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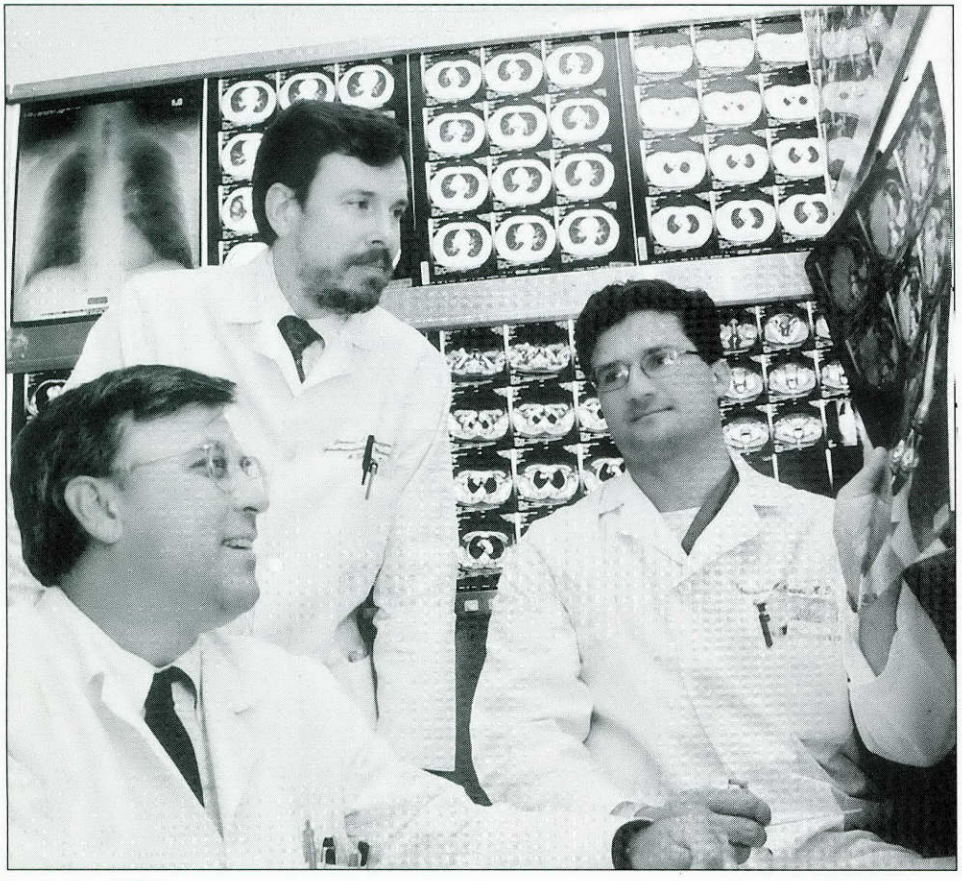
Multidisciplinary Care Improves Treatment, Enhances Quality of Life for Patients with Colorectal Cancer



Dr. John Skibber, *associate professor in the Department of Surgical Oncology,* **Dr. James Abbruzzese**, *professor and chairman of the Department of Gastrointestinal Medical Oncology, and* **Dr. Christopher Crane**, *assistant professor in the Department of Radiation Oncology (left to right), examine computed tomography scans of a patient's colon.*

by Mariann Crapanzano

For each patient who receives a diagnosis of colorectal cancer, the struggle is a personal one, encompassing not only medical treatments but also psychological and social adjustments. Optimizing both the potential for cure and the quality of life for these patients requires the collaborative efforts of many specialists and an unbroken line of communication.

"It's not just what the doctors do in terms of the surgery, radiation therapy, and chemotherapy," said John M. Skibber, M.D., an associate professor in the Department of Surgical Oncology at The University of Texas M. D. Anderson Cancer Center. "It's the whole multidisciplinary approach that helps to achieve the optimal outcome."

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Multidisciplinary Care Improves Quality of Life

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Sphincter-preserving surgery

One result of this approach is an increase in the number of patients with rectal cancer who undergo sphincter-preserving surgery. Patients with locally advanced cancer in the lower part of the rectum have in the past been treated with an abdominoperineal resection and a permanent colostomy. With state-of-the-art staging and surgical techniques, Dr. Skibber said, many of these patients can now undergo a proctectomy and coloanal anastomosis. In this procedure, the rectum and mesorectum are removed, using intraoperative analysis to ensure tumor-free margins, and the descending and transverse colon is freed and then connected by anastomosis to the anal canal, thereby preserving the patient's sphincter and eliminating the need for a colostomy.

"We are strongly interested in sphincter-preserving techniques," said Dr. Skibber, "but not at the cost of a poor cancer operation. And that's a delicate judgment."

The determination of whether a patient is a candidate for sphincter-preserving surgery depends largely upon the precise and accurate staging of the disease. This staging is ideally a joint effort by pathologists, who evaluate tissue samples that are obtained preoperatively, and gastroenterologists and radiologists, who perform endoscopic and imaging studies in conjunction with the surgeon.

Treatment planning and preoperative therapy

Endorectal ultrasound and conventional staging modalities, such as computed tomography (CT) and magnetic resonance imaging (MRI), help determine the involvement of structures surrounding the rectum. Sandeep Lahoti, M.D., an assistant professor in the Department of Gastrointestinal Medicine and Nutrition, and others at M. D. Anderson also routinely use endorectal ultrasound in cases of rectal cancer to evaluate the different layers of the rectal wall and to determine how deeply the tumor invades the wall.

"... other than the presence of metastatic disease, the depth of penetration is the primary prognostic factor in determining how the patient is going to do."

– **John M. Skibber, M.D.,**
associate professor, Department of Surgical Oncology

According to Dr. Lahoti, if endorectal ultrasound, CT, or MRI shows that the tumor extends beyond the inner wall of the rectum, preoperative chemotherapy and radiation therapy may be administered in an attempt to downstage the tumor, in some cases making an unresectable tumor resectable.

"That's important because, other than the presence of metastatic disease, the depth of penetration is the primary prognostic factor in determining how the patient is going to do," said Dr. Skibber. "By the use of endorectal ultrasound, we can identify patients who have high-risk cancers before we operate on them and therefore offer them radiation and chemotherapy before surgery and give them the benefit of possibly having their sphincters preserved."

In a recent study led by Nora A. Janjan, M.D., a professor in the Department of Radiation Oncology, preoperative chemoradiation allowed sphincter-preserving surgery to be performed in 40% of patients who otherwise would have had a colostomy.

Preoperative radiation therapy has the added benefit of reducing the recurrence rate in patients with locally advanced rectal cancer, said Dr. Janjan. And neoadjuvant chemotherapy may benefit these patients by providing early treatment of micrometastatic disease, said James L. Abbruzzese, M.D., professor and chairman of the Department of Gastrointestinal Medical Oncology.

According to Dr. Abbruzzese, improving the effectiveness of chemotherapy for colorectal cancer is an ongoing process. "Medical oncologists collaborate with surgeons and radiation oncologists on neoadjuvant studies to develop new therapies for patients who have more advanced cancers," he said.

Dr. Janjan and Christopher H. Crane, M.D., an assistant professor in the Department of Radiation Oncology, administer radiation therapy to patients with colorectal cancer. In an effort to improve results over those obtained with standard radiation therapy, Drs. Janjan and Crane were instrumental in initiating a concomitant boost radiation protocol in which increased doses of radiation are delivered to the site of the primary tumor during preoperative chemoradiotherapy.

"Preliminary analysis of this phase II protocol indicates that concomitant boost therapy provides an increase in tumor downstaging and sphincter preservation with no apparent increase in toxicity," said Dr. Crane.

Dr. Crane and others at M. D. Anderson are investigating the use of three-dimensional conformal boost radiation therapy, a delivery technique that is more accurate and allows the site of the primary tumor

Clinical Trials for Colorectal Cancer

Clinical trials in progress at The University of Texas M. D. Anderson Cancer Center include the following for patients with colorectal cancer.

- Phase II study of radiofrequency ablation of colorectal cancer liver metastases combined with postablation hepatic arterial infusion of floxuridine alternating with 5-fluorouracil (ID98-035). *Physician: Lee Ellis, M.D.*

  This study is designed for patients with colorectal cancer who have metastatic disease only in the liver that has not responded to systemic chemotherapy. Patients must have no more than six tumors and no tumor larger than 4 cm in its greatest dimension. Participants must also have a life expectancy of at least 16 weeks. Patients are excluded if they have had prior liver irradiation or if they have gross ascites, evidence of cirrhosis, or active duodenal or gastric ulcers.

- A phase I–II study of escalating doses of SU5416 (NSC 696819) in combination with irinotecan (CPT-11) in patients with advanced colorectal carcinoma (ID99-243). *Physician: Paulo Hoff, M.D.*

  Patients with measurable adenocarcinoma of the colon or rectum in a locally advanced or metastatic stage are eligible. Patients must also have adequate hepatic function and have recovered from any prior surgery or radiation therapy. Patients may have received prior chemotherapy but are excluded if they have previously received SU5416, CPT-11, or any topoisomerase I inhibitor.

- Pilot study of graft-versus-tumor induction: High-dose chemotherapy with allogeneic peripheral blood stem cell transplantation for patients with metastatic colon cancer (DM95-106). *Physician: Richard Champlin, M.D.*

  The colon is a target for graft-versus-host reactions that occur after stem cell transplantation, so allogeneic hematopoietic transplants may confer an immune-mediated graft-versus-tumor effect in colon cancer. Patients 18 to 55 years old who have histologically confirmed metastatic colon carcinoma, have received more than one treatment regimen, and have a related HLA-identical donor are eligible. Patients must also have adequate cardiac and pulmonary function. Exclusion criteria include evidence of hepatitis or cirrhosis, HIV, pregnancy, and central nervous system metastases.

- Analysis of patients with locally recurrent rectal carcinoma: Prospective assessment of quality of life, outcome of therapy, and management of pain (ID97-106). *Physician: John M. Skibber, M.D.*

  This study is designed for patients with locally recurrent rectal carcinoma who either speak and understand English or have an interpreter available to answer questions. Participants must have had a period of at least three months between initial treatment and recurrence and may have concurrent distant metastases but no pelvic malignancies other than rectal carcinoma. Those who have had documented pelvic pain syndrome or chronic constipation prior to cancer diagnosis are excluded.

- A phase II chemoprevention study of calcium and aspirin in subjects with previously resected adenomatous polyps of the colon (CAPT Study) (DM93-129). *Physician: Frank A. Sinicrope, M.D.*

  This study is designed for patients 40 to 80 years old who have had a colon adenoma removed within the last five years and who have at least half of their colon intact. Participants must also have no family history of adenomatous polyposis or hereditary nonpolyposis colon cancer and no personal history of gastrointestinal ulcers or bleeding or adverse reactions to aspirin. Patients who have used calcium supplementation at doses greater than 500 mg per day in the four months prior to enrollment or who have a history of pelvic irradiation are excluded. ●

For more information *about these clinical trials, physicians or patients may call the M. D. Anderson Information Line. Those within the United States should call (800) 392-1611; those in Houston or outside the United States should call (713) 792-6161. Visit the M. D. Anderson Cancer Center clinical trials Web site at http://www.clinicaltrials.org for a broader listing of treatment research protocols.*

to receive a larger total dose of radiation while normal tissue is spared.

Treatment of metastatic disease

Neoadjuvant and adjuvant therapies increase response rates and even help cure many patients, but other patients must fight metastatic disease, especially in the liver, said Steven A. Curley, M.D., a professor in the Department of Surgical Oncology.

According to Dr. Curley, some patients with liver metastases may be candidates for surgical resection or radiofrequency ablation—a procedure in which the liver metastases are destroyed with an electrical current delivered directly to the tumor through a needle electrode—with or without placement of a hepatic artery pump for chemotherapy.

"There are a lot of physicians who, when they see a patient with advanced disease or metastatic disease, say there's not a lot that can be done. While that may be true in some cases, it's not true for everybody," Dr. Curley said. "We do have a very aggressive and promising

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Multidisciplinary Care Improves Quality of Life

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multidisciplinary management program to treat liver metastases from colorectal cancer."

Management of bowel function

In addition to fighting the cancer, the multidisciplinary team helps patients manage bowel dysfunction that may result from some treatments for colorectal cancer. Enterostomal therapy nurses work with patients who have undergone a colostomy, helping them learn to care for their stomas and to address the psychological and social issues left in the wake of the procedure.

Annette K. Bisanz, an advanced practice nurse, led the development of practice guidelines and patient education materials for bowel management after colorectal surgery. Bisanz and others provide rehabilitative therapy for patients with bowel dysfunction, particularly those who have had their rectums removed. Many of these patients experience very frequent bowel movements, which often can be managed with diet, appropriate amounts of medicinal fiber, fluid, and medication. With rehabilitative therapy, patients whose bowel functions are profoundly disrupted following surgery can return to very active lives, agreed Dr. Skibber and Bisanz.

Palliative care

Despite advances in multimodality treatments and in staging and surgical techniques for colorectal cancer, some patients are faced with unresectable or extensive metastatic disease that is incurable. Eduardo Bruera, M.D., a professor and chairman of the Department of Symptom Control and Palliative Care, said that advanced, incurable colorectal cancer presents a number of challenges, primarily pain (often from liver metastases or retroperitoneal disease), fatigue, and cachexia. In addition, these patients and their families must confront issues regarding the patient's end-of-life care.

In most cases of incurable disease, pain can be well controlled with oral medications, said Dr. Bruera, something that was not possible as recently as 10 or 15 years ago. In patients for whom oral medication is ineffective, intravenous medication or, occasionally, a nerve block (performed by an anesthesiologist) may provide palliation. Also, the psychological, social, and informational needs of the patient are addressed in a session with various specialists, ranging from physical and occupational therapists to a pastoral care counselor, Dr. Bruera said.

Screening and prevention

Acutely aware of the effects of advanced disease, other specialists work toward preventing colorectal cancer in both high-risk and general populations. In a study published in the June 29, 2000, issue of *The New England Journal of Medicine*, researchers at M. D. Anderson and several other institutions showed that the drug celecoxib significantly reduced the number of colorectal polyps, or adenomas, in patients with familial adenomatous polyposis (FAP). FAP causes the formation of innumerable polyps—precursors to colorectal cancer—inside the bowel and places patients at very high risk for colon cancer. Bernard Levin, M.D., a professor in the Department of Gastrointestinal Medical Oncology and an investigator in the celecoxib study, said that further studies will help delineate the usefulness of the drug in cancer prevention.

In one such study, Frank A. Sinicrope, M.D., an associate professor in the Department of Gastrointestinal Medicine and Nutrition, and others at M. D. Anderson are evaluating whether celecoxib alone and in combination with difluoromethylornithine (DFMO) can cause existing polyps to regress and prevent the formation of new polyps in patients with FAP. Dr. Sinicrope said that celecoxib has also been slated for a trial to determine whether it can prevent the formation of polyps in children and adolescents who have the genetic mutation associated with FAP.

Celecoxib is also administered to control the growth of polyps in some patients with FAP who wish to delay a colectomy. "The drug is not a substitute for surgical resection [in these patients]," said Dr. Sinicrope, "and its utility in the management of patients with FAP has yet to be defined."

Because colon cancer generally develops slowly from one or more benign adenomas, said Dr. Levin, regular screening to detect abnormal changes in the intestine can help to reduce the incidence of cancer. Dr. Levin, who serves as vice president for cancer prevention, and others at M. D. Anderson are also investigating, in multi-institutional studies, methods to detect changes in stool that occur as colon cancer develops, such as genetic mutations in cancer cells that are shed into the stool. According to Dr. Levin, these methods appear to have great promise as screening tools. In the meantime, however, he urges physicians and patients to use available techniques—the fecal occult blood test, flexible sigmoidoscopy, double-contrast barium enema, and colonoscopy—to detect precursors to colorectal cancer and early-stage cancer and, ultimately, to prevent deaths from colorectal cancer. ●

For more information, *contact Dr. Skibber at (713) 792-5165, Dr. Lahoti at (713) 792-2828, Dr. Janjan at (713) 792-3432, Dr. Abbruzzese at (713) 792-2828, Dr. Crane at (713) 792-0782, Dr. Curley at (713) 794-4957, Annette Bisanz at (713) 792-6012, Dr. Bruera at (713) 792-6084, Dr. Levin at (713) 792-3900, or Dr. Sinicrope at (713) 792-2828.*

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CLINICAL PRACTICE GUIDELINES
Quarterly Supplement to *OncoLog*
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About These Clinical Practice Guidelines

This guideline may assist in the diagnostic evaluation of patients with clinical symptoms or positive screening tests (if such testing exists). The clinician is expected to use independent medical judgment in the context of individual clinical circumstances to determine any patient's care.

M. D. Anderson Cancer Center's Practice Guidelines are continually updated as new information becomes available and are being expanded to include the entire spectrum of cancer management. New guidelines for screening and diagnosis are currently under development. Access the most current version of all M. D. Anderson Practice Guidelines from M. D. Anderson's Home Page at http://www.mdanderson.org.

Continuing Medical Education: An expanded version of these materials with CME category 1 credit is available on the Internet. Access Practice Guidelines from M. D. Anderson's Home Page at **http://www.mdanderson.org**.

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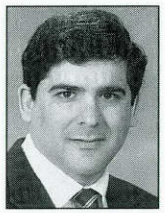

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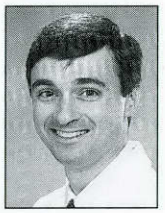

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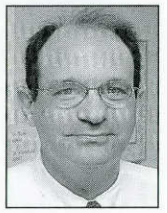

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CLINICAL DISCUSSION: Malignant Melanoma

Scope of This Guideline

This guideline begins with a diagnosis of malignant melanoma confirmed by pathologic evaluation and addresses staging, treatment, and follow-up care in this clinical setting.

Synopsis & Highlights

Overview

Most melanomas (90%) present as cutaneous lesions discovered by self-examination or physician examination, but noncutaneous lesions may also occur in the pigmented cells of the retina or in the mucosa of the oral cavity, nasopharynx, vagina, vulva, or anal canal. The noncutaneous lesions tend to be more advanced when detected.

Melanomas characteristically have two distinct growth phases; the first is a radial growth phase characterized by tumor cells in the epidermis and papillary epidermis, and then a vertical growth phase occurs in which tumor cells begin to penetrate deeper layers of the skin. The propensity for metastasis is characteristically low during the radial growth phase but rises significantly during vertical growth. Melanomas tend to metastasize through regional lymphatics to adjacent and distant skin sites (in-transit metastases) and to regional lymph nodes and also hematogenously to distant sites.

Evaluation & Workup

Biopsy and microstaging

The first step in the evaluation of a suspicious lesion is biopsy for definitive diagnosis and microstaging. Tumor thickness, as measured by Breslow's thickness scale, and depth of penetration, classified by Clark's level, are critical parameters; therefore, full-thickness biopsy is preferred. Excisional, directed incisional, or punch biopsies are all acceptable. Shave or curette biopsies are not appropriate for suspected melanoma, nor are cryosurgery or electrodesiccation techniques, as these methods do not allow for pathologic analysis of tumor depth and margins. Wide excision of the lesion should not be attempted at time of biopsy, as this may compromise later lymphatic mapping studies. Specimens should be analyzed by serial sections rather than frozen sections, and this work should be performed by a pathologist experienced in analysis of skin

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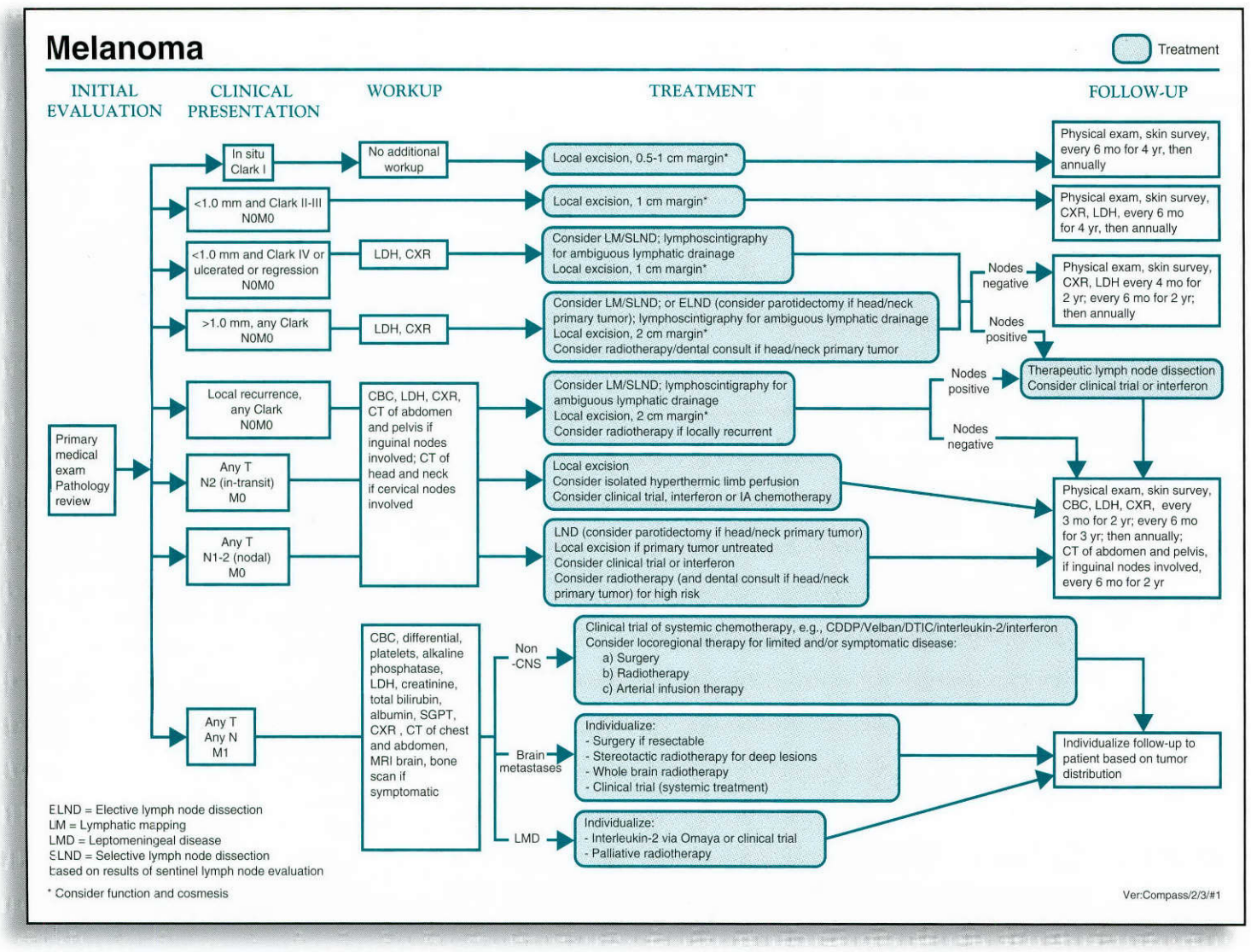
Pull Out



This practice guideline was developed in a collaborative effort between the physicians and nurses at The University of Texas M. D. Anderson Cancer Center and the National Comprehensive Cancer Network. The core development team at M. D. Anderson working on this practice guideline included Dr. Kie Kian Ang, Dr. Omar Eton, Dr. Sharon Hymes, Dr. Jeffrey E. Lee, Dr. Nicholas E. Papadopoulos, Dr. Merrick Ross, and Dr. Gunar Zagars.

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samples. In instances where the initial biopsy is inadequate for complete microstaging, it should be repeated.

Clinical staging

Additional workup is based on the results of microstaging. This should include a thorough history and physical examination for all patients. Patients with in situ lesions require no specific additional workup before undergoing local excision, unless such is indicated by other factors in individual cases. Patients with clinically localized invasive melanomas should have chest x-rays and measurement of LDH levels along with any other preoperative studies indicated by the individual situation, while those with more advanced disease should have additional studies to identify potential metastases, including CT scans of the involved areas. MRI study of the brain is appropriate in patients who present with metastatic disease to identify potentially treatable lesions, and bone scans should be reserved for patients who have symptoms of bone metastases.

Primary Treatment

The primary treatment for clinically localized malignant melanomas is surgical removal of the lesion by wide local excision.

Clark's level I lesions (in situ) that are removed by local excision with margins of 0.5–1.0 cm require no additional investigation or treatment, nor do Clark's level II or III lesions thinner than 1.0 mm if a clear surgical margin of 1 cm or more is achieved.

For lesions thicker than 1.0 mm, as well as for those that are ulcerated or extend into the reticular dermis, a surgical margin of 2 cm is recommended, and lymph node studies are indicated. In centers where it is available, intraoperative lymphatic mapping with sentinel node biopsy is recommended. This is a low-risk surgical procedure with minimal associated morbidity, and it may be done as day surgery, preferably at the same time as the wide local incision. The information obtained is the most accurate indicator in determining lymph node status, disease stage, and underlying patient prognosis and therefore entirely appropriate to use as a basis for recommending further treatment. At M. D. Anderson, it is considered the standard of care for patients presenting with clinically localized melanoma. According to Dr. Lee, "We believe that all patients with at least intermediate-thickness lesions with clinically localized disease should be offered lymphatic mapping as part of initial treatment."

In this procedure, the sentinel lymph node in the lymphatic drainage basin is identified and removed for histologic study. Dr. Ross recommends deferring further surgery to await results of pathologic evaluation of sentinel node biopsy by permanent serial section rather than by frozen section.

When the sentinel node is found to contain metastatic melanoma, lymph node dissection should be performed to remove the remaining nodes in that basin, and adjuvant therapy can be offered. Where no disease is found in the sentinel node, removal of additional nodes is not necessary.

It should be noted that precise evaluation of sentinel nodes by this method is best performed at the same time as wide local excision; in fact, if wide excision is performed without sentinel node biopsy, lymph node mapping may not be accurate later. Where lymphatic mapping is not available or cannot be achieved, elective lymph node dissection may be indicated instead.

Lymphoscintigraphy is recommended prior to surgery in cases where the lymphatic drainage basin is not obvious (i.e., tumor locations that may drain to more than one lymph node basin, including many trunk and head and neck lesions).

Adjuvant Therapy

Adjuvant therapy should be considered following surgical resection of melanoma for patients considered to be at high risk for recurrence as evidenced by lymph node involvement, especially when there is extranodal or extracapsular extension, by matted lymph nodes, or by the surgeon's prerogative. There are several modalities to consider, but this represents one of the most challenging areas of current clinical cancer research.

Systemic therapies

The FDA has approved adjuvant high-dose interferon alpha-2b (Intron® A, Schering Inc.) for a year for patients at high risk for recurrence after resection of a deep primary lesion (over 4 mm in depth) or regional nodal recurrence. According to Dr. Eton, this list may be expanded intuitively to include patients with in-transit disease, although data are few for this subgroup of patients as they are too small a group to study in a randomized trial. This treatment has been shown in phase III trials to consistently improve median time to progression, albeit in a time frame equivalent to approximately the amount of time on therapy. The impact on overall survival rate is modest and can potentially be achieved either by immediate treatment in a proactive adjuvant setting or by later combining Intron A with other agents in the subset of patients who have evidence of disease progression. Although interferon alpha-2b, a cloned biologic agent, is a naturally occurring molecule produced in humans in response to infections and other processes, it should be noted that this regimen uses high doses and is associated with significant but reversible toxicity. However, there are patients who can tolerate this treatment quite well, especially younger patients.

All of our experts agree that enrollment in a clinical trial should be strongly considered for these patients, as promising trends are being noted in current investigations. Biochemotherapy, an aggressive inpatient program that combines biologic (interferon alpha-2b and interleukin-2) and cytotoxic agents, has proven efficacy in stage IV disease and is now under investigation for use in less advanced disease. Other promising areas of investigation include passive and active immunotherapy as well as adoptive cellular immunotherapy and cytokine programs. These continue to be developed as each new insight emerges in the field of molecular immunology. It is hoped over time to harness, augment, or replace natural host defenses using a "cocktail" of these ever more refined products. Finally, as genomic and proteomic technologies are developed, they will allow precise characterization of individual patients' tumors in correlation with clinical course. In turn, drugs designed to address specific critical genetic defects and with considerably reduced toxicity can be developed. *[See the May 2000 issue of* OncoLog *for more information about current investigations in melanoma treatment.]*

Radiotherapy

Radiotherapy has been traditionally considered to be of limited use in the treatment of melanoma because this type of cancer is often radioresistant. However, according to Dr. Zagars, new strategies have made radiotherapy a useful adjunct, and it should be considered where there are factors such as multiple lymph node metastases or extranodal extension that portend a risk for recurrence. Currently at M. D. Anderson, one such strategy consists of high-dose treatments administered over a shorter period of time than conventional radiotherapy. External beam radiation is given directly to the site as a few (5 or 6) treatments in large doses (600 cGy). Therapy is given over a period of 10 to 14 days, for a total of approximately 3000 cGy. However, Dr. Zagars points out, "This is a fairly high-risk treatment that we don't recommend outside of a comprehensive cancer center." Where this is not possible, he recommends conventionally delivered radiotherapy. Radiation therapy in combination with chemotherapy (chemoradiation) is also under investigation in the treatment of patients at high risk for melanoma.

Treatment of Metastases

Isolated hyperthermic limb perfusion

This is a technique for controlling melanoma that has spread to involve dermis or subcutaneous tissue of an affected limb between the primary site and the closest lymph node basin (in-transit metastases). The artery and vein are cannulated and placed on bypass to isolate the blood flow of the limb from general circulation, allowing prolonged perfusion of the area with high doses of chemotherapeutic agents. Generally, the cytotoxic agent melphalan is used, and the limb is heated to a temperature of 40°C. An experimental protocol at M. D. Anderson is currently evaluating improved responses with the addition of tumor necrosis factor. According to Dr. Ross, isolated hyperthermic limb perfusion is frequently very effective and represents an important option for treatment of this difficult category of melanoma. This procedure is, however, a major operation with significant morbidity, best performed at a specialized cancer center.

Intra-arterial chemotherapy and intrahepatic chemoembolization

These are treatment modalities that may be considered for the treatment of symptomatic metastases and, like hyperthermic limb perfusion, are best performed at a center experienced in those procedures.

Brain metastases

Melanoma brain metastases are resistant to most systemic treatment regimens (excepting the nitrosoureas and possibly also temozolomide, a metabolite of dacarbazine (DTIC)), including biochemotherapy. Hence, melanoma metastatic to the brain is treated as a wholly separate disease process, and surgery for single or symptomatic metastases, radiosurgery for fairly small metastases (3 cm or less but still detectable by CT scan), and whole-brain radiation therapy are employed. Stereotactic radiotherapy is used to focus high-dose treatment on a very precise area. In effect, this "radiosurgery" can target and destroy a lesion. Dr. Zagars recommends this for instances where lesions are few and small; this technique is rarely employed for more than two lesions. Stereotactic therapy may be used in conjunction with whole-brain irradiation to boost its efficacy. Studies are ongoing to explore the use of chemotherapy as a "radiosensitizer" to improve clinical results without causing severe toxic effects.

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Follow-up

Our experts recommend posttreatment surveillance for the purpose of early detection of recurrence or a second primary melanoma. An additional consideration for the primary care physician is identification of other family members at risk. For all patients, follow-up visits should be conducted as shown in the guideline or more frequently at the discretion of the physician. At M. D. Anderson, patients receive follow-up care at three-month intervals for at least the first two years after regional recurrence, since this is the period most likely to be associated with progression of disease. Subsequent follow-up visits in the disease-free setting can then be at progressively longer intervals. Patients are carefully educated regarding signs and symptoms of recurrence. During treatment, patient follow-up visits occur at shorter intervals with frequent restaging (as short as six-week intervals in the stage IV setting) to monitor response.

Authors' Perspectives

The first biopsy is a critical event in the course of a patient's treatment for malignant melanoma. Dr. Lee emphasizes that accurate histopathology is very important in evaluation of patients with melanoma and for treatment strategy decisions as well as in counseling patients about the risk of recurrence. It is therefore important that the initial biopsy of a suspected melanoma be performed with that in mind. Full-thickness biopsies should be evaluated by an experienced dermatopathologist. Attempts at wide surgical excision at the time of biopsy are discouraged, as these may compromise later necessary lymphatic study.

Clinical trials are currently the best option for adjuvant therapy for malignant melanoma. Although advanced melanoma has been traditionally considered a resistant solid tumor, Dr. Eton notes that increasingly frequent responses to combined modality therapy are being seen. This means continually improving palliative results in at least 50% of patients. Some of these programs are being aggressively developed in the earlier stage I–III settings to decrease the frequency of disease recurrence in patients and to improve survival time. All of our experts agree that where shown in the guideline as an option, referral to clinical trials often represents the best choice for patients.

Find more information about clinical trials and current protocols available at M. D. Anderson at *http://www.mdanderson.org/research/*.

As with most cancers, there is a strong case for early detection. All of our experts agree that the outcomes in this disease are largely dependent upon disease stage at presentation. According to the National Comprehensive Cancer Network (NCCN), the long-term survival rate exceeds 90% when tumors are < 1.5 mm in thickness. As tumor thickness increases, so does the likelihood of regional nodal involvement, in which survival rates are "roughly halved"; and when distant metastases are present, long-term survival rates are less than 10%. In the case of melanoma, early detection is feasible and economic, as most melanomas may be detected by a simple but thorough skin survey.

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See also:

Melanoma Clinical Trials. M. D. Anderson *OncoLog*, Vol 45, No 5, May 2000

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Wright KL: Early detection of melanoma spread may increase survival benefits of adjuvant therapy. M. D. Anderson *OncoLog*, Vol 45, No 5, May 2000

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Virtual Colonoscopy a Potential Screening Reality

by Mariann Crapanzano

The image on the computer screen simulates the inside of a patient's colon, depicting haustral folds with alternating waves of shadow and light. It can be a still image or a fluid one, navigating through the straightaways and turns of the colon in what is known as a "fly-through sequence." Along the way, any intraluminal polyp or cancer that is detected appears as a three-dimensional rise in the bowel wall.

These irregularities in the wall are real, but the reality-based images are created with virtual colonoscopy, a technique that uses high-speed helical computed tomography (CT) of a patient's abdomen and pelvis to acquire axial scans, which can be reformatted into coronal and sagittal images as well as reconstructed into three-dimensional images of the colonic lumen. Still in its investigational stages, virtual colonoscopy appears to have promise as a screening device for adenomatous polyps and colon cancer.

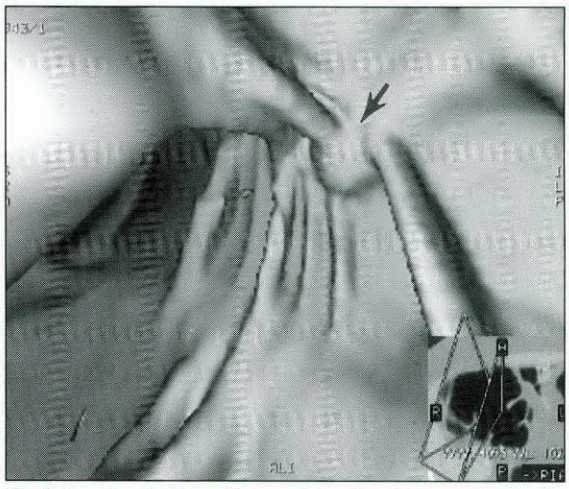
Professor Ronelle A. DuBrow, M.D., and Assistant Professor Revathy B. Iyer, M.D., both of the Department of Diagnostic Radiology at The University of Texas M. D. Anderson Cancer Center, are investigators in a multi-institutional trial to evaluate the use of virtual colonoscopy as a screening tool for average- or moderate-risk patients in a clinical setting. According to Dr. Iyer, each of the more than 1,000 patients in the study will undergo both a virtual and a conventional colonoscopy. The results of both tests will be compared, and the accuracy of the virtual colonoscopy will be determined by how closely its results match those of the proven conventional colonoscopy. A major focus of the study is determining the sensitivity of virtual colonoscopy for detecting colonic lesions, particularly those larger than 5 or 6 mm, which are at highest risk for being or developing into colon cancer, said Dr. Iyer.

During virtual colonoscopy, the bowel is distended by insufflating it with carbon dioxide or air. The CT scan then takes about 25 seconds, said Dr. Iyer. A radiologist interprets both the two- and three-dimensional images, which are preserved and can be reviewed by more than one person. Excluding the time needed to prepare the colon with laxative agents, the entire process can take less than an hour.

Because an endoscope is not used during the procedure, virtual colonoscopy is less invasive than conventional colonoscopy, and the patient does not have to be sedated, said Dr. DuBrow. Its potential as a screening tool, she said, is "to exclude polyps and cancers in asymptomatic patients, who will then not need to undergo conventional colonoscopy." Like conventional colonoscopy, virtual colonoscopy provides images of the entire colon, something that two methods currently being used for colon cancer screening—the fecal occult blood test and flexible sigmoidoscopy—cannot do.

However, the procedure has some limitations. The sensitivity and specificity of virtual colonoscopy as a population-wide screening tool have yet to be determined. Virtual colonoscopy does not allow direct endoscopic visualization of the intestinal lumen as conventional colonoscopy does and cannot always distinguish residual fecal material in the colon. And unlike conventional colonoscopy, said Dr. Iyer, abnormalities that are detected on virtual colonoscopy cannot be biopsied or removed during the procedure.

"I think virtual colonoscopy will be useful as a diagnostic tool, but obviously, it can't be therapeutic," said Sandeep Lahoti, M.D., an assistant professor in the Department of Gastrointestinal Medicine and Nutrition, "so if you do see a polyp or mass, the patient would have to be referred for conventional colonoscopy. The big question is going to be whether this is cost-effective."



Endoluminal views from virtual colonoscopy and computed tomography (inset) show a small polyp (arrow).

Despite this, Dr. Lahoti said that virtual colonoscopy "will probably play a big role in screening" in the future. Dr. DuBrow agrees. "The procedure has tremendous potential as a screening tool," she said. "If the test proves to be sensitive and specific, it could profoundly affect screening for the average-risk population over 50."

This is important because age-appropriate, population-wide colorectal cancer screening could help to dramatically reduce the morbidity and mortality from colon cancer. According to Bernard Levin, M.D., professor of medicine in the Department of Clinical Cancer Prevention and vice president for cancer prevention, colon cancer is unique in that it generally begins with a slow-growing, benign adenoma. Colorectal polyps that are precursors to cancer can be detected through screening and then removed during a conventional colonoscopic examination, thus preventing the development and growth of cancer.

Although the procedure has not yet been proven, Drs. DuBrow and Iyer believe that virtual colonoscopy has the potential to one day join available screening methods in helping to reduce the number of colorectal cancer deaths. ●

FOR MORE INFORMATION, *contact Dr. DuBrow at (713) 794-4539, Dr. Iyer at (713) 792-5043, Dr. Lahoti at (713) 792-2828, or Dr. Levin at (713) 792-3900.*

Cervical Cancer Prevention: Could Spectroscopy Steal the Spot"light"?

by Kerry L. Wright

A woman visits her local gynecologist for routine screening and by the time she leaves has received a diagnosis of cervical cancer and is ready to begin treatment. Fact or fiction? Fiction—for now, but this scenario could soon become reality if a new FDA-approved cervical cancer detection device proves effective in an ongoing clinical trial.

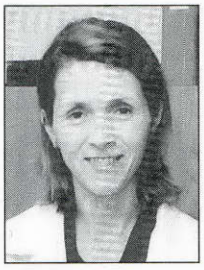
The new device, based on fluorescence and reflectance spectroscopy, will be evaluated for clinical performance, patient satisfaction, and cost-effectiveness in 1,800 women in British Columbia, Canada, and three Houston locations, including The University of Texas M. D. Anderson Cancer Center. If results prove promising, the spectroscope could one day join, or possibly replace, the Pap smear as the standard screening tool for cervical cancer.

"A patient has a Pap smear. They wait two weeks for the results, and they come in for a colposcopy and a biopsy. They wait two more weeks for those results, and then they get treated," explained Michele Follen, M.D., Ph.D., recipient of the Boone Pickens Distinguished Professorship for Early Cancer Prevention and a professor in the Department of Gynecologic Oncology at M. D. Anderson. "If you could use colposcopy and spectroscopy at the first visit and make a diagnosis with good reliability, then you could treat them at visit one instead of doing a screening Pap smear and colposcopically directed biopsies," said Dr. Follen, who is the principal investigator of the Houston portion of the trial.

Trey Kell, *a database coordinator, and* **Karen Rabel**, *an advanced practice nurse in the Department of Gynecologic Oncology, view data collected during a cervical screening examination using a spectroscopy probe.*

The device is being evaluated in two separate experiments: one tests it in a screening mode and the other in a diagnostic mode (in the colposcopy clinic). Each experiment is stratified for patient age and menstrual status. The flat probe is painlessly inserted into a patient's cervix, where it shines light and records fluorescence and reflectance data that are sent back to a computer for analysis.

The fluorescence component detects and allows evaluation of changes in chemical signals and the redox potential of the tissue, which are predictors of cancer.



Michele Follen, M.D., Ph.D.

Rebecca Richards-Kortum, Ph.D.

"The reflectance looks at light as it hits tissue and comes back, and it's really looking at how crumpled the chromatin is in the cells," said Dr. Follen. The more crumpled the chromatin, the more the light scatters and the less it reflects back. The more light the cervix reflects, the more likely it is to be cancerous.

Dr. Follen has been collaborating for nearly 10 years with Rebecca Richards-Kortum, Ph.D., an electrical engineering professor at The University of Texas who developed the probe and its algorithm while in graduate school at the Massachusetts Institute of Technology. The probe has already been used to detect cancers and precancers of the colon, head and neck, mouth, and bladder, and at least one company has already licensed the technique through a patent at The University of Texas. Dr. Follen and colleagues, however, are using the newest model and are the first to report its success and confirm its sensitivity and specificity in the cervix.

"Spectroscopy has a sensitivity between 85% and 90% and a specificity of 80%," said Dr. Follen. In comparison, the Pap smear and colposcopy have approximate sensitivities of 60% and 90% and specificities of 60% and 50%, respectively.

Preliminary analysis of the impact of the probe's increased specificity has shown that if the research-level device were used in conjunction with colposcopy in the United States today, it could save $625 million a year in unnecessary tests or treatments. The spectroscope can be made for as little as $3,500, making its use feasible not only in the United States but also in the Third World, where invasive cervical cancer rates are much higher than the 13,000 new cases reported each year in this country. ●

FOR MORE INFORMATION, *contact Dr. Follen at (713) 745-2564.*

HOUSE•CALL

Sharing Personal Stories: Books Written by People with Cancer

When you or someone close to you has cancer, support can come from many sources—family, friends, health professionals, clergy—but have you ever considered turning to a good book for help and comfort? Below is a list of personal stories—written by people who have experienced cancer—that offer inspiration, hope, and acceptance to those who read them.

Books by Writers

Survivor
by Laura Landro
A *Wall Street Journal* reporter and editor uses her journalistic training to research and understand her diagnosis of chronic myelogenous leukemia. As Laura Landro tells her story, she also teaches readers how to make informed decisions about their own treatment.

Dancing at the Edge of Life: A Memoir *by Gale Warner*
Poet and writer Gale Warner takes us on her 13-month journey with non-Hodgkin's lymphoma as she records her experiences in a journal and comes to terms with her disease and her own mortality.

A Whole New Life
by Reynolds Price
Southern novelist, poet, and writer Reynolds Price recounts his experience with cancer of the spinal cord, which has left him partially paralyzed. His tale begins before his initial diagnosis in 1984 and takes us through his inspirational recovery with the help of medicine, religion, and personal strength.

New York Times Bestsellers and Notable Books

Autobiography of a Face
by Lucy Grealy
Lucy Grealy's bone cancer was diagnosed before her 10th birthday and cured only after a third of her jaw was removed. This is her memoir of living with disfigurement, dealing with rejection from her peers, and striving for acceptance.

It's Always Something
by Gilda Radner
Gilda Radner, best known for her days as a young comedienne on *Saturday Night Live*, wrote this book after her ovarian cancer was diagnosed in the 1980s. Keeping her sense of humor throughout, Radner shares her perspective on life and cancer.

Books by Doctors

Healing Lessons *by Sidney J. Winawer and Nick Taylor*
In this book, a prominent cancer specialist must face his own wife's metastatic stomach cancer. It is the story of a doctor seeing cancer from a new perspective and of a woman desperately searching for a cure for her life-threatening illness.

Prostate Cancer: A Doctor's Personal Triumph
by Saralee Fine and Robert Fine
Dr. and Mrs. Robert Fine had been together for 40 years when Dr. Fine was told he had prostate cancer. This book recounts the couple's search for the appropriate treatment and includes a wealth of resources for accessing accurate medical information.

Other Suggested Titles

No Time to Die
by Liz Tilberis
Liz Tilberis, former editor-in-chief of *Harper's Bazaar*, gives us a behind-the-scenes look at the world of fashion magazines as she displays fierce determination in her battle with ovarian cancer.

That's Unacceptable
by Rebecca L. Libutti
First treated for a sinus infection, Rebecca L. Libutti later discovered that the cause of her debilitating headaches was a rare brain tumor called glioblastoma multiforme. Libutti tells an inspiring story of courage and survival in the face of a potentially terminal disease.

Cancer…There's Hope
by Richard and Annette Bloch
Richard Bloch, co-founder of the tax return preparation company H&R Block, Inc., tells his no-nonsense story of surviving lung cancer in the 1970s. The Blochs also emphasize the importance of having a positive mental attitude and obtaining the best medical care available. Copies of this title and other books by the same authors are available free from the R. A. Bloch Cancer Foundation (www.blochcancer.org) at 1-800-433-0464.

Most of the titles listed above, as well as many, many more, have been recommended by and are available through The Learning Center at The University of Texas M. D. Anderson Cancer Center. A list of books for children can be found on The University of Pennsylvania Cancer Center Web site, OncoLink (http://cancer.med.upenn.edu/). Additional titles can be found by calling the Cancer Information Service at 1-800-4-CANCER. ●

For more information, contact your physician or contact the M. D. Anderson Information Line:

(800) 392-1611 *within the United States, or*

(713) 792-6161 *in Houston and outside the United States.*

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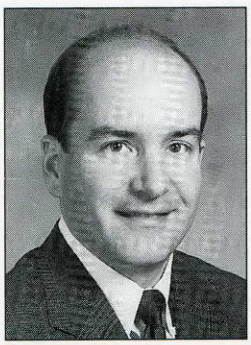
Treating Cancer with a Team Approach

David L. Callender, M.D.
Senior Vice President and
Chief Medical Officer



Fueled by research, new discoveries continue to increase our understanding of cancer and improve our treatment methods—from standard therapies such as chemotherapy, radiotherapy, and surgery to new approaches such as immunotherapy and gene therapy. Similarly, the tools of the pathologist and diagnostic imaging specialist are improving, allowing for earlier and more complete detection and diagnosis. Supportive care interventions for patients with cancer are also getting better and have become a major focus of cancer treatment centers today.

As our methods improve, however, the complexity of treatment grows. To achieve the best outcome, interventions must be carefully timed and monitored, and caregivers from all of the involved disciplines must communicate well and work together closely. This type of communication and cooperation among caregivers and with their patients is greatly enhanced when all are together at one site. The University of Texas M. D. Anderson Cancer Center helped pioneer the concept of multidisciplinary care under one roof over 50 years ago, and multidisciplinary care is now the principal model for cancer care at comprehensive cancer centers across the United States.

The benefits of effective multidisciplinary care are (1) a more complete evaluation, (2) precise diagnosis, (3) individualized treatment planning, (4) well-coordinated treatment delivery, and (5) appropriate and convenient posttreatment management.

At M. D. Anderson, we continue to refine our methods of providing multidisciplinary care to our patients. We now bring together physicians, nurses, and support personnel in Multidisciplinary Care Centers (MCCs), which focus on the patient and his or her particular cancer and associated problems. Team members evaluate the patient, perform sophisticated diagnostic testing in close consultation with pathologists and imaging specialists, and craft an individualized treatment plan. The MCC team then monitors all subsequent care of the patient.

While patients may receive treatment in different areas of the institution, the MCC is their home base for contact with their caregivers. As a result, the MCC team members and their patients get to know each other very well, and these relationships allow physicians to better serve the specific needs of their patients.

We believe disease-focused MCCs that allow for improved communication between the patient and the caregiver team and promote coordination and cooperation between specialists are even more necessary as new discoveries and new technologies improve our ability to treat patients with cancer.

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