Dr. Jim Evans and his "Ode of a Geneticist"

Dr. Jim Evans, associate professor of medicine and leader of the Lineberger Cancer Genetics program, spoke at the Lineberger Club meeting. He ended his talk with a poem he wrote for the occasion:

Like Columbuses of latter day
We chart the genome's DNA
We splice, we snip, we recombine
On risks of cancer, boldly opine

Perhaps with the Tarheel basketball team
We could tweak a chromosome or splice a gene
To make a eugenic team of dreams
Coached by a young clone of Dean's

But genetics has its darker side
For if the wrong experiment's tried
We might end up with a player or two
Who bleeds a deeper shade of blue...

As his patron, Michelangelo
Had the Medicis long ago
And backing Walter Raleigh's team
Was fair Elizabeth, England's Queen
Vasco de Gama had the King of Portugal
But we lucked out ...We have you all

The future of medicine, pundits say
Lies within our DNA
But without you our noble mission
Would be forlorn, an empty vision

So, from gene and cell and chromosome,
We wish to make our thanks well known,
We sing your praises on this special day,
From the bottom of our DNA

calendar of events

JUNE

9th **Susan G. Komen Breast Cancer Foundation NC Triangle Race for the Cure.** Raleigh, NC.

SEPTEMBER

20th **Pink Ribbons Project Dancers in Motion Against Breast Cancer Performance/ Benefit.** Carolina Theatre, Durham, NC.

OCTOBER

5th **Board of Visitors Meeting.** Lineberger Cancer Center, Chapel Hill, NC.

13th **Patient/Family Symposium.** Friday Center, Chapel Hill, NC.

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UNC Lineberger Comprehensive Cancer Center

Cancer Lines

University of North Carolina School of Medicine & UNC Hospitals

Spring 2001

UNC LINEBERGER COMPREHENSIVE CANCER CENTER

the inside line . . .

More Effective Mammography: Is Digital the Answer?

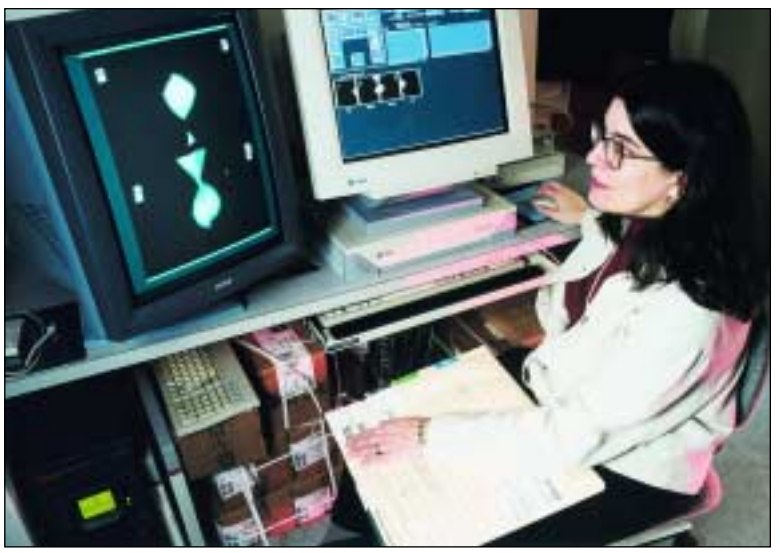
"Physicians have been using X-rays to detect breast cancer for years," notes Etta Pisano, professor of radiology and director of breast imaging at the UNC Lineberger Comprehensive Cancer Center. Studies have shown that between 80 and 90 percent of malignancies are visible on mammography. "It would be foolish to supplant a technology that's known to reduce breast cancer mortality."

But Pisano and her colleagues are working with a technology that might further reduce mortality and potentially improve the early diagnosis of breast cancer—digital mammography.

Current technology misses some 15,000 to 45,000 breast cancers in the more than 32.5 million mammograms performed annually in the United States. Prior studies and early clinical experience have shown that digital mammography offers better visibility, particularly near the skin line and the chest wall, and in dense breast tissue.

The digital mammography machine used at UNC, in addition to easier detection and better imaging, can reduce exam time by half that of traditional film-based mammograms. Improved images also may eliminate many of the call-backs necessary with traditional mammography.

That's important because approximately one in eight



Dr. Etta Pisano views a digital mammogram.

American women will develop breast cancer in her lifetime. With more than 180,000 cases diagnosed each year, it's the second most common cancer in women after skin cancer and the leading cause of cancer death among women 40 to 55. According to the American Cancer Society, the 5-year survival rate after treatment for localized breast cancer is

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Colon Cancer Screening: Not As "Accepted" By Public, But Vital and Effective

"All adults over age 50 are at sufficient risk for colorectal cancer to warrant screening," says Michael Pignone, Assistant Professor of Medicine in the Division of General Internal Medicine. "While some groups are at higher risk because of a family history of colorectal cancer or the presence of inflammatory bowel disease, the absence of a high-risk condition does not mean that one is at low or no risk."

According to the American Cancer Society, an estimated 47,700 people died of colon cancer in 2000, the third most common cancer in men and women. When detected in an early, localized stage, the 5-year relative survival rate is 90 percent; however, only 37 percent of colorectal cancers are discovered at that stage.

Early detection is critical. After the cancer has spread to adjacent organs or lymph nodes, the rate drops to 65 percent or to 8 percent in patients with distant metastases. Despite that, only 25-35 percent of adults have had a screening test recently for colorectal cancer. "The low rates of screening are a consequence of poor communication," Pignone notes. "Many patients do not realize they are at risk and many providers do not routinely offer screening to patients over age 50." And many people don't have access to regular, affordable health care, so they don't have the opportunity to be screened.

"Another reason may be apathy," adds David Ransohoff, professor of medicine, Lineberger member and an epidemiologist. "For reasons we don't fully understand, colorectal cancer screening is much less popular, or 'accepted,' by the public than, say, screening for prostate cancer, or mammography for women 40-49, even though the evidence is strong that colorectal cancer screening reduces mortality and has very few side-effects."

For all these reasons, researchers at UNC are engaged in a number of initiatives to increase screening for colorectal cancers and improve prevention. "This is a point of emphasis for North Carolina and its advisory committee on cancer control and coordination," says Dr. Joseph Pagano, Director Emeritus and chair of the state committee.

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Director's Message

Dr. Shelton Earp

What do a digital camera and the Trojan horse have in common? They're both prototypes for new technology to help make cancer diagnostic tests and therapies more precise. UNC Lineberger is a leader in meeting this challenge.

To make one of the tests that diagnose breast cancer more precise, Dr. Etta Pisano is pioneering a promising new technology called digital imaging. This process uses a computer image of the breast rather than a film x-ray. The new technology is the same as that used for digital cameras. This advance means potentially better images and information. For patients it means less radiation since additional views aren't necessary: the image captured by the computer can be manipulated and re-examined by the radiologist.

To answer definitively whether digital imaging is superior to film x-ray at detecting breast abnormalities, Dr. Pisano will lead a 19-center three-year study funded by the National Cancer Institute involving 49,500 women. The $27 million grant is the largest ever awarded to a radiologist.

In related news, Dell Computer and Microsoft have made a gift of 100 high-end computers and software to be used in parallel computation by Dr. Julian Rosenman in his quest to obtain faster and more accurate 3-dimensional images of a particular tumor. This will allow precise focusing of multiple radiation beams converging on the tumor while sparing normal tissue. Julian's and Etta's work are both results of the highly successful collaborations with UNC's internationally renowned computer science department. Such collaboration and teamwork are the hallmarks of a multidisciplinary cancer program at a great university.

On another front, ideal cancer therapy targets tumor cells while sparing healthy ones. But how do you sneak the therapy into cells but only have it attack the cancer cells? Pack the therapy in a genetically altered cold virus—a Trojan Horse—that can multiply in a cancer cell. Dr. Dell Yarbrough is doing just that with a new therapy for head and neck cancers. He is using a cold virus to deliver therapy that will only be amplified in cells carrying a mutated protein, the kind found in certain cancers. Modifications in this delivery approach are being developed in Dr. Yarbrough's lab for a second generation of clinical trials.

We're teaming up with the new UNC Genomics program led by Dr. Terry Magnuson and will tell you more about this new Carolina initiative in the next issue of *Cancer Lines*. In the meantime, enjoy a wonderful summer: please remember to wear sunscreen.

UNC LINEBERGER COMPREHENSIVE CANCER CENTER

UNC Lineberger is designated a comprehensive cancer center by the National Cancer Institute.

Cancer Lines is a semi-annual publication of the UNC Lineberger Comprehensive Cancer Center, The University of North Carolina School of Medicine at Chapel Hill.

Dr. H. Shelton Earp, III, Director
Dr. Joseph S. Pagano, Director Emeritus
Dianne G. Shaw, Director of Communications/Executive Editor
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Colon Cancer

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(Left to right) *Drs. Michael Pignone, David Ransohoff and Robert Sandler.*

At UNC, Pignone and others developed and tested a video-based decision aid for patients that informs them about the options for screening and helps them discuss screening with their doctors. The study, one of the largest trials ever done on the effectiveness of decision aids in real clinical practices, found that the video increased screening rates significantly. The test was so successful they are developing a similar program for the Web that they plan to test next year.

Additionally, the Internal Medicine clinic has instituted a reminder system for patients undergoing fecal occult blood testing. The system has increased return rates by 10-15 percent over baseline.

Research shows that five simple activities can lower the risk of colon cancer by as much as 70 percent, according to Robert Sandler, professor of medicine and co-director of UNC-CH's Center for Gastrointestinal Biology and Disease and Linberger member. To reduce colorectal cancer people should:

- Avoid obesity
- Engage in regular physical activity
- Limit alcohol consumption and don't smoke
- Eat a sensible diet high in vegetables and fruit and low in red meat
- Consider using supplements of calcium and folic acid

Taking calcium or folic acid supplements can reduce polyps from which it's estimated 90 percent or more of colon cancers evolve. In a 1999 national study, Sandler and his colleagues found that calcium supplements moderately reduce the risk of recurring polyp growth in the colon and may reduce the risk of colon cancer.

Researchers found overall a 24 percent decrease in the number of polyps and a 19 percent decrease in the risk of polyp recurrence.

Approximately 20 epidemiologic studies have found that people who regularly use aspirin and other non-steroidal anti-inflammatory drugs have 40 to 50 percent lower risk of colorectal cancer and adenomatous polyps.

However, no randomized trials have yet proven that aspirin-like drugs cause this reduction. Two studies, funded by the National Cancer Institute, are underway at UNC to determine the link.

Sandler and others also are working on a population-based study to determine the impact of risk factors, access to health care and insurance and poverty on colon cancer mortality rates; and a study on diet and its effect on the colon's lining.

Approaching colon cancer prevention and screening from several disciplines results in more comprehensive research and clinical treatment. "Multidisciplinary collaboration is important because it unites people with different types of expertise to work together to solve a problem. To best tackle colon cancer screening and prevention, we need expertise in psychology, health education/behavior change, epidemiology, physician learning, gastroenterology, information sciences and oncology," Pignone concludes. "Lineberger helps us do that."

Scrapbook

Lineberger Fellows. Six Lineberger fellows were honored for demonstrated excellence in research. The Board of Visitors began the program in 1987 to promote and encourage graduate students to pursue cancer research. The fellowships are made possible by Best Distributing Company in Goldsboro; the Cancer Resesearch Foundation of America in Arlington, VA; and Mr. and Mrs. Sanford Doxey, Jr. of Wilmington. *Pictured (left to right):* Helena Furberg–public health science, preceptor Dr. Robert Millikan; Jennifer David Peck–public health science, preceptor Dr. Barbara Hulka; Nathan Felix–laboratory science, preceptor Dr. Jenny Ting; Susan Steck-Stoff–public health science, preceptor Lenore Arab; Wolfgang Resch–laboratory science, preceptor Dr. Ron Swanstrom; and Betty P. Liu–laboratory science, preceptor Dr. Keith Burridge.

Seed Grant Recipients. UNC Lineberger Seed Grant recipients were honored at a recent Board of Visitors meeting. *(Left to right) back row:* Dr. David Ollila; Dr. Jozef Spychala; Dr. Shelton Earp, Center director; Dr. Beverly Mitchell, Center associate director; *front:* Dr. Carol Shores; Dr. Valerie Murrah and Dr. Bill Funkhouser. The grants support new and growing UNC-CH research projects in innovative areas. The grant program helps launch smaller projects that could lead to more in-depth studies in the future. The grants were made possible by: the Schechter Foundation, the Brody Brothers Foundation and the Felix Harvey Foundation, all of Kinston; the Foundation for the Carolinas of Charlotte; the A.E. Finley Foundation Inc. of Raleigh; the Cemala Foundation Inc. and the Hillsdale Fund Inc., both of Greensboro.

Tomlinson Lab Continues Tradition

Larry and Sarah Tomlinson of Charlotte are not your ordinary Carolina couple. Like many alumni, they were both born and raised within a few miles of Chapel Hill and have parents, siblings, and now children, who attended UNC. While at UNC Mr. Tomlinson played on the tennis team and was a member of the SAE fraternity, and he is a member of Carolina Living Legends. The Tomlinsons have been lifelong supporters of the place that is so near to their hearts, but their roots here at the University run much deeper. Mrs. Tomlinson's grandfather was Dr. Francis P. Venable, chemistry professor and then president of the University from 1900 to 1914, who was instrumental in laying the solid foundation on which UNC has built its scientific research programs.

Mr. and Mrs. Tomlinson have been very active supporters of UNC for many years. However, it was not until Mr. Tomlinson's brother, Carroll, was diagnosed with prostate cancer in 1983 that they were introduced to the Lineberger Comprehensive Cancer Center. In 1985, after Carroll Tomlinson lost his life to cancer, the Tomlinsons joined the Center's Board of Visitors and the fight against this disease.

The Tomlinsons' most recent gift will benefit UNC's scientific community. Their generous gift to the University is a charitable remainder trust, which has funded the Larry and Sarah Tomlinson Lab in the Lineberger Comprehensive Cancer Center.

The Lab will be home to Dr. Terry Van Dyke and her team of 20 scientists. Dr. Van Dyke is director of the Animal Models Core here at UNC and is co-chair of the National Cancer Institute's Mouse Models of Human Cancer Consortium. One of the main projects in her lab is the development of mouse models that produce human cancers, such as breast and prostate cancer, and lymphoma.

The Tomlinson Lab is the result of one of many different kinds of planned gifts. Gifts to Lineberger can be made in forms from property to stocks, retirement plan assets to trusts. Although donations of outright gifts such as cash and property are fairly simple, the benefits of making gifts such as annuities and trusts can be attractive options. Depending on which type of planned gift one chooses, tax benefits can be immediately realized or they are delayed to benefit one's heirs. Gifts can be designed so that income payments from an investment benefit Lineberger while ownership of the asset is retained (a charitable lead trust), or so that the property is transferred to Lineberger but a beneficiary receives a predetermined income payment from the trust, as is the case with the Tomlinsons' charitable remainder trust.

The array of gift planning opportunities available does cover a wide assortment of options. For more information on planned gifts for Lineberger, please call the Development Office at (919) 966-5905 to request information. Though the benefits are different for the various types of planned gifts, the one constant is the benefit of helping the clinicians and scientists at Lineberger work toward a cure for this disease that touches all our lives.

Profile

Trailblazer in Mouse Model Research

Terry Van Dyke didn't *always* want to be a cancer researcher. "When I was 5, I decided I wanted to be a nurse," recalls the professor of Biochemistry and Biophysics at UNC. "But in my spare time, I wanted to be a cowgirl. My mom says that kids from the neighborhood used to come around our house and ask for 'Dale.' I had told everyone my name was Dale Evans!"

Encouraged by an inspirational biology teacher in 10th grade, Van Dyke let go of her nursing and cowgirl aspirations and decided to pursue molecular biology. "Asking questions and getting answers through experimentation has always been fascinating to me," she says. "I've always loved trying to figure things out."

Van Dyke received her BS and PhD in molecular biology from the University of Florida. She did her post doc work at the University of New York at Stony Brook with Arnold J. Levine and then followed Levine to Princeton. In 1986, she got the opportunity to run her own laboratory at the University of Pittsburgh—where she stayed for 7 years and earned tenure.

"When you start your lab, you have to be very focused, like a horse with blinders," she recalls. "About the time I got tenure is when I took a deep breath and asked myself 'now what do I want to do?' There weren't many people at Pittsburgh at that time doing what I was interested in, so my husband (Jude Samulski, director of the UNC Gene Therapy Center) and I started looking around and were attracted to the intellectual climate at UNC. We've been here about seven and a half years now."

Van Dyke continues to pursue her love of figuring things out through her research in cancer cell biology. "As a researcher, the thing that's fascinating about cancer is that it's not a single disease, but hundreds of diseases and it takes different things for different cells to become a cancer," she explains. "What we'd like to understand is exactly what goes wrong in the cells so that people who do drug design can actually develop ways to inhibit the cancers."

Currently, Van Dyke and her team are developing a therapy by genetically manipulating mice. "You can do in the mouse pretty much what you can do in a test tube," she says. "You can go in and alter a specific gene and say 'what happens if I make this alteration?' Things you see happening in human cells you can mimic in the mouse and ask 'does it really lead to cancer?'"

The problem with cancer research in humans is that scientists study the disease after the fact and cannot establish cause and effect relationships.

"That's why our mouse model studies are so cool," Van Dyke says. "The technologies have developed tremendously over the last 20 years and it's just exhilarating the different kinds of things we can do."

As a professor, wife and the mother of two teenagers, she admits she doesn't have a lot of spare time. "But I do enjoy playing tennis, reading, and the occasional artsy-craftsy project." Van Dyke is also currently co-chairing a national consortium funded by the NCI and has been very involved in trying to build the field of genetics at UNC. "I guess you could say my days are pretty jam-packed!"

Briefs

Study offers new evidence that garlic protects against cancers

A new study at UNC by Lenore Arab and colleagues shows that people who consume raw or cooked garlic regularly face about half the risk of stomach cancer and two thirds the risk of colorectal cancer as people who eat little or none.

Their study was a meta-analysis, a mathematical combination of numerous other studies to develop a clearer picture of such issues as cancer and heart disease. The group reviewed 300 scientific papers related to diet and cancer and then combined and analyzed data from 22 describing the best, most relevant human research related to garlic from around the world.

Previous research has shown that a compound in garlic called allium partially protects animals against cancer, and some scientists believe it has the same effect in humans. "After controlling for various risk-factors, we found that when we pooled the results, this preventive effect was largely confirmed," says Lenore Arab, professor of epidemiology and nutrition at the UNC-CH schools of public health and medicine and Linebeger member. "We didn't have enough information to be able to say the same about garlic's possible effects on other forms of cancer."

Researchers could not show similar benefits from taking garlic supplements, possibly because the active ingredients are destroyed by processing or by sitting on store shelves for a long time. "Many scientists believe garlic helps prevent stomach cancer because it has anti-bacterial effects against a bacterium, Helicobacter pylori, found in the stomach and known to promote cancer there," Arab says.

Study shows why muscle decays mysteriously in cancer, AIDS and other illnesses

Scientists at UNC-CH's Lineberger Comprehensive Cancer Center believe they have discovered a major reason why muscles often decay in patients with cancer, AIDS, late-stage heart disease, severe burns and numerous chronic diseases. Their research focuses on cachexia, an important syndrome that could lead to an effective treatment for the condition.

The new study shows that cachexia, which kills an estimated one third of cancer patients, results from activation of a factor, NF-kappa B. This natural substance attaches to DNA inside cell nuclei and turns genes on and off like a switch. In this instance it prevents expression of a key regulatory protein called MyoD from replenishing muscle tissue as it does in healthy people.

"Cancer cachexia, which causes patients to literally waste away, has been documented for at least 100 years, but it wasn't until about 20 years ago that researchers discovered a cytokine protein called tumor necrosis factor and that the factor could elicit cachexia," notes postdoctoral fellow Denis Guttridge. "What we have done is to identify a key part of what's happening mechanistically inside muscle cells to cause cachexia."

"Since we now know how to inhibit NF-kappa B, this will lead to therapies for reducing cachexia, which may well lead to significant improvement in the quality of life of patients who have chronic diseases like cancer and AIDS," Guttridge says.

Studies plumb tumor resistance to treatment

Cancer tumors with cells low in oxygen often survive and continue to grow despite the treatments thrown at them. Mahesh Varia, professor of radiation oncology at UNC-CH and a Lineberger member, has developed a method of identifying these hypoxic tumors which may lead to a greater understanding of treatment resistance and help doctors more effectively predict the outcome of cancer therapies.

James Raleigh, professor of radiation oncology and Lineberger member, invented the one clinically advanced method, the pimonidazole hypoxia marker, that identifies tumor hypoxia at the cellular level. "We spent a number of years proving it in the laboratory and with animals in a veterinary setting

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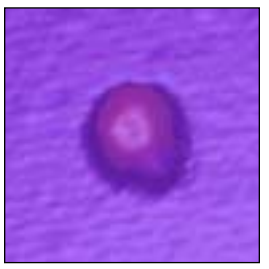
New Studies for Head and Neck Cancers

Dr. Dell Yarbrough examines a patient for the clinical trial.

Cancers of the head and neck are the fifth-most common in the U.S. with 65,000 new cases and 18,000 deaths annually. Tobacco and ethanol use and abuse account for 75 percent of these cancers. The standard therapy for early cancers is surgery or radiation therapy alone; advanced tumors are treated with combination therapy (either surgery plus radiation or radiation plus chemotherapy).

One promising new treatment involves the cancer-killing adenovirus CI-1042 (also known as ONYX-015). This is a souped-up cold virus designed to infect and selectively destroy cancer cells. In February, researchers in the UNC Multidisciplinary Head and Neck Oncology Program embarked on a clinical trial using the oncolytic virus to treat recurrent head and neck squamous cell carcinoma.



Atomic-force microscope image showing DNA unfolding out of an adenovirus. PHOTO COURTESY OF ATSUKO NEGISHI, UNC PHYSICS AND ASTRONOMY.

Adenoviruses are 20-sided viruses that contain DNA and replicate by rupturing the host cell's membrane, killing the host cell and releasing new viral particles. Normal cells can deactivate the virus using the p53 protein. This important cell regulator (p53) is lost in 50 percent of head and neck cancers meaning that the cancer cells can no longer protect themselves from the virus.

"Since cancer cells are the only cells within the body that have altered p53 activity this virus (CI-1042) selectively kills cancer cells while sparing their normal neighbors," explains Dell Yarbrough, assistant professor, Otolaryngology/Head and Neck Surgery and Biochemistry and Biophysics. Dr. Yarbrough is a long-term Chapel Hill resident, having arrived as a Morehead scholar and subsequently graduated from UNC's medical school and housestaff training program.

This trial further investigates the use of chemotherapy alone versus chemotherapy plus CI-1042. "Earlier trials have shown that 60 percent of previously treated cancers will respond to the combination of CI-1042 and chemotherapy," Yarbrough says. Research studies also suggest that adenovirus and chemotherapy may have synergistic anti-tumor activity.

Additionally, there was no increased chemotherapeutic toxicity associated with the addition of the adenovirus. "The adenovirus can be associated with transient fevers and chills (flu like symptoms), but in general the chemotherapy side effects are not increased by addition of the adenovirus", Yarbrough says. That could mean a more effective treatment and increased survival rates.

In addition to the ONYX-015 trial, the program team is actively involved in developing organ preservation protocols (primarily for tongue and larynx cancer using a combination of chemotherapy and radiation therapy.

"We are also evaluating whether or not sentinel node technology is accurate to predict cervical metastasis in head and neck cancer," Yarbrough says."The advantage of sentinel node biopsy, if it proves to be accurate, would be that by removing only one or a few lymph nodes from the neck we would be able to accurately determine if the neck needs further treatment. This would allow us to avoid the unwanted side effects associated with treating patients without neck disease."

The team also is evaluating a molecular method of determining if a head and neck cancer has spread to neck nodes."The theoretical advantage is that the molecular technique (RT-PCR) should be more accurate and less costly than standard pathologic examination," Yarbrough says. Last year, the team discovered that CAT scanning can be used to determine if surgery will be necessary after chemotherapy and radiation therapy.

The Head and Neck Program includes physicians, researchers and staff from the Departments of Otolaryngology/Head and Neck Surgery, Radiation Oncology, Hematology Oncology, Plastic and Reconstructive Surgery, Dentistry, Radiology, Pathology, and Speech Pathology. Says Yarbrough, "This is a truly multidisciplinary team working together to advance knowledge regarding the treatment of head and neck cancer and to provide total care for the head and neck cancer patient."

clinical trials underway

For information about these and other clinical trials, call 919-966-4432 or visit the UNC LCCC website at http://cancer.med.unc.edu under "Patient Resources."

Solid Tumors (LCCC 9903) This is a Phase I UNC Lineberger-developed trial designed to determine the highest dose of paclitaxel that can be safely tolerated when it is given as a weekly 1-hour infusion on a 2 out of 3 week schedule. Another purpose of this Phase I study is to understand how the paclitaxel is absorbed, distributed, used and removed from the body. This trial will be open to patients with solid tumors (i.e. breast, ovarian, head and neck, prostate, lung, gastrointestinal) who have had previous therapy for their disease. This trial will be open for accrual first part of March 2001. *PI, Claire Dees, MD*

Hematologic and Solid Tumors (LCCC 2020) This is a Phase I UNC Lineberger-developed trial designed to determine the highest dose of PS-341 that can be safely tolerated while receiving Doxil. While patients with hematologic malignancies and those with solid tumors will be treated in separate groups, all will receive the same drug and follow the same schedule of dose escalation. Patients who have had previous therapy and relapsed will be eligible for this trial. This trial will be open for accrual end of March 2001. *PIs, Robert Orlowski, MD and Claire Dees, MD*

Hodgkin's and Non-Hodgkin's Lymphoma (LCCC 9929) This is a Phase II UNC Lineberger-developed trial designed to determine the efficacy of three chemotherapy drugs (ifosfamide, carboplatin, etoposide) administered one after another three weeks apart. Another purpose of this study is to assess the ability of this sequence of chemotherapy drugs to mobilize and harvest stem cells for future use. This trial is open for accrual at UNC and will be open at four other cancer centers. *PI, Thomas Shea, MD*

Non-small Cell Lung Cancer Stage I/II (LCCC 2012) This is a Phase II UNC Lineberger-developed trial designed to determine the efficacy of using a combination of chemotherapeutic drugs (gemcitabine, carboplatin, paclitaxel). This treatment will be repeated every 21 days for three cycles prior to surgery in patients with limited disease. This trial will be open for accrual the first part of March 2001. *PI, Mark Socinski, MD*

Lineberger

Carolina Cancer Focus. At the January 14th women's basketball game against NC State, members of Carolina Cancer Focus handed out over 7000 ribbons in honor of ovarian cancer and informational flyers about cancer prevention. Pictured *(left to right)*: Shanna Fox, James Haltom, Shelley Koon, Michael Abel, Lisa Wald, Brennan Bouma and Krishna Gelot.

Outstanding Service. Board of Visitors member Dee Dee McKay of Charlotte received the Center's Outstanding Service Award. She was cited for her service in many vital capacities over the years—as Board chair, as an advocate for the Center, and "as an amazing source of optimism, strength and grace."

Hammond Chair in Childhood Cancer Established. A $1.5 million gift will establish the G. Denman Hammond Chair in Childhood Cancer, honoring Dr. G. Denman Hammond, president and CEO of the National Childhood Cancer Foundation and the founding director of the University of Southern California Comprehensive Cancer Center. The professorship is made possible by a gift from an anonymous donor in honor of Dr. Hammond. A national recruitment to fill the endowed chair will begin this summer.

Dr. Hammond, a distinguished alumnus of the University of North Carolina at Chapel Hill, was a student at the UNC School of Medicine, then only a two-year program, who subsequently received the M.D. degree from the University of Pennsylvania.

"This is an outstanding legacy for one of the University of North Carolina at Chapel Hill's most distinguished undergraduate and medical school alumni," said Shelton Earp. "Dr. Hammond's extraordinary career helped change the way we treat children with cancer."

Shown here (left to right) Dr. Hammond; Dr. Julie Blatt, chief, pediatric oncology; and Dr. Shelton Earp, Center director.

Briefs

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and found it was feasible and low-tech," says Raleigh. Now, the U.S. Food and Drug Administration has given the go-ahead to test as a diagnostic tool the pimonidazole hypoxia marker in human tumors.

"Our interest in tumor hypoxia is twofold: One, if these tumors don't do as well with radiation, chemotherapy or surgery, then it's important that we assess that before we embark on treatment," Varia explains. "The other important interest is in finding out why these hypoxic tumors are behaving badly." Varia, Raleigh and their collaborators have demonstrated that the pimonidazole marker is a valuable approach to studying the mechanisms of hypoxia-associated poor prognosis.

Tumors from more than 200 patients worldwide are being tested for hypoxia using this method. Beyond cancer treatment planning, clinical investigators at UNC-CH and elsewhere are looking at the hypoxia marker for studying alcohol-associated liver damage, wound healing and liver transplant success. "It's a very novel tool that can be applied not only in cancer research but widely in medical investigations," Raleigh noted.

UNC, Dell, Microsoft partnership could dramatically improve cancer radiation treatments

UNC has received a large computer cluster for a clinical study to determine possible ways in which radiation therapy can be more effectively tailored for individuals. Dell Computer Corp. and Microsoft Corp. provided the technology that could one day enable research that dramatically improves the accuracy of radiation therapy treatments through the use of parallel-computing processes and Monte Carlo simulations.

Julian Rosenman, professor of radiation oncology and a member of the UNC Lineberger Comprehensive Cancer Center, is principal investigator for the new study. "Medicine's current methods for calculating radiation doses, while highly sophisticated, are just not good enough," Rosenman said. "We know that dose calculations can contain errors as large as 10 to 15 percent in some situations. These errors could adversely affect survival rates, particularly in patients with lung, head or neck cancers."

Monte Carlo simulations have helped calculate radiation doses since nuclear testing began in the 1940s. But on regular computers, Monte Carlo simulations are notoriously slow, requiring a week's worth of 24-hour-a-day computing just to calculate one radiation dose. As a result, Monte Carlo simulations are not practical for setting dose codes for cancer patients. But perhaps with faster, parallel-operating computers, they could be, Rosenman said.

"We have always felt that if we could just get the calculations up and running fast enough, we could use Monte Carlo simulations in a clinical setting," Rosenman said. "To the best of my knowledge, no one is yet ready to use Monte Carlo code clinically. We could be the first." As surgical and chemotherapy treatments for cancer become more sophisticated, Rosenman notes, radiation therapy needs to move forward as well. "We need faster, more accurate computing ability. It's one more reason why this partnership with Microsoft and Dell is so important."

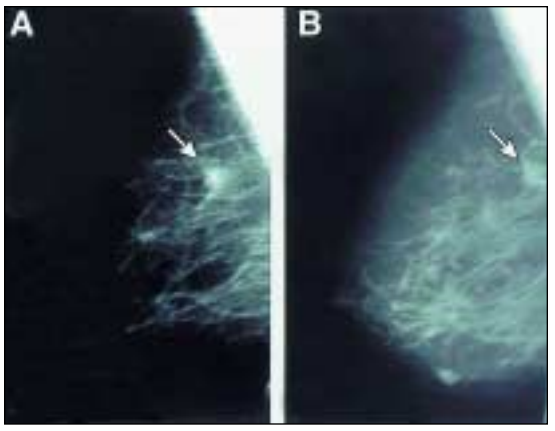
More Effective Mammography

continued from page 1

more than 95 percent, but it drops significantly to less than 20 percent after treatment for metastatic breast cancer. Early detection, then, is crucial.

Film Versus Digital

In conventional mammography, differences in tissue densities and composition show up as contrasting areas in the image, enabling physicians to see tumors or changes in tissue. However, traditional film presents two challenges to radiologists. First, it cannot be altered after it's acquired. To get different perspectives, technologists have to take more pictures, exposing the patient to more radiation. Or radiologists have to use a hot light and magnifying glass to get a different look.



Mammograms of the same breast using digital mamography (A) and conventional X-ray (B). Dr. Pisano's study will help determine whether digital mammography has the potential to give more precise information about the breast possibly leading to fewer callbacks for false positive or unclear results.

Second, because breast tumors and healthy breast tissue are very similar in density, up to 20 percent of cancers cannot be detected at all on X-ray film. In addition, when suspicious lesions are found on a mammogram, doctors generally choose to do a breast biopsy to make a clear determination. The annual breast biopsy volume in the U.S. is approaching almost 1,000,000 per year, with benign diagnoses made between 80 and 90 percent of the time.

By contrast, digital mammography offers an image that can be manipulated after it is acquired. "If you've ever used a digital camera, you know how simple it is to adjust the image after you've taken the picture," says Pisano, who also serves as head of the International Digital Mammography Development Group. "You can easily rotate, zoom or adjust the contrast or brightness." Digital mammography offers the same functionality for technicians and the digital pictures are easier to store, retrieve and transport, particularly via the Internet.

Putting it into Practice

While it seems likely digital imaging could improve cancer detection, Pisano and the FDA want quantifiable proof before they give up on the traditional screen-film technology.

"We don't know that digital mammography is better yet," Pisano cautions. "We're still very early in its history. From a physics perspective, we certainly think it should provide earlier detection in dense-breasted women. But while early studies suggest reduced false positives, we don't know yet that digital mammography will find more breast cancer."

That's why Pisano is leading an international study of 49,500 women in the United States and Canada to evaluate whether digital mammography is as good as or better than traditional mammography in detecting breast cancers. Nineteen centers in the United States and Canada, including UNC Lineberger, are participating in the study funded by the National Cancer Institute. The study is expected to enroll patients for 3 years.

That's all good news for radiologists who tend to prefer digital images over film because they provide better information on which to base diagnoses, according to a small study led by Pisano last year. She and her team asked 12 certified, working radiologists in Chapel Hill, Dur-ham, Raleigh and Graham to look at, compare and grade images from traditional X-rays and digital mammography for screening and diagnosis of breast masses and calcifications.

> *"With digital mammography they can take different looks at the same image to get exactly the information they need without exposing the patient to additional radiation."*

"It was clear that the radiologists preferred to look at different versions of the image for each of the three tasks," Pisano says. "What they liked for screening is not the same thing they liked for diagnosis of masses or diagnosing calcifications. The bottom line is that they need multiple versions of the same image to get as much information out of each image as they can. With digital mammography," she says, "they can take different looks at the same image to get exactly the information they need without exposing the patient to additional radiation."

Pioneering Technology

"In general, radiology technology has moved to digital over the last 20 years," explains Pisano. "Mammography is the last field to go digital."

Tests and clinical trials of digital breast imaging began in 1992, but the technology didn't receive FDA approval until February 2000. Currently, only GE's Senographe has the FDA's stamp of approval, but Pisano expects one or two other manufacturers to receive the green light this year.

At present, there are only 20 to 30 places in the country using digital mammography and only a handful use it in a clinical setting, and UNC was one of the pioneers.

"For some time, researchers in the Computer Science department have been working on image processing—how to get increased information in images," Pisano says. "That gave us a significant head start for the work we're doing with digital mammography."

In fact, the algorithm used to help the troubled Hubble telescope see better is the same one that will probably be used in the future to help digital mammography see cancers better in the breast. "UNC is one of the world leaders in image processing research, computer science and biomedical engineering."

Hatchell Donation. UNC women's basketball Coach Sylvia Hatchell donated $5,000 to gynecologic cancer research at UNC Lineberger at halftime of the January 14th game against NC State. Last summer she had a cancer "scare." After her experience and to express her gratitude, she had pledged to donate $5.00 for each women's basketball season ticket sold. Shown with her are *(above, left to right)*: Dr. Linda Van Le, UNC Lineberger gynecologic oncology program; Dr. Bill Nebel, Coach Hatchell's Chapel Hill gynecologist; Dr. Shelton Earp, Center director; Dr. John Boggess, UNC Lineberger gynecologic oncology program.