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Cancer research news for clinicians

Cancer Prevention:

Meta-Analysis Of Randomized Trials Shows Aspirin Reduces Colon Polyp Recurrence

Regular aspirin use is associated with a statistically significant reduction in the development of colorectal adenomas, which are precursor lesions to colorectal cancer, in individuals at high risk of developing colorectal cancer.

Multiple lines of evidence, including data from randomized clinical trials, suggest that aspirin may reduce the risk of colon adenomas and perhaps cancer. A quantitative summary of the clinical data—and a more precise estimate of the magnitude of the benefit associated with aspirin use—has been missing.

Bernard Cole, of the University of Vermont performed a meta-analysis of all available randomized clinical trials that examined adenoma formation in participants assigned to regular aspirin use or placebo. The study was

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Breast Cancer:

Pregnancy-Associated Breast Cancer More Likely Diagnosed At Advanced Stage

Young women who develop breast cancer during their pregnancy, or who are diagnosed within one year of their pregnancy, have no difference in rates of local recurrence, distant metastases and overall survival compared to other young women with the disease, according to researchers at The University of Texas M. D. Anderson Cancer Center.

However, the largest single-institution study to look at pregnant breast cancer patients finds that women with Pregnancy Associated Breast Cancer (PABC), are more likely to be diagnosed later with advanced stages of the disease and, thus, have necessary treatment delayed.

The findings are published in the March 15 issue of the journal Cancer.

"Breast cancer in young women is a highly aggressive disease, and it's important that we study it in hopes of making a difference in terms of treatment," said Beth Beadle, a radiation oncology resident at M. D. Anderson and the study's first author. "When we looked at our young breast cancer population, a relatively large percentage had disease affiliated with pregnancy. We thought it would be really instructive to review our data to determine how we can best serve these women."

It's estimated that up to 3.8 percent of pregnancies are complicated by breast cancer, and approximately 10 percent of breast cancer patients under

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NSAIDs Associated With Cut In Risk Of Colon Adenomas

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published in the Feb. 10 issue of JNCI.

Among 2,698 participants who underwent colonoscopic follow-up after randomization, 37% of the participants assigned to placebo developed adenomas compared with 33% of those assigned to aspirin. Moreover 12% of the participants assigned to placebo developed advanced adenomas compared with 9% of the participants assigned to aspirin. The pooled analysis indicated that regular aspirin use resulted in an absolute risk reduction of 6.7% for developing adenomas relative to placebo.

"The substantial size of the relative reduction in risk seen in our analysis (28% for advanced adenomas) and seen in clinical trials that evaluated the effect of aspirin on colorectal cancer risk (26% reduction) indicates the potentially important health benefits of aspirin use," the authors write. "Of course, these benefits need to be considered in the context of all of the health effects of aspirin, positive and negative."

In a different, observational study, conducted at the end of a randomized placebo-controlled trial, researchers found that continued use of nonsteroidal anti-inflammatory drugs (NSAIDs) is associated with a reduction in the risk of developing colorectal adenomas, which are precursor lesions to colorectal cancer.

The randomized placebo-controlled Aspirin/Folate Polyp Prevention Study showed that regular use of low dose aspirin (81 mg) reduced the risk of colorectal polyp formation in individuals at high risk compared with placebo. To determine whether continued NSAID use might be beneficial, researchers invited the study participants to enroll in an follow-up study. This observational study examined their NSAID use and the risk of a diagnosis of colorectal adenoma at their next colonoscopy, on average 4 years after the end of randomized aspirin treatment.

John Baron, of Dartmouth Medical School, found that individuals who were initially assigned to low-dose aspirin in the randomized trial and continued to take NSAIDs four or more days per week during the follow-up period had a statistically significantly lower risk of adenomas than those who were assigned to placebo during the randomized trial and used NSAIDs less than two days per week during the observational study. The risk of adenomas among frequent NSAID users was 26.8 percent versus 39.9 percent among placebo subjects who later used NSAIDs sporadically.

"These findings imply that aspirin does not lose its antineoplastic properties over time and that these effects persist and may even be accentuated with prolonged NSAID use," the authors write.

Analysis Finds Exercise Lowers Colon Cancer Risk

An ambitious new study has added considerable weight to the claim that exercise can lower the risk for colon cancer.

Researchers at Washington University School of Medicine in St. Louis and Harvard University combined and analyzed several decades worth of data from past studies on how exercise affects colon cancer risk. They found that people who exercised the most were 24 percent less likely to develop the disease than those who exercised the least.

"What's really compelling is that we see the association between exercise and lower colon cancer risk regardless of how physical activity was measured in the studies," said lead study author Kathleen Wolin, a cancer prevention and control expert with the Siteman Cancer Center at Barnes-Jewish Hospital and Washington University. "That indicates that this is a robust association and gives all the more evidence that physical activity is truly protective against colon cancer."

Each year more than 100,000 people in the U.S. are diagnosed with colon cancer and about 40,000 are diagnosed with rectal cancer. The study suggests that

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if the American population became significantly more physically active, up to 24 percent, or more than 24,000, fewer cases of colon cancer would occur each year.

Wolin's report was published Feb. 10 online in the British Journal of Cancer. In the study, she and her colleagues gathered the results from all relevant studies published in English on the effect of physical activity on colon cancer risk.

They eliminated from consideration any studies that combined both colon and rectal cancer because exercise has not been shown to affect rectal cancer risk—including such studies would have led to an underestimation of the effect of exercise on colon cancer risk. In all, they analyzed 52 studies going back as far as 1984, making their analysis the most comprehensive to date.

They found that the protective effect of exercise held for all types of physical activity, whether that activity was recreational, such as jogging, biking or swimming, or job related, such as walking, lifting or digging.

"The beneficial effect of exercise holds across all sorts of activities," said Wolin, also assistant professor of surgery. "And it holds for both men and women. There is an ever-growing body of evidence that the behavior choices we make affect our cancer risk. Physical activity is at the top of the list of ways that you can reduce your risk of colon cancer."

The difference between people who were the most physically active and those who were the least varied from study to study in Wolin's analysis. As an example, in a 2007 study by Wolin and colleagues, women who walked the most realized a 23 percent reduction in their risk of colon cancer. Those highly active women walked briskly for five to six hours each week. By comparison, the women in that study who walked the least walked only a half hour each week.

Breast Cancer:

Diagnosis Is Often Delayed In Breast Cancer In Pregnancy

(Continued from page 1)

age 40 develop the disease during pregnancy, said the researchers. As the age for first and subsequent pregnancies increases and intersects with advances in imaging and screening, this statistic will only continue to climb, said George Perkins, associate professor in M. D. Anderson's Department of Radiation Oncology.

"Because we see care for large volume of patients who are young, as well as those who are young and pregnant, we wanted to see if there was something additive going on that is attributed to pregnancy, or if the response to treatment and behavior of the disease is a phenomenon of young age itself," said Perkins, the study's senior author.

For the retrospective study, Beadle, Perkins and their colleagues reviewed the records of 652 M. D. Anderson breast cancer patients, all were 35-years-old or younger at the time of diagnosis and treated at M. D. Anderson between 1973 and 2006. Of those women, 104 (15.6 percent) had PABC – 51 developed their cancer during their pregnancy and 53 developed the disease within one year post-pregnancy. Median follow-up for PABC patients compared to non-PABC patients was 95.5 months versus 91 months respectively.

When comparing the PABC and the non-PABC cohorts, the researchers found no statistical difference between the 10-year rates of: locoregional recurrence (23.4 percent, PABC; 19.2 percent, non-PABC), metastasis (45.1, percent PABC; 38.9 percent, non-PABC), or overall survival (64.6 percent, PABC; 64.8 percent, non-PABC).

"What we did find, however, is that women with PABC presented with more advanced disease, both in the breast and lymph nodes," said Beadle. "These women seem to have a significant delay in diagnosis, and their symptoms were not identified as breast cancer for an extended period of time – putting them at a disadvantage by withholding necessary treatment."

In an analysis of the 51 PABC patients who developed breast cancer during their pregnancy, 26 received some form of treatment; 25 received no therapy. Of those 25, 22 patients (88 percent) had disease symptoms that were not evaluated; three had a breast cancer diagnosis but were advised not to begin treatment until after delivery.

In PABC patients, the overall survival in those who received therapy was 78.7 percent, compared to 44.7 percent in those who receive none, though researchers caution that these statistics reflect a small sample size. Regardless, the researchers say it's important to note that there was no difference in the statistic by decade, reiterating there's still progress to be made in terms of diagnosing and treating the disease during pregnancy.

"Women really need to be aware of changes to their breasts that persist, even during pregnancy and to discuss these changes immediately with their doctor," said Perkins. "The study also proves that there's a vital opportunity for physicians to focus on complete breast care during a patient's pregnancy, and should include cancer as a possible diagnosis. Persistent

complaints should be monitored aggressively, with breast exams, imaging and biopsy, all being conducted as necessary."

50-Gene Set Identifies Known Types Of Breast Cancer

A set of 50 genes can be used to reliably identify the four known types of breast cancer, according to research conducted at Washington University School of Medicine in St. Louis and collaborating institutions.

Using this 50-gene set, oncologists can potentially predict the most effective therapy for each breast tumor type and thereby personalize breast cancer treatment for all patients.

"Unlike a widely used genomic test that applies only to lymph-node negative, estrogen-receptor positive breast cancer, this new genomic test is broadly applicable for all women diagnosed with breast cancer," said breast cancer specialist Matthew Ellis, a member of the Siteman Cancer Center at Barnes-Jewish Hospital and Washington University.

The study was reported Feb. 9 online in the Journal of Clinical Oncology.

Breast cancer results from genetic abnormalities in breast tissue, but not all breast cancers have identical genetic alterations. Ellis and his colleagues analyzed the gene activity of more than 1,000 breast tumors to identify and validate the genetic signature of each of the four types of breast cancer. Although the cancer types are distinguished by thousands of genetic differences, the researchers were able to narrow the list down to a set of 50 of these genes that could uniquely identify each type.

These tumor types have been previously defined and are known as luminal A, luminal B, HER2-enriched and basal-like.

The latter three types are generally considered types with a poor prognosis. Another genomic test commonly used in clinical practice, OncotypeDX, does not identify all four tumor types.

"Our test is the first to incorporate a molecular profile for the basal-like type breast cancers," said Ellis, professor of medicine in the Division of Medical Oncology at Washington University School of Medicine. "That's important because these breast cancers are arguably the most aggressive yet the most sensitive to chemotherapy.

"By identifying them we can ensure they are treated adequately."

Breast cancer experts typically also identify a fifth breast cancer type known as normal-like. The 50-gene set also recognizes the normal-like type. But the researchers found that instead of being a fifth type of breast cancer, the normal-like classification is an indicator that a sample contains insufficient tumor cells to make a molecular diagnosis and that a new sample needs to be taken.

In this study, the researchers also compared the activity of the 50-gene set to how well 133 breast cancer patients responded to standard chemotherapy. They found that their genetic test was highly sensitive and very predictive for chemotherapy response.

The test was more predictive than typically used clinical molecular markers such as estrogen receptor status, progesterone receptor status or HER2 gene expression status.

They found that luminal A was not sensitive to the chemotherapy, suggesting that patients with this good-prognosis type can forgo chemotherapy in favor of hormone-based therapy. They showed that among the poor-prognosis tumor types, basal-like breast cancer was the most sensitive to the chemotherapy and luminal B the least.

"Luminal B tumors are a very poor prognosis group, and none of the current conventional therapies are particularly effective against it," Ellis said. "The ability to identify luminal B tumors accurately makes it possible to develop better therapies for this type."

Ellis said more than 20 drugs are available to treat breast cancer. The researchers are now investigating how each tumor type responds to these drugs to help determine the best treatment for each. Their 50-gene set can be assayed in preserved tumor samples left over from standard diagnostic procedures, so the group plans to study tumor samples from breast cancer cases going back a decade or more.

Since the patients in these cases have already been treated, the researchers can relatively quickly discover how well various therapies worked for each breast cancer type.

The genomic test technology is patented and will be distributed through University Genomics, a company co-owned by Washington University, the University of Utah and the University of North Carolina. University Genomics is working with Associated Regional and University Pathologists Inc., a reference laboratory at the University of Utah, to provide a site where the 50-gene test will be available.

Ellis is one of the inventors of the test and holds patents for the technology.

Study Identifies Risk Factors To Predict Contralateral Cancer

A preventive procedure to remove the unaffected breast in breast cancer patients with disease in one breast may only be necessary in patients who have high-risk features as assessed by examining the patient's medical history and pathology of the breast cancer, according to researchers at The University of Texas M. D. Anderson Cancer Center.

Their findings, published in the March 1 issue of Cancer, may help physicians predict the likelihood of patients developing breast cancer in the opposite breast (contralateral breast cancer), stratify risk and counsel patients on their treatment options.

"Women often consider contralateral prophylactic mastectomy (CPM) not because of medical recommendation, but because they fear having their breast cancer return," said Kelly Hunt, professor in the Department of Surgical Oncology at M. D. Anderson and lead author on the study. "Currently it is very difficult to identify which patients are at enough risk to benefit from this aggressive and irreversible procedure. Our goal was to determine what characteristics defined these high-risk patients to better inform future decisions regarding CPM."

According to the researchers, approximately 2.7 percent of women diagnosed with breast cancer choose to have CPM. Recent statistics have shown that the rate of CPM in women with stage I-III breast cancer increased by 150 percent from 1998 to 2003 in the United States. Potential reasons breast cancer patients choose to undergo CPM include risk reduction, difficult surveillance and reconstructive issues such as symmetry and/or balance.

To begin to classify such risk factors, researchers reviewed the cases of 542 women with breast cancer only in one breast who received CPM to remove the second breast at M. D. Anderson from January 2000 to April 2007. Out of this group, 435 patients had no abnormal pathology identified in the opposite breast, 25 patients had contralateral breast cancer identified at surgery, and 82 patients had abnormal cells (atypical ductal hyperplasia, atypical lobular hyperplasia and lobular carcinoma in situ) that indicate a moderate to high-risk for breast cancer development in the contralateral breast found at the time of surgery.

Further analysis of the patients with contralateral breast cancer revealed that a five-year Gail risk of 1.67 percent or greater; an invasive lobular histology; and multiple tumors in the original breast were all strong predictors for contralateral breast cancer. Patient race, estrogen receptor status and progesterone receptor status were not associated with increased risk.

"We went from having very little information on the benefit of this procedure for individual patients to identifying three independent and significant risk factors," Hunt said. "Each provides valuable insight into how likely a woman is to develop the disease in her other breast and enables physicians to make an educated recommendation if a patient will potentially benefit from CPM."

The Gail model, typically used for patients without breast cancer, evaluates factors such age, age at menarche, number and findings of previous breast biopsies, age at first live birth and number of first-degree relatives with breast cancer, has been validated in several studies to calculate the risk of developing an invasive breast cancer over the next five years. The five-year risk of 1.67 percent is traditionally used as the cutoff point for the definition of "high risk."

"We've always known contralateral breast cancer risk is not the same for all women and it is unnecessary to perform preventive mastectomies routinely. As we begin to clarify the specific risk factors, the number of women undergoing CPM may decrease and those with a low to moderate-risk may be more open to less extreme options for risk reduction, such as hormonal therapy and newer agents for prevention of breast cancer."

Leukemia:
Two Drugs Combined Better Than One Alone, Study Finds

Researchers from the Children's Cancer Hospital at The University of Texas M. D. Anderson Cancer Center reported that two specific drugs combined appear to be five times more effective than either agent alone against leukemia in the prepublished online issue of BLOOD Jan. 30.

For the first time, the researchers showed that the novel proteasome inhibitor, NPI-0052, shares similar functions as the histone deacetylase (HDAC) inhibitor, vorinostat. These cross-over similarities between the two anti-cancer agents increased cell death in chronic lymphocytic leukemia five-fold in preclinical tests. For acute leukemia, the efficacy was even greater.

"Our previous research on cell lines showed us that NPI-0052 was stronger than other proteasome inhibitors in fighting leukemic cells," said Claudia Miller, first author of the paper and graduate student at M. D. Anderson through The University of Texas

Graduate School of Biomedical Sciences at Houston. "We wanted to improve the clinical efficacy of NPI-0052, so we started combining it with other agents and found that it was most potent when combined with HDAC inhibitors."

Joya Chandra, associate professor of Pediatrics and senior author on the study, worked with Miller analyzing the cause of the drugs' synergy in primary leukemia cells from human samples.

"We knew the two agents worked better together, but we were very surprised to find that the proteasome inhibitor and the HDAC inhibitor acted alike," Chandra said. "That's one of the reasons these two agents are so potent against leukemia."

The traditional role of proteasomes is to clean out mutated or damaged proteins within cells, which promotes cell growth and allows cancer cells to rapidly reproduce. Proteasome inhibitors, such as NPI-0052, block this process, resulting in apoptosis, or cell death, of the malignant cells.

HDAC inhibitors work by allowing DNA strands within a cell to uncoil, which influences gene expression of that cell. The expression or repression of the cell's genes tips the balance in favor of the cancer cell to undergo cell death or to stop growing.

In the study, Chandra found that the two agents overlapped in function when the HDAC inhibitor repressed the proteasome from acting, and the proteasome inhibitor modified a protein that binds to DNA. This, in turn, enabled the cancer cell's DNA to uncoil, allowing for gene expression that promoted cell death.

"Combining the two anti-cancer agents should allow clinicians to use a lower dosage of each drug, which hopefully will result in fewer side effects for the patient," Chandra said. "For pediatric patients in particular, the fewer side effects they have from treatment could mean a better quality of life as survivors in the long run."

NPI-0052 is currently being tested with solid tumor malignancies and recurrent lymphoma in Phase I human clinical trials at M. D. Anderson. A combination trial to test NPI-0052 with vorinostat is in the planning.

Lymphoma:
Rituximab Maintenance Improves Survival In Relapse

Patients with relapsed or refractory follicular lymphoma who continue on maintenance rituximab therapy after chemotherapy have better overall survival than patients who do not receive this treatment, according to a meta-analysis of randomized trials in the Feb. 10 online issue of the Journal of the National Cancer Institute.

Most patients with follicular lymphoma respond to initial therapy but many experience disease relapse. Previous trials have showed that rituximab plus chemotherapy improves overall survival in these patients compared with chemotherapy alone. However, it has not been clear if continuing rituximab treatment beyond the completion of chemotherapy further prolongs overall survival.

To determine the impact of maintenance rituximab on overall survival, Liat Vidal, of the Rabin Medical Center in Petah-Tikva, Israel, and colleagues pooled data from five randomized trials that compared maintenance therapy with no maintenance therapy. Overall survival data were available for 985 patients.

Rituximab maintenance therapy was associated with a 40% improvement in overall survival relative to observation or retreatment with rituximab at relapse. The improvement in overall survival was statistically significant for patients with relapsed or refractory lymphoma, but not for previously untreated patients. Patients treated with rituximab maintenance therapy, however, had nearly twice the rate of infection-related adverse events as patients who did not have prolonged rituximab therapy.

"Our results suggest that rituximab maintenance therapy for up to 2 years, either as four weekly infusions every 6 months or as a single infusion every 2 – 3 months, should be added to standard therapy of patients with relapsed or refractory follicular lymphoma after successful induction treatment," the authors write. "The higher rate of infections with rituximab therapy should be taken into consideration when making treatment decisions."

Endometrial Cancer:
Shorter Hospital Stay After Robot-Assisted Surgeries

Patients with endometrial cancer who have minimally invasive robotic-assisted hysterectomies tend to have quicker surgeries and shorter hospital stays compared with patients who have similar laparoscopic surgical procedures, according to new research from The Ohio State University Comprehensive Cancer–James Cancer Hospital and Solove Research Institute.

Until now, little data existed to confirm the benefit of minimally invasive robotic-assisted surgery for

patients with endometrial cancer, also known as uterine cancer.

The findings are published online in the journal Gynecologic Oncology, and presented during a national meeting of the Society of Gynecologic Oncologists Feb. 5-8 in San Antonio, Texas.

The study analyzed the results of surgeries for 105 patients conducted at The James between March 2006 and April 2008 using the da Vinci robot, compared to 76 patients who received minimally invasive laparoscopic surgery for uterine cancer, said principal investigator Jeffrey Fowler, director of the Division of Gynecologic Oncology and chief of staff at The James.

"Our study found that robotic hysterectomy and lymph node removal for uterine cancer results in shorter hospital stays and faster overall recovery with fewer complications compared with laparoscopic surgery," said Fowler, who also is a researcher at Ohio State's Comprehensive Cancer Center. "While this is still a major surgery, robot-assisted minimally invasive methods can greatly reduce blood loss, pain and scarring and risk of infection. We can now also use the technology in heavier patients."

Fowler and his colleague David Cohn were among the first surgeons nationwide to be certified to perform minimally invasive robotic-assisted surgery on patients with gynecologic cancer. Fowler and Cohn, who both specialize in gynecologic oncology, are routinely using robotic instrumentation to perform hysterectomies and lymph node dissections for treating uterine cancer, and they train other surgeons in the technique.

For years, robotic-assisted surgery has been used in heart and prostate surgeries. In 2005, the Food and Drug Administration approved the minimally invasive technique for treatment of gynecological disorders, including hysterectomies (removal of the uterus) and myomectomies (removal of uterine fibroids). Typically, these procedures have required large abdominal incisions that result in more blood loss and longer hospital stays and recovery times, said Fowler.

Minimally invasive laparoscopic surgery is less invasive than open abdominal surgery. A laparoscope viewing tube is inserted into the abdomen through a small incision, allowing the surgeon to examine the abdominal and pelvic organs on a video monitor. Other small incisions are made to insert instruments to perform procedures.

Doctors began using laparoscopic surgery in 1993 to treat early stage uterine cancer. The benefits of a laparoscopic approach are lower blood loss and transfusion rates, shorter hospital stay, faster post-operative recovery and superior short-term quality of life. However, laparoscopic surgery usually requires longer operations and a steeper learning curve for surgeons compared to robotic-assisted surgery, particularly among obese patients.

Lymph nodes are also removed during the procedure and examined for the presence of cancerous cells to help determine whether the cancer has spread. This procedure can be accomplished using both minimally invasive surgical techniques, but is more difficult during laparoscopic surgery, Fowler said.

"Typically, patients with uterine cancer tend to be overweight or obese with high blood pressure and diabetes, and therefore are at greater risk for post-surgical complications, especially wound healing," said Fowler. "Our study showed that overweight or obese patients can benefit most from this approach.

"We have found that robotic-assistance enables greater precision during surgery," Fowler said. "When it comes to treating patients with uterine cancer, this is now the procedure of choice in our practice."

Cervical Cancer:
Cervix Moves Significantly During Radiation for Cancer

Radiation and gynecologic oncologists at the Moores Cancer Center at the University of California, San Diego are concerned that many women with cervical cancer may not be receiving the optimal dose of radiation during treatments specific for the shape of the tumor because the cervix may be moving too much.

They recommend that radiation oncologists need to take such movement into account to make sure the cervix remains in the treatment field.

The team presented its findings, the first to look at cervix movement during radiation therapy, on Feb. 6 at the Society of Gynecologic Oncologists' annual meeting on Women's Cancer in San Antonio.

The researchers found that the cervix moved significantly more than previously thought during radiation therapy, possibly affecting treatment. As a result, radiation oncologists may have to spare less healthy tissue than they would like to effectively treat the cancer.

According to Catheryn Yashar, assistant professor of radiation oncology at the UC San Diego School of Medicine and chief of breast and gynecological radiation services at the Moores UCSD Cancer Center, who led the work, one of the difficulties in using radiation in treating cervical cancer is that the cervix frequently

moves during and between treatments. This may be caused by the bladder filling, pockets of gas in the rectum and tumor shrinkage as the therapy progresses, making treatment planning difficult when using precise radiation therapy such as IMRT (intensity modulated radiation therapy).

To determine how much the cervix was moving during radiation therapy, Yashar monitored 10 patients diagnosed with cervical cancer between 2007 and 2008. All patients had two cervical "seeds" placed, which enabled images to be taken of the cervix. Yashar's team looked at more than 500 scans, or 50 per patient. While the researchers found that cervical movement during and between treatments may average from 2 to 5 millimeters, they were surprised to find that the cervix moved in some cases as much as 10 times more, or 2 centimeters, between and even during daily treatments.

"The study implies that you have to be very careful from the beginning to the end of treatment," Yashar said. "To account for movement and to be sure the cervix is in the treatment field, you have to either give large treatment margins, which decreases the sparing of normal tissues, like bladder and rectum, or you have to use image guidance. Image guidance monitors the position of the cervix and signals when changes in the radiation treatment plan are necessary."

IMRT can be effective in treating cervical cancer, and compared to irradiating the entire pelvis, it can potentially spare surrounding structures, such as the bowel and bladder, from radiation, Yashar said.

"What is unique with this study is that we use two gold seeds as surrogate markers for the cervix and performed daily imaging both before and after treatment. That shows us not only the movement of the cervix between Monday and Tuesday but also between the beginning and end of treatment. It's not the average daily motion, but rather the maximum motion that is the most important.

"We need research to be able to predict which patient's cervix might move 2 cm during treatment. We have to go back and look at those patients who have the maximum movement during treatment and see if we can figure out why that is and predict it."

NCI Cooperative Group, Cancer Center Trials Listed

The National Cancer Institute's Cancer Therapy Evaluation Program approved the following clinical research studies last month. For further information, contact the principal investigator listed.

Phase I

8190, A Dose Ranging Trial of Adenovirus CCL-21 Transduced MART-1/gp100 Peptide-Pulsed Dendritic Cells Matured Using Cytokines for Patients with Chemotherapy-Resistant Metastatic Melanoma. Moffitt Cancer Center and Research Institute, Weber, Jeffrey, (813) 745-2007.

Phase II

8209, A Phase II Study of Sequential and Concurrent Chemoradiation for Patients with Advanced Nasopharyngeal Carcinoma. Stanford University, Colevas, Alexander, (650) 724-9707.

ADVL0821, A Phase II Study of IMC-A12 (Anti-IGF-I Receptor Monoclonal Antibody) in Children with Relapsed/Refractory Solid Tumors. Children's Oncology Group, Weigel, Brenda, (612) 626-5501.

E6508, A Phase II Study of L-BLP25Æ and Bevacizumab in Unresectable Stage IIIA and IIIB Non-Squamous Non-Small Cell Lung Cancer After Definitive Chemoradiation. Eastern Cooperative Oncology Group, Patel, Jyoti, (312) 695-4549.

S0802, A Randomized Phase II Trial of Weekly Topotecan with and without AVE0005 (Aflibercept) in Patients with Platinum Treated Extensive Stage Small Cell Lung Cancer. Southwest Oncology Group, Jahanzeb, Mohammad, (901) 722-0532.

S0919, A Phase II Study of Idarubicin and Ara-C in Combination with Pravastatin for Relapsed Acute Myelogenous Leukemia. Southwest Oncology Group, Advani, Anjali, (216) 445-9354.

Phase III

E2905, Randomized Phase III Trial Comparing the Frequency of Major Erythroid Response to Treatment with Lenalidomide (RevlimidÆ) Alone and in Combination with Epoetin Alfa (ProcritÆ) in Subjects with Low- or Intermediate-1 Risk MDS and Symptomatic Anemia. Eastern Cooperative Oncology Group, List, Alan, (813) 745-6086.

Other

AOST08B1, Retrospective Study of Genetic Risk Factors for Osteosarcoma. Children's Oncology Group, Savage, Sharon, (301) 496-5785.

SWOG-S9313B-ICSC, Evaluation of the Expression of the Cancer Stem Cell Marker ALDH1 as a Predictor of Adjuvant Chemotherapy Response in Breast Cancers of High Risk Women in SWOG-9313. Southwest Oncology Group, Hayes, Daniel Fleming, (734) 615-6725.