



THE LEADING EDGE

REFERRING PHYSICIAN UPDATE

A cancer-care collaboration among Fred Hutchinson Cancer Research Center, UW Medicine and Children's Hospital & Regional Medical Center

FALL 2003 ISSUE 5

Neoadjuvant protocols aim for pathologically complete response

While the number of women diagnosed with breast cancer continues to rise, the number who die of the disease continues to decline, thanks in part to continuing efforts to develop new treatment regimens that increase effectiveness while reducing toxicity.

At the Seattle Cancer Care Alliance, a multidisciplinary team of breast cancer specialists including radiologists, surgeons, pathologists, medical oncologists and radiation oncologists collaborates on protocol development.

The team is currently developing several neoadjuvant protocols, two of which are designed for patients with surgically resectable (stage I–IIIA) breast cancer. The two protocols incorporate the best current thinking from each discipline including breast imaging with MRI, PET and sentinel lymph node mapping to more accurately stage patients before treatment.

Dr. Georgiana Ellis and Dr. Hannah Linden are the University of Washington professors leading the neoadjuvant treatment trials with co-investigators Dr. Julie Galow and Dr. Robert Livingston. Drs. Anderson, Byrd, Mann, Moe and Yeung of the University of Washington Department of Surgery provide surgical expertise.

Drs. David Mankoff and Connie Lehman from the UW and Fred Hutchinson are conducting concurrent imaging and treat-

ment trials using MRI and experimental PET imaging of estrogen uptake and tumor biochemistry. The goal is to allow patients and physicians to monitor tumor response throughout treatment. The combination of neoadjuvant regimens and imaging trials provide new options for SCCA breast cancer patients.

“We’ve tried to create a palette of clinical trials for women to choose from,” Linden says. “Women and their physicians can choose the neoadjuvant regimen, with or without the imaging trials, or they can undergo standard treatment with the option to participate in other adjuvant trials.”

Linden will lead the neoadjuvant trial for hormone receptor positive women, which will involve sentinel node biopsy, with aggressive hormone therapy, followed by chemotherapy. MRI and PET monitoring are used throughout the trial. The patient will then proceed to surgery. The goal is to achieve a pathologically complete response before surgery. Dr. Ellis has developed and piloted the chemotherapy regimen for Linden’s trial. The regimen uses a potent chemotherapy combination using newer agents less toxic than those currently used for patients with more aggressive tumors lacking hormone receptors or over expressing HER2/neu.

“The advantage of this approach is that you can see whether the tumor is responding to treatment in contrast with empiric treatment following—Continued on page 4

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Fred Hutchinson Cancer Research Center
UW Medicine
Children's Hospital and Regional Medical Center

Working together to cure cancer

Doc-to-Doc



F. Marc Stewart, MD
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Professor of Medicine,
University of Washington

Member, Fred Hutchinson
Cancer Research Center

As Medical Director of the Seattle Cancer Care Alliance I would like to welcome you to *The Leading Edge*, the SCCA's Referring Physician Update. Each quarter a new topic will be highlighted to give you the latest news on leading edge therapies that SCCA physicians are offering.

In conjunction with national breast cancer awareness month, this issue is dedicated to women's cancers and highlights some of the SCCA physicians involved in breast and gynecological cancer research and treatment. Each article includes contact numbers if you would like additional information.

Additionally, each issue will include a handy reference card describing some of the Fred Hutchinson Cancer Research Center and University of Washington clinical trials currently open and enrolling at our SCCA building.

We will occasionally include patient educational tools—please feel free to comment on how we may provide you with information to help you educate your patients.

Brachytherapy treatment for breast cancer

By Dr. Michelle Yao—UW Medical Center's Cancer Center has launched a new program for the treatment of early-stage breast cancer using high-dose-rate interstitial brachytherapy for adjuvant therapy after breast-conserving surgery.

Current standard treatment for early-stage breast cancer includes adjuvant external-beam radiotherapy to the whole breast, delivered five days a week over a period of approximately six weeks, with the goal of decreasing local tumor recurrence after lumpectomy. Interstitial brachytherapy involves the temporary placement of plastic catheters directly into the tumor bed following lumpectomy. These catheters can then be "afterloaded" with a radioactive source to deliver a highly localized dose of radiation to the tumor bed. Using a high-dose-rate Iridium-192 source, the catheters will be loaded twice a day for four or five days to give a biologically equivalent dose to conventional external beam treatment.

Interstitial brachytherapy has a long history of use in many cancer sites and has been used for several years for the delivery of tumor bed "boost" treatment in conjunction with external beam adjuvant breast radiotherapy. Several studies using interstitial brachytherapy for partial breast irradiation as sole radiation treatment, including a multi-institutional cooperative group trial, have been completed. Data from a total of several hundred women demonstrate local recurrence rates at three to four percent, very comparable to what is seen with external beam therapy.

The primary advantages of brachytherapy treatment over external beam treatment include very localized treatment volume with maximal sparing of surrounding normal tissues (lung, heart) from unnecessary radiation exposure, as well as a shorter treatment course (one week vs. six-plus weeks). These characteristics make this treatment especially ideal for breast cancer patients who might have prior exposure

to radiation treatment (e.g., for Hodgkin's lymphoma), for working women, or for women who live at some distance from a radiotherapy center.

Eligibility criteria for this treatment include primary tumor size ≤ 3 cm, completely resected with negative resection margins, and negative axillary nodes without extracapsular extension. Patients with multicentric disease, lobular histology, extensive intra-ductal component, or underlying collagen vascular disease will be excluded. Please contact Dr. Michelle Yao at 206-598-4121 with questions or patient referrals.

An integrated approach to breast cancer evaluation, treatment and monitoring

By Barbara Berg—From the time a woman finds a suspicious lump until her treatment plan is mapped out, she may have consulted with as many as four specialists. Such multi-faceted medical care can be a logistical burden for patients and doctors.

That's why the Breast Cancer Specialty Center (BCSC) at the Seattle Cancer Care Alliance takes a team approach. Dr. Ben Anderson, a University of Washington breast surgeon, oversees the SCCA specialty center and is medical director of the Breast Health Center at UW Medical Center-Roosevelt.

"With the level of complexity in clinical care and research today, it's not realistic for any individual to be a specialist in all areas," said Anderson who is also a member of the Cancer Prevention Research Program at Fred Hutchinson Cancer Research Center. "Only through collaboration can we get to the next generation of treatment advances."

The BCSC is a—Continued on page 3

Specialized prevention program offers assistance to referring physicians and their patients

The Seattle Cancer Care Alliance treats an average of 450 new gynecological cancer patients a year. Women with gynecological cancer are treated in a multidisciplinary team approach coordinated by their primary gynecologic oncologist.

But care need not start with a diagnosis of cancer. Women known to be at high risk for breast or ovarian cancer, may be directed to UW Medicine's Breast and Ovarian Cancer Prevention Program, at the Seattle Cancer Care Alliance.

"We take a tailored approach to prevention," says Dr. Elizabeth Swisher, University of Washington assistant professor of obstetrics and gynecology, and director of the Breast and

SCCA partner physicians currently participate in over 50 clinical trials for ovarian, cervical and endometrial cancer.

Ovarian Cancer Prevention Program. This approach begins with risk confirmation and assessment along with evaluation of lifestyle and

personal risk factors. A team including a gynecologic oncologist, breast surgeon, genetic counselor, medical geneticist, and medical oncologist first meet one-on-one with the patient and then all together as a group.

"The team helps each woman develop a plan to lower and manage her risk for breast or ovarian cancer," says Whitney Neufeld-Kaiser, program manager. The prevention program works with referring care providers in implementing their patient's prevention plan. Additionally, the program provides education to patients and



A woman facing gynecological cancer can meet with her oncologist, surgeon, genetic counselor and radiation oncologist to discuss options and create a plan to take to her home physician.

physicians about clinical trials aimed at cancer prevention or screening.

For information, or to refer a patient, call 206-616-5241.

Integrated Approach—From page 2

multidisciplinary specialty center where a patient diagnosed with breast cancer undergoes an integrated evaluation of her cancer and treatment options. The initial patient consultation includes a surgeon, a medical oncologist and a radiation oncologist, all of whom specialize in breast cancer. Radiologists specializing in breast imaging conduct mammography, ultrasound and MRI for diagnosis and disease progression. Such consolidation of medical services in one location fosters productive

Screening Tool Offered

Enclosed is a sample tool to help you identify patients at high risk due to a family history of cancer. Your patients can fill it out in the waiting room. Then you can review and ask any clarifying questions.

If you see...

- Several relatives with the same or related cancers (e.g. breast and ovarian);
- Cancer at a younger age than normal for that cancer;
- Multifocal or bilateral cancer;
- Two primary cancers in the same person

your patient may be at risk for an inherited cancer syndrome.

You may want to consult with or refer your patient to a cancer genetics specialist. Call NCI's Cancer Information Service at 1-800-422-6237 or the UW's Genetic Resource Line at 1-800-562-GENE to find a cancer genetics specialist near you.

collaboration between the specialists and streamlines care for patients.

"It's one thing to get a report sent to you and entirely another thing to walk down the hall and go over a case with your colleague," Anderson said. "I don't think many centers have this level of integration."

Anderson credits Drs. Roger Moe and Robert Livingston, UW breast-cancer specialists, for their early vision in the 1980s of multidisciplinary cancer care, which they helped develop at UW Medical Center.

Neoadjuvant—From page 1

removal of the tumor,” Linden says. “This allows you to use the imaging information to tailor the treatment to the individual response. The disadvantage is that you

In addition to treatments based on NCI standard therapy guidelines, SCCA patients also have access to the latest advances in treatment through its research partners:

■ **Fred Hutchinson Cancer Research Center**

■ **UW Medicine**

chemotherapy regimen developed by Ellis and her colleagues. Patients will receive a course of dose dense combination chemotherapy and bone marrow support with G-CSF, followed by a course of paclitaxel.

Lehman’s imaging team will measure tumor size with a newer MRI technique that uses gadolinium injections to enhance image contrast and yield higher resolution images. A computer reconstructs this information to produce multiple images of thin slices of the breast before and after the contrast injection, allowing more accurate measurement of treatment progress.

The women will undergo a pretreatment MRI and biopsy, and another MRI one to three days after starting hormone or chemotherapy. A third MRI will be done following the 12-week course of dose dense combination chemotherapy and another at completion of the systemic therapy prior to surgery at which time another core biopsy will be taken.

have to be comfortable with leaving the tumor in place.”

Ellis designed and leads the treatment trial for women with operable breast cancer that is either hormone receptor negative or HER2 positive. The Ellis trial involves sentinel lymph node biopsy followed by a

“We use MR imaging to monitor whether the tumor is getting bigger or smaller,” Lehman says. We hope these new methods will tell us, at a much earlier time point, whether the chemotherapy (or hormone therapy) is working or not.”

Mankoff’s team in nuclear medicine has developed experimental tools to monitor the biology of the tumor, and has previously shown that changes in blood flow to the tumor predict response to treatment. His studies will allow measurement of estrogen uptake by the tumor prior to treatment for patients with tumors that express hormone receptors and measurement of hypoxia in patients with tumors lacking hormone receptor.

Prior work has suggested that hypoxia may be an important resistance factor in tumors that do not respond. The PET scans will also help monitor response. The PET images, which look at tumor biochemistry, are complementary to the MRI studies, .

Another advantage of this neoadjuvant approach with continuous monitoring, Linden says, is that patients and physicians won’t have to wait five years for results of the trials. Information from pathology and imaging should provide enough data to analyze within two years.

The treatment trials began enrolling October 1 and expect to recruit 50 patients over the next two years. Physicians who would like more information, or want to refer patients to these trials can call Tracy Headley, SCCA patient care coordinator at 206-288-1024.

RESOURCES

How do I refer a patient?

Call our Intake Office at 206-288-1024.

■ **General Oncology**
patient case discussions will be transferred to the appropriate Patient Care Coordinator.

■ **Marrow or Stem Cell Transplant**
patient referral cases will be transferred to the Clinical Coordinator Office.

We will review the case with you to determine if it would be beneficial for the patient to come to SCCA for treatment.

What happens after referral?

The SCCA is committed to ongoing communications with referring physicians to maintain seamless patient care.

The UW offers a secure electronic connection through U-Link to give you instant access to your patient’s information and updated records while at SCCA. Contact the Physician Liaison Program at 206-598-4972 to sign up. Current users may access U-link at: <http://mindscape.mcis.washington.edu/>

Just want to consult with a specialist at the SCCA?

Use the MEDCON Consultation service to consult with UW physicians who practice at SCCA. Call 206-543-5300 in the Seattle area or toll-free 800-326-5300. The consultation is free.

Advanced imaging offers greater confidence in screening and treatment

Breast Imaging in the SCCA Radiology Department provides physicians and their patients with an array of advanced imaging technology ranging from digital mammography to ultrasound, PET and MRI.

“This is a very exciting time in imaging,” said Dr. Connie Lehman, a UW radiologist and director of breast imaging at the SCCA. “We have new imaging tools beyond mammography which enhance our ability to effectively detect, diagnose, and treat patients with breast cancer.”

According to Lehman, one function of imaging is to detect and evaluate tumors early through noninvasive methods.

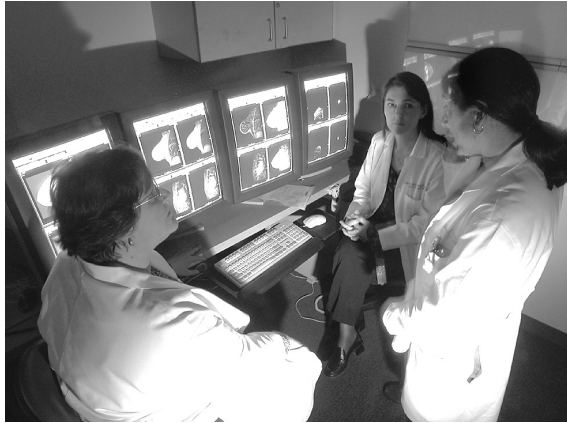
“The earlier we can detect a cancer, the better the chances for a cure,” she said. “The first step is to evaluate whether a lump is cancerous. We’d like to do this without unnecessary biopsies. In an ideal world, we’d have very few biopsies of benign tumors.”

Imaging also is used for patients with known cancers. Once a patient is diagnosed with breast cancer, it is important to know the extent of disease. Lehman says that in a small number of women, cancer goes undetected in the contralateral breast, primarily because the cancer is undetectable on mammography.

In an effort to improve the ability to detect these cancers, Lehman is heading an international bilateral MR imaging trial. The objective is to determine the ability of contrast MR imaging to

detect cancer in the contralateral breast of women with a recent breast cancer diagnosis and no known disease by mammography or clinical breast exam.

The enrollment goal is 1,000 women, and is being conducted at 22 sites in the U.S., Canada and Europe.



Drs. Ellis, Lehman, and Linden examine imaging and discuss cases together for the best possible patient treatment plan.

In another project aimed at improving early diagnosis of breast cancer, the SCCA breast-imaging group was the first in the region to perform biopsies under MR guidance.

“When we find a lesion on MRI that is not visible

on mammography or ultrasound, we need to be able to biopsy the suspicious region under MRI guidance,” Lehman said. “The Seattle Cancer Care Alliance is the first to test a new method of vacuum-assisted breast biopsy under MRI guidance.”

Overall, Lehman is enthusiastic about the comprehensive approach to detection, diagnosis and treatment of breast cancer at the SCCA.

“The collaborations we are able to do with the surgeons, medical oncologists and radiologists at the SCCA make it possible to make inroads in this disease,” she says.

For more information regarding any of the breast imaging available at the SCCA, call the Breast MR Research Line at 206-288-7808.

Educational Opportunities

OCTOBER 16, 17, 18: ***Challenges and Controversies in Breast Cancer CME***

Location: Bell Harbor International Conference Center, Seattle, WA

Audience: Clinical Practitioners

Contact: 206-543-1050

OCTOBER 27: ***Current Therapies in Women’s Cancers***

Location: Richland Hampton Inn, Richland, WA

Audience: Internal Medicine, OBGyn, Family Practitioners, Surgeons, Radiologists, Oncologists

Contact: Reza Macaraeg, 206-288-6999

NOVEMBER 3–4: ***Foundations in Chemotherapy Practice***

Location: Shoreline Conference Center, Shoreline, WA

Audience: Nursing CEU
Contact: 206-543-1047

NOVEMBER 18: ***Leukemia Treatment, Myelodysplasia & Research***

Location: Olympic Medical Center, Port Angeles, WA.

Audience: SCCA Network Affiliate Clinical Practitioners
Contact: Lynda Minor, 360-417-7429



Fred Hutchinson Cancer Research Center
UW Medicine
Children's Hospital and Regional Medical Center

The Seattle Cancer Care Alliance brings together the best of three internationally renowned cancer-care institutions: Fred Hutchinson Cancer Research Center, UW Medicine, and Children's Hospital and Regional Medical Center.

Our Mission:

- Provide premier, patient-focused cancer care.
- Support the conduct of cancer clinical research and education.
- Enhance access to improved cancer interventions, and advance the standard of cancer care, regionally and beyond.

www.seattlecca.org

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Connecting physicians to comprehensive breast and ovarian programs

There may be no more comprehensive resource for breast and ovarian cancer care than that offered by the Seattle Cancer Care Alliance. SCCA gives physicians access to UW Medicine and Fred Hutchinson Cancer Research Center breast and gynecologic oncologists and researchers who integrate the latest advances in cancer biology, prevention, detection, and treatment research into

The program is trusted as the Northwest's premier breast cancer care resource, with the region's most sophisticated continuum of specialty care services.

Prevention
The Breast and Ovarian Cancer Prevention Program provides breast and ovarian cancer risk assessment and cancer prevention planning. This specialized program offers a multidisciplinary, personalized approach to cancer risk assessment, prevention, and screening for women known to have a high risk of developing breast or ovarian cancer.

The Medical Genetics Cancer Genetics Clinic provides services for women with a family history of breast or ovarian cancer who have not had formal cancer risk assessment and genetic counseling. A team of medical geneticists and genetic counselors reviews personal and family health history to assess both the likelihood of a heritable cancer syndrome and a patient's risk of developing cancer. Genetic testing and/or DNA banking is offered as appropriate.

comprehensive clinical care. Through the SCCA, community physicians can connect with surgeons, medical oncologists, radiation oncologists, radiologists, pathologists, geneticists and internists.

For Information:

| | |
|---|---------------------|
| Breast and Ovarian Cancer Prevention Program | 206-616-5241 |
| Cancer Genetics Clinic | 206-616-2135 |
| Breast Health Center | 206-598-5500 |
| Mammography Scheduling | 206-598-7343 |
| MRI Scheduling | 206-288-1434 |
| Treatment Planning and Care | 206-288-1024 |

Detection and Diagnosis

The Breast Health Center provides prompt evaluation of breast lumps, abnormal mammograms, nipple discharge, or breast pain. To provide a diagnosis and treatment plan, our breast disease specialists closely integrate the clinical evaluation with breast imaging studies to ensure that patients receive a thorough evaluation and accurate diagnosis.

Breast Imaging Services at the SCCA offer standard and advanced imaging technologies including computer-aided stereotactic biopsy, MRI and nuclear medicine techniques including lymphoscintigraphy, PET, and MIBI imaging.

Treatment Planning and Care

The Breast Cancer Specialty Center offers a review of a patient's case by a multidisciplinary team of breast cancer specialists. These doctors include specialists in breast-cancer surgery, radiation oncology, medical oncology, pathology and radiology. A plastic surgeon will join the team if the patient is considering breast reconstruction. The team jointly develops a treatment plan and then meets with the patient to review and discuss the plan, and if appropriate will continue to care for the patient through treatment completion.