A Publication of
M. D. Anderson Cancer Center
Making Cancer History®

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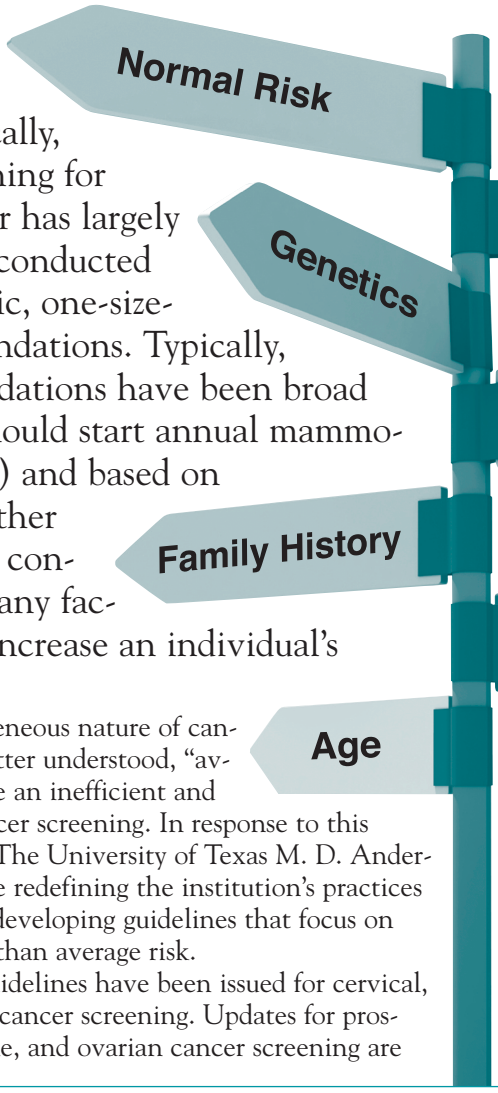
REPORT TO PHYSICIANS
FEBRUARY 2010 VOL. 55, NO. 2

OncoLog

Risk-Based Cancer Screening

M. D. Anderson's revised guidelines offer more precise, individualized recommendations on screening for common cancers.

By John LeBas



Historically, screening for cancer has largely been conducted according to basic, one-size-fits-all recommendations. Typically, these recommendations have been broad (e.g., "women should start annual mammograms at age 40") and based on "average risk" rather than taking into consideration the many factors that might increase an individual's risk of cancer.

But as the heterogeneous nature of cancer has come to be better understood, "average risk" has become an inefficient and outdated basis for cancer screening. In response to this change, specialists at The University of Texas M. D. Anderson Cancer Center are redefining the institution's practices for cancer screening, developing guidelines that focus on individual risk rather than average risk.

Already, revised guidelines have been issued for cervical, breast, and colorectal cancer screening. Updates for prostate, liver, skin, uterine, and ovarian cancer screening are scheduled to roll out later this year. The guidelines are available in streamlined versions designed for the public and more detailed formats geared toward physicians.

The revised guidelines take into account the fact that not all people have a similar risk of developing a particular cancer—even groups of people who, for example, have a similar age or family history of cancer. "We can now define risk of cancer much more precisely, so that individuals and their physicians can make better decisions about when to start screening, when to stop screening, and what cancers to screen for," said Therese Bevers, M.D., professor in the Department of Clinical Cancer Prevention and medical director of the Cancer Prevention Center at M. D. Anderson.

Importantly, the guidelines also address the problem of overscreening (the unnecessary or excessive testing of patients at a low risk of cancer). "Cancer screening itself burdens the patient with risks," Dr. Bevers said. "We always want to be sure the benefits of screening outweigh the risks, and our

(Continued on **page 2***)*

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Risk-Based Cancer Screening

(Continued from **page 1***)*

revised guidelines should help us do a better job of that."

Individualized approach

Cancer screening specifically refers to testing for cancer before there are any clinical signs of disease. It falls second on M. D. Anderson's five-part cancer continuum: Risk assessment/reduction → Screening → Diagnosis →Treatment → Survivorship.

The more tailored approach to early cancer detection being adopted by M. D. Anderson is not revolutionary, Dr. Bevers explained—in fact, it is one that the institution's physicians have employed in the clinic for many years. But the guidelines are novel in that the approach is now in writing and being communicated to the public. "We don't know that the public fully understands how to assess their risk of certain cancers or which screening tests are best for them," Dr. Bevers said. "Our new guidelines address the need for more specific recommendations."

"We always want to be sure the benefits of screening outweigh the risks, and our revised guidelines should help."

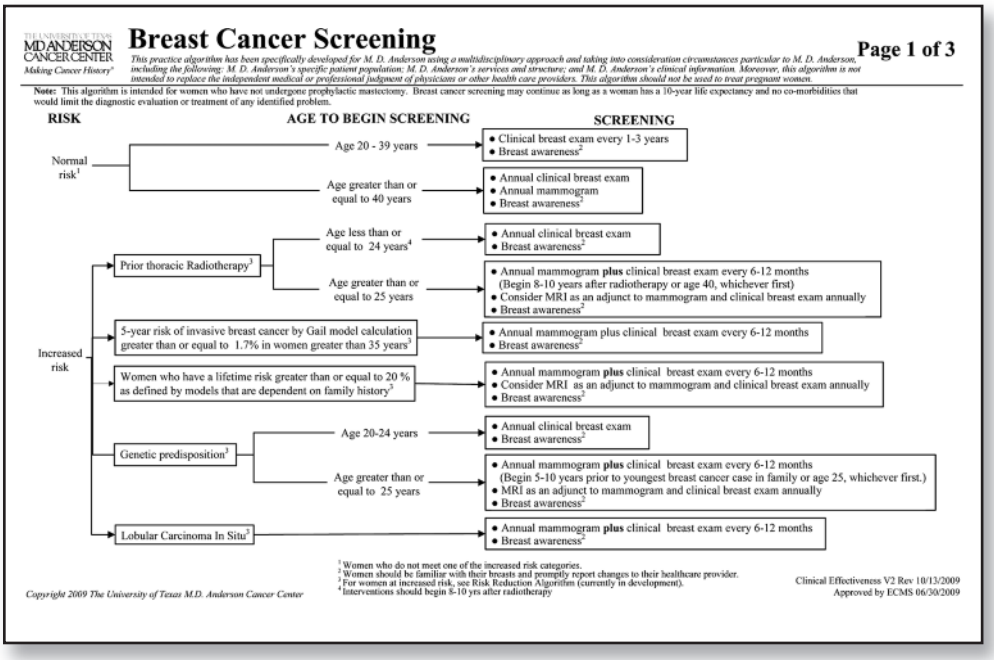
– Dr. Therese Bevers

Consider, for example, M. D. Anderson's new guidelines for cervical cancer screening, which amend the conventional wisdom that women who have ever had sex should undergo annual Pap tests to detect cancer or precancerous lesions of the cervix. The new recommendation is that women at average risk under age 21 years have a liquid-based Pap test within 3 years of first vaginal intercourse, followed by annual Pap tests until three consecutive negative tests are obtained. Then, according to the guidelines, Pap tests should be done every 2 years unless the woman develops an increased risk of cervical cancer (see box for details). Furthermore, beginning at age 30, a woman who has a negative test for high-risk human papillomavirus (HPV) types in addition to a negative Pap test could transition to testing every 3 years unless her risk increases.

"These changes result from the recognition that not all women are at the same risk of cervical cancer," said Helen E. Rhodes, M.D., an associate professor in the Department of Gynecologic Oncology. "Women with high-risk HPV types and other risk factors identified in the guidelines are most at risk of developing cervical malignancy, and they benefit the most from screening tests that can catch cancer at its earliest stages. Conversely, women who don't have these risk factors are likely undergoing unnecessary testing which can, in fact, be detrimental owing to the potential overtreatment of preinvasive cervical disease."

It may seem counterintuitive that screening regularly for a disease so insidious and devastating as cancer can actually have harmful effects for some patients. "The overriding belief is that there are no risks in screening," Dr. Bevers said. "But there are risks: the risk

Selected flow charts showing revised screening guidelines for physicians illustrate how the approach to testing has become increasingly individualized. Full-size charts for physicians and patients are available online at www.mdanderson.org (see page 4).



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Breast Cancer Screening — Page 1 of 3

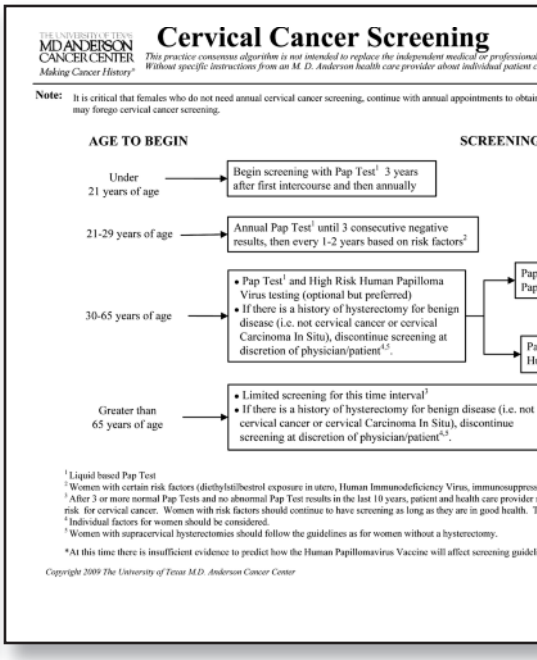
This practice algorithm has been specifically developed for M. D. Anderson using a multidisciplinary approach and taking into consideration circumstances particular to M. D. Anderson, including the following: M. D. Anderson's specific patient population; M. D. Anderson's services and structure; and M. D. Anderson's clinical information. Moreover, this algorithm is not intended to replace the independent medical or professional judgment of physicians or other health care providers. This algorithm should not be used to treat pregnant women.

Note: This algorithm is intended for women who have not undergone prophylactic mastectomy. Breast cancer screening may continue as long as a woman has a 10-year life expectancy and no co-morbidities that would limit the diagnostic evaluation or treatment of any identified problem.

RISK	AGE TO BEGIN SCREENING	SCREENING
Normal risk[1]	Age 20 - 39 years	• Clinical breast exam every 1-3 years • Breast awareness[2]
	Age greater than or equal to 40 years	• Annual clinical breast exam • Annual mammogram • Breast awareness[2]
Increased risk	Prior thoracic Radiotherapy[3] — Age less than or equal to 24 years[4]	• Annual clinical breast exam • Breast awareness[2]
	Prior thoracic Radiotherapy[3] — Age greater than or equal to 25 years	• Annual mammogram **plus** clinical breast exam every 6-12 months (Begin 8-10 years after radiotherapy or age 40, whichever first) • Consider MRI as an adjunct to mammogram and clinical breast exam annually • Breast awareness[2]
	5-year risk of invasive breast cancer by Gail model calculation greater than or equal to 1.7% in women greater than 35 years[3]	• Annual mammogram plus clinical breast exam every 6-12 months • Breast awareness[2]
	Women who have a lifetime risk greater than or equal to 20 % as defined by models that are dependent on family history[3]	• Annual mammogram **plus** clinical breast exam every 6-12 months • Consider MRI as an adjunct to mammogram and clinical breast exam annually • Breast awareness[2]
	Genetic predisposition[3] — Age 20-24 years	• Annual clinical breast exam • Breast awareness[2]
	Genetic predisposition[3] — Age greater than or equal to 25 years	• Annual mammogram **plus** clinical breast exam every 6-12 months (Begin 5-10 years prior to youngest breast cancer case in family or age 25, whichever first.) • MRI as an adjunct to mammogram and clinical breast exam annually • Breast awareness[2]
	Lobular Carcinoma In Situ[3]	• Annual mammogram **plus** clinical breast exam every 6-12 months • Breast awareness[2]

[1] Women who do not meet one of the increased risk categories.
[2] Women should be familiar with their breasts and promptly report changes to their healthcare provider.
[3] For women at increased risk, see Risk Reduction Algorithm (currently in development).
[4] Interventions should begin 8-10 yrs after radiotherapy

Clinical Effectiveness V2 Rev 10/13/2009
Approved by ECMS 06/30/2009



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Cervical Cancer Screening

This practice consensus algorithm is not intended to replace the independent medical or professional Without specific instructions from an M. D. Anderson health care provider about individual patient

Note: It is critical that females who do not need annual cervical cancer screening, continue with annual appointments to obtain may forego cervical cancer screening.

AGE TO BEGIN	SCREENING
Under 21 years of age	Begin screening with Pap Test[1] 3 years after first intercourse and then annually
21-29 years of age	Annual Pap Test[1] until 3 consecutive negative results, then every 1-2 years based on risk factors[2]
30-65 years of age	• Pap Test[1] and High Risk Human Papilloma Virus testing (optional but preferred) • If there is a history of hysterectomy for benign disease (i.e. not cervical cancer or cervical Carcinoma In Situ), discontinue screening at discretion of physician/patient[4,5].
Greater than 65 years of age	• Limited screening for this time interval[3] • If there is a history of hysterectomy for benign disease (i.e. not cervical cancer or cervical Carcinoma In Situ), discontinue screening at discretion of physician/patient[4,5].

[1] Liquid based Pap Test
[2] Women with certain risk factors (diethylstilbestrol exposure in utero, Human Immunodeficiency Virus, immunosuppress
[3] After 3 or more normal Pap Tests and no abnormal Pap Test results in the last 10 years, patient and health care provider risk for cervical cancer. Women with risk factors should continue to have screening as long as they are in good health.
[4] Individual factors for women should be considered.
[5] Women with supracervical hysterectomies should follow the guidelines as for women without a hysterectomy.

*At this time there is insufficient evidence to predict how the Human Papillomavirus Vaccine will affect screening guidel

> **"Women with high-risk HPV types and other risk factors identified in the guidelines benefit the most from screening tests."**
>
> **– Dr. Helen E. Rhodes**

of mental and emotional anguish from false-positive test results, more invasive and unnecessary testing following false-positives, and the risk that the patient becomes desensitized to the need for future screening.

"Our historical approach to screening has had good and bad effects," she continued. "We've gotten people to understand the benefits of screening, which has saved thousands of lives by catching early cancers at treatable stages. But now people tend to think that any screening is good." In an example of this, some women receive annual ultrasonography screening for breast tumors in addition to annual mammograms—apparently believing that this two-pronged screening approach is more effective at detecting cancer.

"But there is no definitive benefit from this approach—it is excessive screening," Dr. Bevers explained. "In fact, if a woman is at high risk of breast cancer, then magnetic resonance imaging (MRI) is probably better than ultrasonography, and better still would be to alternate MRI and regular mammography."

It remains important (and is recommended) for women and men to receive annual checkups from their physician, even if those checkups don't include cancer screening.

Recognizing risk

The issue of how and when people should undergo screening for cancer has at times been controversial, as illustrated last year when the U.S. Preventive Services Task Force recommended that across-the-board mammography be conducted every 2 years for women age 50 years and older, rather than the widespread practice of annual mammography starting at age 40 years. M. D. Anderson disagrees with the recommendation, citing evidence that the benefits of annual mammography beginning at age 40 years outweigh the harms but that mammography should begin earlier for some women with an increased risk of breast cancer.

Obviously, a key component of the revised guidelines is the ability to recognize a patient as being at greater-than-average risk of developing malignancy. This recognition takes into account a patient's personal medical history, family history of cancer, and genetic predisposition as established by blood tests for cancer predisposition genes.

The colorectal screening guidelines, for example, have been changed to reflect the implications of family history and polyps discovered on prior colonoscopy. The guidelines essentially ask the following questions: Does the patient have a family history of colorectal cancer? How many polyps were discovered during the patient's last colonoscopy? What type of polyps were they?

The answers to those questions lead to different paths for when to conduct screening for colorectal cancer. For example, a prior history of adenomatous polyps confers an increased risk of ma-

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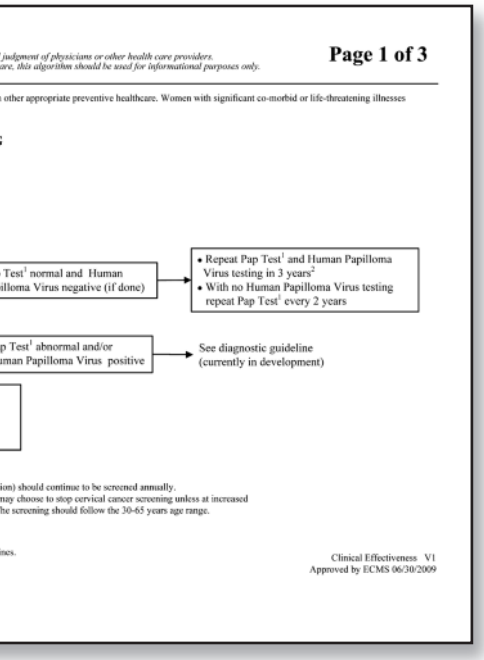

judgment of physicians or other health care providers.
are, this algorithm should be used for informational purposes only.

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other appropriate preventive healthcare. Women with significant co-morbid or life-threatening illnesses

Test[1] normal and Human
illoma Virus negative (if done)

- Repeat Pap Test[1] and Human Papilloma Virus testing in 3 years[2]
- With no Human Papilloma Virus testing repeat Pap Test[1] every 2 years

p Test[1] abnormal and/or
uman Papilloma Virus positive

See diagnostic guideline
(currently in development)

ion) should continue to be screened annually.
ay choose to stop cervical cancer screening unless at increased
he screening should follow the 30-65 years age range.

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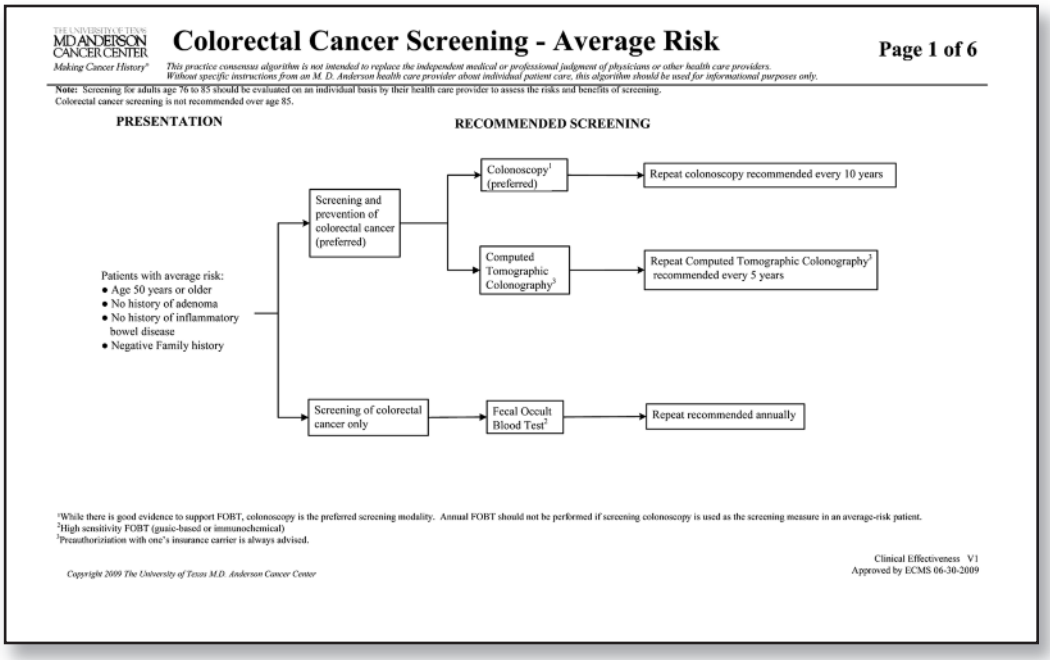
Clinical Effectiveness V1
Approved by ECMS 06/30/2009



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Colorectal Cancer Screening - Average Risk

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This practice consensus algorithm is not intended to replace the independent medical or professional judgment of physicians or other health care providers. Without specific instructions from an M. D. Anderson health care provider about individual patient care, this algorithm should be used for informational purposes only.

Note: Screening for adults age 76 to 85 should be evaluated on an individual basis by their health care provider to assess the risks and benefits of screening.
Colorectal cancer screening is not recommended over age 85.

PRESENTATION

RECOMMENDED SCREENING

Patients with average risk:
- Age 50 years or older
- No history of adenoma
- No history of inflammatory bowel disease
- Negative Family history

Screening and prevention of colorectal cancer (preferred)
- Colonoscopy[1] (preferred) → Repeat colonoscopy recommended every 10 years
- Computed Tomographic Colonography[3] → Repeat Computed Tomographic Colonography[3] recommended every 5 years

Screening of colorectal cancer only
- Fecal Occult Blood Test[2] → Repeat recommended annually

[1]While there is good evidence to support FOBT, colonoscopy is the preferred screening modality. Annual FOBT should not be performed if screening colonoscopy is used as the screening measure in an average-risk patient.
[2]High sensitivity FOBT (guaic-based or immunochemical)
[3]Preauthorization with one's insurance carrier is always advised.

Clinical Effectiveness V1
Approved by ECMS 06-30-2009

(Continued from **page 3***)*

lignancy, and thus the recommended screening interval for patients with adenomatous polyps is shortened according to the characteristics and number of polyps found. "Older screening guidelines for colorectal cancer were much less specific, suggesting more frequent colonoscopy for patients in whom adenomatous polyps were found but not customizing recommendations according to the polyps' characteristics or number," Dr. Bevers said.

Likewise, M. D. Anderson's revised screening guidelines also recommend ages at which to stop screening, something believed be to unique among cancer screening protocols. "Is it appropriate for an 80-year-old to get a mammogram?" Dr. Bevers asked hypothetically. "Perhaps. But if that person has medical problems that would preclude the diagnostic evaluation or treatment of any problem, it may not be appropriate to pursue mammographic screening.

"This is not necessarily an age-related issue. There are individuals who, because of comorbidities, are not appropriate candidates for screening. For example, a 55-year-old woman who has end-stage heart disease should probably not get a mammogram. In every situation, there should be a discussion between the patient and his or her physician that focuses on the patient's individual characteristics."

Future efforts

As part of the screening guideline overhaul, the institution also plans to develop supporting documents that further explain how patient-specific factors affect risk of cancer. "Ongoing laboratory and clinical research is continually increasing our understanding of how cancer develops and spreads," said Ernest Hawk, M.D., M. D. Anderson's vice president for cancer prevention and population sciences. "By making our knowledge about cancer available to patients in easy-to-understand screening guidelines, we can help patients better understand their own cancer risk and make educated decisions about screening." ●

For more information, visit www.mdanderson.org/prevention.

Screening Guidelines In Brief

BREAST CANCER

Starting at age 20 years, women at all risk levels should become familiar with how their breasts look and feel and immediately report any changes to their doctor. Women age 40 years and older at average risk should get annual mammograms and breast exams by a physician. For women at increased risk, the type and frequency of screening depend on factors that confer an increased risk, including:

- History of radiation treatment to the chest
- Family history of breast cancer
- Genetic predisposition to breast cancer
- Diagnosis of lobular carcinoma in situ
- Gail Model score of greater than 1.7%

CERVICAL CANCER

It is recommended that women at average risk of cervical cancer under age 21 years get a liquid-based Pap test within 3 years of initiating vaginal intercourse. These women should continue to have Pap tests annually until three consecutive negative test results are obtained. After that, M. D. Anderson recommends screening every 2 years unless a woman develops an increased risk of cervical cancer based on risk factors including:

- History of cervical cancer or severe cervical dysplasia
- Persistently testing positive for high-risk human papillomavirus (HPV) types
- Exposure to diethylstilbestrol (DES) before birth
- Human immunodeficiency virus (HIV) infection
- An immune system that does not function properly

Beginning at age 30 years, it is recommended that women undergo testing for high-risk HPV types in addition to the Pap test. If both tests are negative, a woman may go to screening every 3 years unless she develops an increased risk based on the risk factors listed above or unless the optional HPV test was not done.

COLORECTAL CANCER

M. D. Anderson recommends a colonoscopy every 10 years (preferred), a virtual colonoscopy every 5 years, or a yearly fecal occult blood test for men and women age 50 years and older who are at average risk. For men and women at higher risk, the type and frequency of exams depend on the following factors:

- Personal history of precancerous (adenomatous) polyps
- Personal history of colorectal cancer
- Family history of colorectal cancer or precancerous (adenomatous) polyps
- Genetic diagnosis of familial adenomatous polyposis
- Genetic history of hereditary nonpolyposis colorectal cancer or a clinical history suggesting such
- Inflammatory bowel disease (ulcerative colitis or Crohn's disease) ●

Source: M. D. Anderson news release

M. D. Anderson's new cancer screening guidelines are available in two formats, one designed for the general public and one designed for physicians. The general public versions can be accessed at www.mdanderson.org (navigate to the "Cancer Screening Guidelines" hyperlink on the homepage), while more detailed guidelines intended for physicians can be accessed through myMDAnderson (visit http://myMDAnderson.org to log in or create an account).

Electromagnetic Navigation Biopsy for Peripheral Lung Lesion Diagnosis

By Joe Munch

Cancer in the periphery of the lung can be difficult to diagnose. The standard methods of diagnosing peripheral lung lesions, notably image-guided transthoracic or bronchoscopic biopsy, can put patients who are weak or suffer compromised breathing at a high risk of lung collapse. Bronchoscopy may also be imprecise or impossible to perform because of peripheral lesions' distance from the main bronchi.

"No medical procedure is without risks, including biopsy," said George Eapen, M.D., an associate professor in the Department of Pulmonary Medicine. "The question becomes, is it better to take the chance of a lung collapse with a transthoracic approach or put the patient at a different risk—non-diagnosis of cancer—with a bronchoscopic procedure that has a lower diagnostic yield? This is the quandary we're facing."

To address limitations in diagnosing peripheral lung lesions, M. D. Anderson is now using a tool that employs technology similar to that found in GPS devices. The tool allows navigation of the smallest airway passages to reach lesions for which standard diagnostic procedures would be impossible or too risky.

Importance of biopsy in lung cancer patients

Most lung tumors, including those in the peripheral lung, go undetected until after they have metastasized. Because a patient's prognosis largely depends on the extent of disease at diagnosis, it is important to identify tumors early and definitively so that the proper treatment can begin immediately. The only sure way to make a definitive diagnosis of lung cancer is to perform a biopsy.

CT-guided transthoracic needle biopsy (TNB), the conventional method of biopsying suspicious masses in the peripheral lung, has a diagnostic yield of about 90% but violates the lung lining and thus carries a high risk of lung collapse, a potentially fatal complication in fragile patients with highly compromised breathing.

In such patients, the risk of lung collapse can be mitigated with the use of transbronchial biopsy, in which a bronchoscope is advanced through the patient's trachea and bronchus to acquire tissue samples. Compared to TNB, the transbronchial approach has a smaller risk of lung collapse because it does not violate the lining of the lungs but also results in a smaller diagnostic yield. In addition, while the smallest bronchoscope is 2.8 mm in diameter, many of the air passages in the lung are even smaller, making it difficult or impossible

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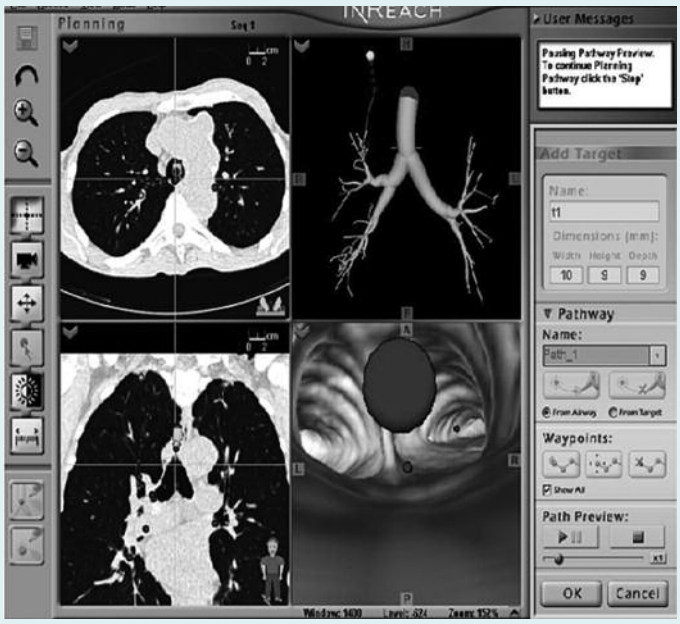
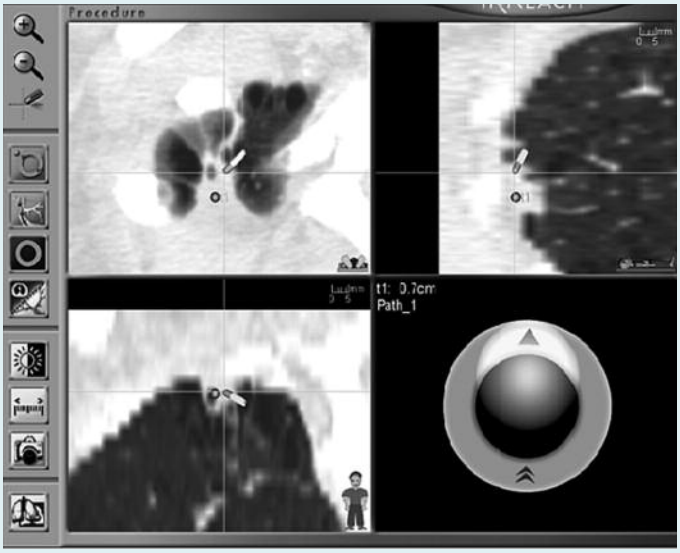
Importance of Images in Electromagnetic Navigation Biopsy



Electromagnetic navigation biopsy is preceded by careful radiologic mapping. The technology uses computed tomography and other imaging to create three-dimensional and virtual reconstructions of the region to be biopsied (as shown above and below in representative screen grabs from treatment planning software). These three-dimensional and virtual reconstructions are then used to compute a precise path that the physician follows to biopsy lesions in the hard-to-reach periphery of the lung.



Electromagnetic Navigation Biopsy for Peripheral Lung Lesion Diagnosis

(Continued from **page 5***)*

to reach many lesions in the peripheral lung.

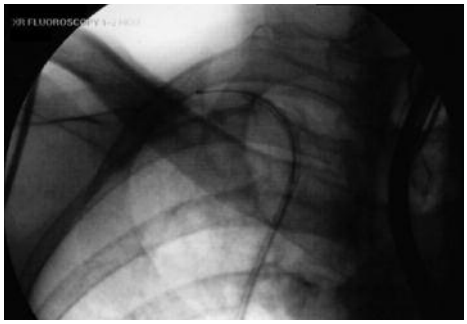
Electromagnetic navigation

Traditionally, in patients for whom biopsy was not an option—or was a very risky option—potentially malignant lesions in the lung periphery would be approached with "watchful waiting," which carries the risk of late detection of disease progression. Biopsy with electromagnetic navigation bronchoscopy, which uses GPS-like technology to guide an ultra-thin steerable catheter with twice the range of a conventional bronchoscope, may be a viable option for some of these patients. At M. D. Anderson's Cardiopulmonary Center, electromagnetic navigation bronchoscopy is performed with the inReach system (superDimension, Inc., Minneapolis, MN). M. D. Anderson is the second institution in the Texas Medical Center and one of more than 100 in North America to use the technology.

In electromagnetic navigation bronchoscopy, CT is first used to locate the lesion. The physician then uses software to review the CT data slice by slice to trace a path from the lesion to an adjacent airway to increasingly larger airways accessible by a conventional bronchoscope. The physician makes a series of reference points at easily identifiable bronchoscopic landmarks—e.g., the main carina and upper lobe takeoff—to leave a trail of virtual bread crumbs leading to the lesion.

In the clinic, the patient is situated on an electromagnetic board. The modified CT data with reference points are then entered into the inReach system, which transposes the data into the three-dimensional magnetic field occupied by the patient. The patient's chest is marked with three reference points to account for respiratory fluctuations.

A conventional bronchoscope catheter is advanced into the patient's lung, and the physician advances a smaller catheter with a sensor through the tube. The physician then touches the sensor to the actual anatomical points that correspond with the reference points placed on the planning CT earlier; the machine in turn calculates a divergence ratio to allow for error. The physician then uses the virtual road map to navigate the bronchi to the lesion. Once the lesion is located, endobronchial tools are used to collect tissue samples.



Fluoroscopy shows a brush approaching a lesion for sample collection following navigation to the lesion.

Weighing options

At M. D. Anderson, which has a team of aggressive and highly skilled interventional radiologists, many patients with peripheral lung lesions who have good lung function and overall health are suitable candidates for TNB. "Our interventional radiologists are very good at diagnosing peripheral lung lesions with conventional methods," said Dr. Rodolfo Morice, M.D., a professor in the Department of Pulmonary Medicine. Newer nonelectromagnetic navigation technologies are being evaluated as well.

> **"The most fragile patients, the most compromised patients, are the ones who really benefit from electromagnetic navigation bronchoscopy."**
>
> **– Dr. George Eapen**

However, as Dr. Eapen explained, "The most fragile patients, the most compromised patients, are the ones who really benefit from electromagnetic navigation bronchoscopy." Patients who have undergone failed conventional transbronchial biopsy may also benefit, Dr. Eapen said.

Electromagnetic navigation bronchoscopy is not without its potential shortcomings. The inReach system uses preoperative CT data to construct its virtual pathway to the lesion, and according to Dr. Morice, these non–real-time data can sometimes result in navigation errors and lower diagnostic yield. He also said that the technology may actually be limited by one of its advantages over TNB—its minimally invasive approach to lesions through airways in the lungs.

"Theoretically, any lung lesion should be reachable through an airway," Dr. Morice said. "When the CT scan shows an airway going right into the lesion, you know that you're going to get to the lesion. However, if it shows an airway that goes to the periphery of the lesion, you may still get to the lesion, but the diagnostic yield may not be as good as it would be if the airway was going into the lesion."

Other applications

Ultimately, Dr. Eapen regards the electromagnetic navigation bronchoscopy system as a superb aiming device for current and future technologies for diagnosing and treating lung cancer. For example, the system could be used in conjunction with optical coherence tomography to examine lesion characteristics in situ without the use of tissue or to deliver less risky therapies—microwave ablation, radiofrequency ablation, thermal vaporization—bronchoscopically with precision. The system can also be used to biopsy lymph nodes for staging purposes and treatment planning.

"Electromagnetic navigation bronchoscopy adds an extra level of precision in terms of the diagnostic yield. It enables us to go after lesions that conventionally we would not be able to because the risk of failure is so high," Dr. Eapen said. "But it's not a magic bullet. It is a tool like any other tool that adds value to our ability to do what we want to do." ●

For more information, contact Dr. Eapen at 713-563-4256 or Dr. Morice at 713-563-4257.

HOUSE•CALL

Couples and Cancer: Cancer-Related Issues Can Disrupt Relationships

Cancer patients and their loved ones experience a wide range of stressful emotions, including shock, anger, fear, and even hopelessness. For couples dealing with cancer, the added stress can undermine the stability of the relationship.

"Being diagnosed with cancer changes everything," said Phyddy Tacchi, a licensed marriage and family therapist and advanced practice nurse in the Department of Psychiatry at The University of Texas M. D. Anderson Cancer Center. "Every domain of the couple's relationship eventually begins to be affected by cancer."

Ms. Tacchi, who provides counseling to individual patients as well as couples dealing with cancer, said changes in a couple's relationship often result from the partner taking on many of the patient's functions and responsibilities. "I find that looking at the couple's relationship is more beneficial than just looking at the patient," she said. "Cancer affects the whole family, and treating patients in a vacuum ignores a large part of their lives."

Cancer-related issues

Ms. Tacchi typically works with a couple for 2 weeks to help them develop coping strategies to handle the emotional effects of cancer. She said that although the issues affecting couples will vary depending on their age and the stage of their relationship, to one extent or another the following five major issues affect all couples dealing with cancer:

- **Emotions.** Understanding the emotions related to cancer is the most important issue facing couples, according to Ms. Tacchi. She said couples should realize that each partner will express emotions differently. For example, a caregiver may hide feelings for fear of burdening the patient with his or her emotions, but the patient may interpret this as a lack of caring.

- **Uncertainty.** "Cancer forces us to come to grips with the fact that we don't control our own lives as much as we think we do," Ms. Tacchi said. Dealing with the unknown adds stress to the relationship.

Fotosearch

- **Finances.** The treatment costs and/or lost income associated with cancer can affect a couple's retirement, their children's college education, and their ability to buy a home or maintain their home.

- **Spiritual concerns.** Spiritual questions about life, death, suffering, and afterlife come to the forefront for those affected by cancer. Many couples don't share the same views or want to talk about them. A couple might also have to make decisions about end-of-life issues like a funeral, will, living will, and do-not-resuscitate order. Such mortality issues can be a strain, especially for young couples.

- **Sex.** Some treatments cause body image changes, which can affect libido or make the patient feel undesirable. Many chemotherapy regimens dampen sexual desire.

Working it out

Although many patients and caregivers have told her the emotional part of dealing with cancer is harder than the physical part, Ms. Tacchi said that the couples she counsels usually find common ground that keeps them committed and dedicated to one another.

"That doesn't mean there's no conflict, but some sense of 'in sickness and in health' takes over," she said. "Even though a cancer journey is rocky at the beginning, most couples really do find a way to gravitate toward each other, and in the end they often say they grew closer as a result of all of this."

Help is available

Most insurance plans will cover couples counseling such as the kind Ms. Tacchi provides, although patients should confirm this with their carriers. Many cancer treatment centers sponsor support groups and other services for couples dealing with cancer. The American Cancer Society also has a list of support resources available on its Web site at http://www.cancer.org/docroot/SHR/SHR_2.asp. ●

For more information, talk to your physician, or:

- *visit www.mdanderson.org*
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OncoLog, February 2010
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IN BRIEF

Researchers Find Glioblastoma's Resistance to Treatment Rooted in Immunosuppression

Cancer "stem cells" leading to glioblastoma multiforme, an aggressive brain tumor, suppress the body's ability to destroy the cancer, investigators at M. D. Anderson Cancer Center have discovered.

However, the researchers also found a way to potentially overcome this immunosuppressing effect: prompt the stem cells to differentiate into noncancerous brain cell types. The findings were published in January in the journal *Clinical Cancer Research*.

"We've known for years that glioblastoma and cancer patients in general have impaired immune responses," said Amy Heimberger, M.D., an associate professor in the Department of Neurosurgery and senior author of the study. "Our research uncovers an important mechanism that shows how that happens. The cancer stem cells inhibit T cell response, and it is these T cells that recognize and eradicate cancer."

The team worked with cancer stem cells that expressed the CD133 tumor marker, could form neurospheres in culture, could develop into glioblastoma in mouse brains, and could differentiate into neurons, astrocytes, and glial cells. The stem cells were shown to interfere with T cell response to tumorigenesis in three ways:

- By producing immunosuppressive cytokines that prevented the responses of T cells.
- By inducing some T cells to become regulatory T cells, which halt immune response.
- By killing T cells via apoptosis (programmed cell death).

These immunosuppressing activities were reversed when the team placed the undifferentiated stem cells in a culture medium that caused them to differentiate into neurons, astrocytes, or glial cells, said first author Jun Wei, Ph.D., an instructor in the Department of Neurosurgery. In a separate paper published recently in the journal *Molecular Cancer Therapeutics*, the research team reported that the immunosuppressing effect of glioblastoma stem cells could also be reversed by inhibiting the STAT3 signaling pathway with small interfering RNA or the experimental drug WP1066.

Dr. Heimberger said the findings could contribute to the development of vaccines or other immunotherapeutic agents against glioblastoma stem cells. Patients with glioblastoma live only an average of 14 months after initial diagnosis, and attempts to attack the cancer with other therapies have met with limited success. In fact, researchers believe the biology of glioblastoma stem cells is at least partly responsible for the disease's notorious resistance to chemotherapy and radiation. ●

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