy can be omitted or given at lower, less toxic doses.

"The idea is to remove cancers and either avoid radiation or chemotherapy completely or give a lower dose of radiation or radiation and chemotherapy after surgery in patients who need adjuvant therapy," Dr. Gross said. He also pointed out that TORS is most effective when performed at high-volume centers by surgeons experienced in the procedure.

Transoral robotic surgery trials

At MD Anderson, clinical trials to evaluate how TORS can be best used to treat tongue base or tonsil cancer



"The technology is catching up with the needs of the kinds of patients we're seeing today."

– Dr. Neil Gross

and the extent to which the surgery can improve quality of life are under way or on the horizon. In one such ongoing trial, Dr. Gross, Brandon Gunn, M.D., an associate professor in the Department of Radiation Oncology, and their colleagues are investigating ways to track patients' recovery from either TORS or proton radiation therapy for early-stage, HPV-positive tongue base or tonsil cancer. Because most of these patients can expect a cure, many are particularly concerned about not only survival but also their quality of life and how quickly they can return to normal activities. Thus, the trial will not only assess patient-reported symptoms, such as swallowing ability and fatigue, but also employ wearable activity monitors to gather data on patients' physical activity, including distances walked, altitude changes, and sleep habits. The trial will help determine whether activity levels measured in this way correlate with the symptoms that patients describe and thus whether data collection with activity monitors can be used in bigger clinical trials that compare quality of life following different treatments.

"Many of these patients are really dragging after treatment, and it takes a long time to recover. Some patients may not get all the way back to normal activity levels," Dr. Gross said. "And again, these patients tend to be younger, so they tend to be used to busy, active lives. If suddenly they can't be active, that's a big change."

In another trial expected to open at MD Anderson by the middle of this year, patients with tongue base or tonsil

cancer will receive an immune checkpoint inhibitor before undergoing TORS. The patients' initial tumor biopsy specimens, taken before the immunotherapy drug is given, will be compared with their resected tumors to assess the immunotherapy's biological effects. Moreover, investigators hope to learn whether giving the immunotherapy drug before TORS reduces the need for adjuvant radiation or chemotherapy. Patients with HPV-positive disease and those with HPV-negative disease will be included.

These and other trials will help guide the use of TORS in the multidisciplinary treatment of patients with tongue base and tonsil cancers. As the technology continues to improve and as the instruments become smaller and more agile, TORS may someday be used to resect cancers at even harder-to-reach sites in the throat, including the larynx, trachea, and upper esophagus.

"The technology is catching up with the needs of the kinds of patients we're seeing today," Dr. Gross said. "Ultimately, it's not about the instrument; it's about the patient." ■

"The idea is to remove cancers and either avoid radiation or chemotherapy completely or give a lower dose of radiation or radiation and chemotherapy after surgery in patients who need adjuvant therapy."

– Dr. Neil Gross

FOR MORE INFORMATION

Dr. Neil Gross.....713-745-8483

To learn more about ongoing clinical trials of treatments for tongue base or tonsil cancers at MD Anderson, visit www.clinicaltrials.org.

Implantable Devices Monitor for Cardiac Events in Cancer Survivors and Patients on Chemotherapy

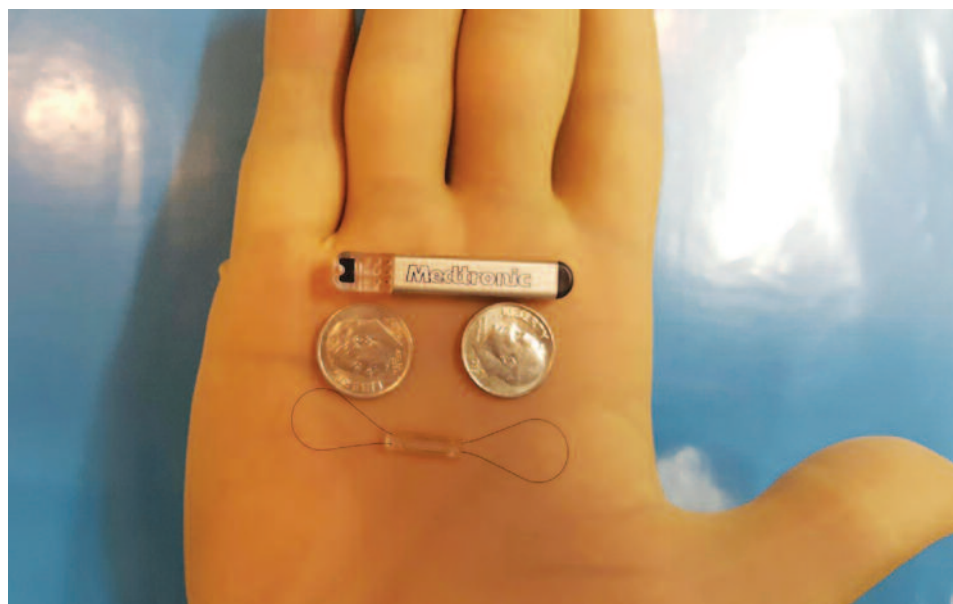
By Jill Delsigne

Cancer survivors are more likely to die from heart disease than cancer, and therefore patients must be closely monitored for heart problems during and after cancer treatment. Such surveillance can be done continuously with new implantable cardiac monitoring devices.

The need for cardiac monitoring is evidenced by estimates of heart failure in cancer patients during chemotherapy; such estimates range from 3% to 50% depending on the drugs used. And the risk of heart disease remains long after the treatment is finished. “When caring for cancer survivors, it’s important to recognize their vulnerability to atrial fibrillation and heart failure caused by previous chemotherapy and to be vigilant for these heart problems,” said Jean-Bernard Durand, M.D., an associate professor in the Department of Cardiology at The University of Texas MD Anderson Cancer Center.

Treatment-related heart problems

Chemotherapy and radiation therapy can increase the risk of cardiovascular problems such as severe hypertension, cardiomyopathy, ischemia, atrial fibrillation, and congestive heart failure. Chronic cardiotoxicity can occur



Two implantable cardiac devices—Reveal LINQ (top), which detects abnormal heart rhythms, and CardioMEMS, which monitors heart rate and arterial pressure—enable physicians to monitor patients remotely in real time. Image courtesy of Dr. Jean-Bernard Durand.

within weeks of treatment or up to 20 years after treatment.

The cardiac side effects of systemic drugs vary. Cytotoxic chemotherapeutic drugs such as doxorubicin (and other anthracyclines) cumulatively weaken the heart muscle. Biologic therapies such as trastuzumab also can weaken the heart muscle during treatment, but trastuzumab-related cardiomyopathy is often reversible with medical therapy. Taxanes and other chemotherapeutic drugs cause abnormal heart rhythms during treatment in some patients. And angiogenesis inhibitors can cause blood pressure spikes and increase the risk of blood clots and heart failure.

Radiation therapy can trigger long-term cardiac effects if the heart is incidentally exposed to radiation. These long-term effects include coronary artery disease, damage to the heart valves, damage to the heart’s electrical system, heart muscle stiffening, and inflammation.

“These devices can help patients continue chemotherapy and can help cancer survivors avoid trips to the emergency room.”

– Dr. Jean-Bernard Durand

Implanted monitors

Implantable cardiac monitors such as the CardioMEMS system and the Reveal LINQ system can provide diagnostic information that can help physicians monitor patients constantly and remotely to detect cardiac events before they become serious.

The Reveal LINQ system, used to detect abnormal heart rhythms and to monitor unexplained fainting, is implanted just under the skin in the chest

Implantable Devices Monitor for Cardiac Events

[Continued from page 5]

in an outpatient procedure that takes less than 5 minutes. Patients also receive a bedside machine that collects the heart data and sends the data to a central database and directly to the smartphone of the implanting physician. If patients notice a cardiac event symptom, they can press a button on the bedside machine to send a report to the database instantly. Physicians can program the device by setting parameters for how often data are downloaded and what ranges of abnormal heart rhythms warrant notification of the physician and patient by database monitors.

Dr. Durand uses the Reveal LINQ system to monitor patients around the world. When a patient in Dubai experienced palpitations, Dr. Durand was able to call him to discuss his symptoms. The patient took a beta blocker and thus avoided a trip to the emergency department. “Patients are monitored and cared for 24/7; even halfway around the world, my patients can feel comfortable knowing that their hearts are constantly being monitored and that I’m always there for them, at any time,” Dr. Durand said.

This system also allows physicians to help patients associate what they feel with the data that document cardiac events. Dr. Durand said, “Patients are often surprised to receive a call from the database service when their heart rates are abnormal. Implantable cardiac monitors help patients understand that they don’t necessarily perceive heart rate spikes.”

The Reveal LINQ device can collect data for up to 3 years, but Dr. Durand said that most patients’ heart conditions can be diagnosed with 60 days of monitoring after cancer treatment. However, Dr. Durand said, “Most patients like keeping the device until the battery runs out because it’s like a safety net.”

Unlike the Reveal LINQ device, the CardioMEMS system does not use batteries and can monitor arterial pressure and heart rate throughout a patient’s lifetime. The CardioMEMS device, about the size of a paperclip, is permanently implanted in the pul-

“[M]y patients can feel comfortable knowing that their hearts are constantly being monitored and that I’m always there for them, at any time.

– Dr. Jean-Bernard Durand

monary artery during a right heart catheterization procedure. The device monitors pressure in the pulmonary artery and transmits data wirelessly to an external electronic system, and then the data are transmitted directly to the physician. “I can monitor patients on my cell phone,” Dr. Durand said. “Once I noticed a 10% increase in arterial pressure in a patient. I called him and advised him to take a water pill; we caught the problem quickly enough to avoid a trip to the emergency room.”

MD Anderson is the only cancer center in the world with a fully integrated cardiac device program for cancer patients. In addition to **Dr. Durand**, the team consists of **Kaveh Karimzad**, M.D., an associate professor in the Department of Cardiology, who is one of the only oncoelectrophysiologists in the world; **Marc Rozner**, M.D., Ph.D., a professor in the Departments of Anesthesiology and Perioperative Medicine and Cardiology, who studies the use of imaging modalities and radiation therapy for cancer patients with implanted cardiac monitors; and **Darla Labasse**, R.N., a cardiac device specialist in the Cardiopulmonary Center.

Implanted cardiac monitoring devices have several advantages over traditional external monitoring devices. Implanted devices continuously record data for years, whereas external devices are used for short-term data collection (1–30 days). With implanted devices, patients are not encumbered by recording pads or wires. Finally, implanted devices allow physicians to analyze data from before, during, and after cardiac events and to track patterns over time.

Ongoing research

Dr. Durand and his team currently are conducting two studies involving implantable cardiac monitoring devices in cancer patients. In a retrospective study, Dr. Durand and his colleagues are investigating how many patients who qualify for implantable cardiac monitoring devices have been approached by physicians about this possibility.

In a clinical trial that will soon begin enrolling patients, Dr. Durand and his colleagues will investigate whether Reveal LINQ devices can help cancer patients with atrial fibrillation continue chemotherapy; if the devices detect an early potential heart problem and the problem is addressed, patients may be able to continue life-saving treatments instead of temporarily halting chemotherapy, which is the current standard practice.

Dr. Durand said that cancer patients and survivors with unexplained episodes of passing out, palpitations, or frequent visits to the hospital with symptoms of heart failure may qualify for implantable cardiac monitoring devices as part of the diagnosis and treatment of their heart conditions. Dr. Durand said, “These devices can help patients continue chemotherapy and can help cancer survivors avoid trips to the emergency room, which is important because hospital visits make patients more vulnerable to developing blood clots, pneumonia, or drug-resistant bacterial infections.” ■

FOR MORE INFORMATION

Dr. Jean-Bernard Durand713-792-6239



Colorectal Cancer Screening

Regular screening is key for fighting and preventing colon and rectal cancers

Colorectal cancer is the second most common cause of cancer-related death in the United States.

But the U.S. National Cancer Institute estimates that up to 90% of deaths from cancers of the colon and rectum could be prevented by routine screening.

For people at average risk, The University of Texas MD Anderson Cancer Center recommends that screening for colorectal cancer start at age 50 years.

Types of screening

Most colorectal screening tests examine the colon and rectum for tissue growths called polyps. Polyps usually are not harmful, but some can gradually develop into cancer. Screening can identify potentially dangerous polyps before cancer develops or spreads.

Colorectal cancer screening commonly involves one of the following tests.

Colonoscopy. This thorough examination uses a flexible instrument tipped with a lighted video camera to inspect the rectum and entire colon for abnormalities. During the exam, doctors can use the instrument to remove polyps or take tissue samples for examination. Most people receive sedation before this exam, as the procedure causes some discomfort. For people age 50 years or older at average risk of colorectal cancer, colonoscopies should be performed every 10 years.

Virtual colonoscopy. MD Anderson offers this less-invasive alternative to a traditional colonoscopy. Using computed tomography, doctors produce pictures of the colon and rectum. No sedation is needed. If the images reveal any polyps or other abnormalities, a traditional colonoscopy will be needed to remove them. Generally, a virtual colonoscopy should be done every 5 years. Check with your insurance provider about whether this new test is covered under your medical plan.

Sigmoidoscopy. This test is similar to a colonoscopy and allows doctors to see and remove suspicious polyps, but a sigmoidoscopy examines only the rectum and lower part of the colon (the descending colon and the sigmoid colon). A sigmoidoscopy is less invasive than a colonoscopy but cannot see polyps on the other side of the colon. A sigmoidoscopy should be repeated every 5 years.

Double-contrast barium enema.

This test views the lining of the rectum and colon for abnormalities. In this procedure, the colon is filled with radiographic contrast material by an enema, air is added to expand the colon, and then a series of x-ray scans are performed. As in a virtual colonoscopy, if any polyps are found, a colonoscopy will be needed to remove them. This screening should generally be repeated every 5 years.

Stool tests. Three take-home stool tests for colorectal cancer screening have been approved by the U.S. Food and Drug Administration. Two of these, the fecal immunohistochemical test (FIT) and the fecal occult blood test (FOBT), test for substances that suggest blood in the stool sample. The other, the DNA stool test, detects altered DNA in stool. Blood or altered DNA may be a sign of colorectal cancer, but a full colonoscopy will be needed to confirm the presence of cancer. Because stool tests may not be able to identify precancerous abnormalities that could be removed to prevent colon cancer, MD Anderson prefers colonoscopy or virtual colonoscopy. If a stool test is used, the FIT or FOBT should be repeated every year or the DNA test every 3 years.

For colonoscopy, virtual colonoscopy, sigmoidoscopy, and double-contrast barium enema, people usually must prepare the day before the test by consuming only clear liquids and

by using laxatives or enemas.

Your doctor can help you compare benefits of each screening test with the risks involved and develop a strategy that is right for you. In addition to regular screening, MD Anderson recommends that you pay attention to signs that something might be wrong, like bleeding or a change in your bowel movements, and report these signs to your doctor immediately.

What is your risk?

You and your doctor can discuss your personal and family history to customize your screening routine. If you are at average risk of colorectal cancer, MD Anderson recommends you begin regular screening at age 50 years and continue through age 75 years.

People with an increased risk of colorectal cancer are advised to begin screening at a younger age and/or repeat tests more frequently, depending on the reason for the increased risk. You may have an increased risk of colorectal cancer if you have an inflammatory bowel disease such as chronic ulcerative colitis or Crohn disease or if you or a family member had or have colorectal cancer, precancerous colon polyps (adenomas), or a hereditary cancer syndrome such as familial adenomatous polyposis or hereditary nonpolyposis colorectal cancer (Lynch syndrome).

Regular screening and staying aware of your body can help detect colorectal cancer early, when it may be more easily treated, or remove polyps before they can turn into cancer. ■

—K. Werner

FOR MORE INFORMATION

- Ask your physician
- Call askMDAnderson at 877-632-6789
- Read MD Anderson's colorectal cancer screening guidelines at <http://bit.ly/1nMOpV1>

USEFUL RESOURCES

Clinical Trials Information

Clinical trials often provide cutting-edge treatment for patients with advanced cancer after standard treatment options have failed. With information about which clinical trials are currently enrolling patients, physicians can guide such patients to new possibilities for treatment.

With one of the world's largest clinical trials programs, The University of Texas MD Anderson Cancer Center has about 1,000 clinical trials open at any given time. Some of these are trials of experimental agents or new techniques of radiation or surgery, while others test new combinations of existing treatments or test an agent approved for one type of cancer in a different type. In addition to trials of new cancer treatments, MD Anderson offers trials of new technologies or techniques for cancer prevention, diagnosis, and survivorship.

Physicians and patients can search MD Anderson's online database of clinical trials by cancer type, treatment type, principal investigator, or National Institutes of Health identification number (NCT No.). The Web site has drop-down menus to facilitate searches and a search



tool that allows users to find trials using specific terms (e.g., HER2-negative metastatic inflammatory breast cancer).

For patients, the clinical trials Web site offers links to pages that give general information about clinical trials and explain the differences between phase I, II, III, and IV trials. This information can help patients make informed decisions about whether to participate in a trial.

For physicians, the Web site tells how to contact MD Anderson research staff for specific information about particular trials.

The clinical trials database and links to patient information are available at www.clinicaltrials.org. The physician information is available at www.mdanderson.org/for-physicians/clinical-trials.html. ■

"Useful Resources" introduces tools for community physicians and other medical professionals available free of charge on MD Anderson's Web site.

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