Inside Surgery

BREAST CARE AT UCSF

UCSF’s Carol Franc Buck Breast Care Center (BCC) offers women multidisciplinary expertise in the diagnosis and treatment of a disease that ranks as the most prevalent malignancy among U.S. women.

Led by Laura Esserman, MD, a nationally recognized leader in breast cancer treatment, the UCSF Mount Zion-based center, part of the UCSF Comprehensive Cancer Center, combines high-quality, patient-centered care with rigorous scientific research. Providers form a collaborative team of experts in surgical, medical and radiation oncology, pathology, radiology, psychology and genetic counseling. Additional staff offer psychosocial support, advice on nutrition and information about complementary and alternative medicine.

Using information science to improve patient care

Harnessing the power of informatics and management sciences to advance the quality of breast cancer care is central to BCC Director Laura Esserman’s ongoing efforts to improve patient care. In recognition of her work, Esserman, who also holds an MBA from Stanford Graduate School of Business, has recently been awarded a $7 million grant from the Department of Defense Breast Cancer Research Program to create a national Center of Excellence (COE) in breast cancer care delivery. A primary goal of the COE is to develop a prototype clinical information system specifically designed to promote collaborative decision making among physicians and patients. Conceptualized as a knowledge management system, it differs from current electronic medical record systems by emphasizing the integration of standardized patient data, routinely collected at the point of care, with information from other hospital and research databases. This will provide a platform that helps providers, in consultation with patients, to tailor treatment to individual biology and patient preference. It also allows providers to evaluate the impact of clinical decisions based on outcomes generated at both the BCC and other centers nationwide.

A second and equally important goal of the COE is to develop tools for helping physicians scientifically assess and communicate a patient’s risk of cancer occurrence, recurrence and death. These risk assessment...
LETTER FROM THE CHAIR

Two aspects of cancer care are showcased in this issue of Inside Surgery: the Carol Franc Buck Breast Care Center and the UCSF endocrine surgery program. Both are based at the Comprehensive Cancer Center at UCSF/Mount Zion. Awarded the National Cancer Institute’s highest designation — “comprehensive” — for uniting innovative research and state-of-the-art patient care, the Center provides multidisciplinary evaluation and treatment for a variety of types of cancer patients, all at one site. Oncologists, pathologists, surgeons, radiation oncologists and other specialists operate from adjacent offices in the Center. This physical proximity streamlines the evaluation and treatment process, and fosters the interdisciplinary collaboration that have for many years been hallmarks of the UCSF community.

I am also pleased to single out the hard work of UCSF surgeon Jeffrey Pearl, MD, who serves as associate dean of the UCSF Medical School at Mount Zion. Dr. Pearl has worked tirelessly to involve the San Francisco community in this newly revitalized part of our campus. He has helped to oversee the complex movement of selected programs from the main campus to Mount Zion, and continues to champion this unique teaching and patient care resource. His latest effort is the organization of a public lecture series on forensics, which will be held in the remodeled Herbst Hall auditorium at Mount Zion.

Community support is also evident in the level of financial assistance provided to UCSF programs by outside groups. The Breast Care Center has been the grateful recipient of financial support provided by donors ranging from major corporations to private individuals. Endocrine research, which is highlighted in the story beginning on page 6, has also been generously supported by several individuals and family foundations. Their support keeps these multifaceted programs vibrant and growing.

Nancy L. Ascher, MD, PhD
Professor and Chair, Department of Surgery
models compare a patient’s profile to population-based statistics, integrating demographics, tumor biology, treatment and outcomes. Again, the goal is to develop systems that support the ability to tailor treatments based on biology and risk.

The COE is currently developing and testing decision-support models for patients who are at high risk for developing breast cancer, for those who have been diagnosed with ductal carcinoma in situ (DCIS), and for those who are considering adjuvant therapy following surgery for primary breast cancer. Although based at UCSF, the COE is an international effort, bringing together leaders from various fields and institutions. Participants include investigators from UC Davis, the Northern California Cancer Center, Stanford University Department of Management Science and Engineering, Harvard University School of Business, the Patient Safety Institute, University of Texas Southwestern, Massachusetts General, the Foundation for Informed Decision Making, and the United Kingdom Advanced Computation Laboratory.

**Same-Day assessment**

The Center’s Same-Day Assessment program is an example of the care systems supported by the COE grant. The program coordinates provider schedules so that patients who require evaluation for a mass or abnormal mammogram can undergo clinical examination, imaging and needle biopsy procedures on the same day. This allows patients to quickly learn whether they have a serious breast problem, allowing them to schedule treatment more rapidly than would ordinarily be possible. The Center’s facilities, which include on-site diagnostic mammography, biopsy, and cytopathology, help facilitate this process.

Two innovative clinical trials are associated with Same-Day Assessment. One is the development of a proteomics blood test (analysis of blood proteins) as an adjunct to screening for breast cancer, either before or after mammography. The second involves identifying patients with DCIS for novel studies (see below).

**Optimizing doctor-patient communication**

The Program for Collaborative Care uses trained facilitators to help patients prepare for consultations and to moderate doctor/patient meetings. Its goal is to improve the quality of treatment decisions by helping physicians and patients communicate more effectively. In a process called consultation planning, facilitators help patients map out their questions and concerns before a meeting with a breast cancer specialist. A printed flowchart, the consultation plan, is created for each patient highlighting questions, concerns, and issues. Both the patient and the physician receive a copy of the plan, which guides discussion of treatment options.

**Bringing mammography to underserved women**

UCSF’s Mammovan, the only mobile mammography service in the San Francisco Bay Area and the only one in the world equipped with the highest-quality digital screening technology, brings the expertise of UCSF clinicians to women who would otherwise not receive breast cancer screening. The Mammovan travels to 22 sites that comprise the Community Health Network of San Francisco, offering no-cost examinations and counseling to underserved populations. Working under the auspices of San Francisco General Hospital and under the direction of Cheryl Ewing, MD, the UCSF Mammovan screens 3,000 women a year.

For information, contact Shoshana Levenberg at 415/353-7355.

**A wide spectrum of research**

Over the past five years, the number of investigator-initiated trials originating at the BCC has increased significantly, and staff have assumed leadership roles in large, multicenter studies, including those sponsored by national and international cooperative groups. The Center’s clinical trials unit, under the direction of Hope Rugo, MD and Laura Esserman MD, is currently recruiting patients for 30 open trials on topics including breast cancer prevention, imaging, behavioral studies, biologically targeted therapies and complementary/alternative medicine. John Park, MD, PhD, is in charge of innovative clinical translational research bringing cutting-edge molecular therapeutics to patients at UCSF and elsewhere. The Center also collaborates with breast cancer advocates on the design and implementation of new trials.
Measuring tumor response with MRI

Studies of neoadjuvant chemotherapy, currently standard treatment before breast cancer surgery, have shown that some patients benefit greatly from it, while others do not. BCC director Laura Esserman, MD, is leading a multi-institutional study of women undergoing neoadjuvant chemotherapy for stage II and stage III breast cancer. The aim is to identify biomarkers that would predict response to therapy. Participants’ response to treatment is monitored with serial magnetic resonance imaging (MRI) and core biopsies. One goal of this study is to identify non-responsive patients within approximately a week of chemotherapy and then to identify novel therapeutics most likely to succeed in those patients.

In addition to UCSF, study sites include the University of Pennsylvania, University of North Carolina-Chapel Hill, University of Alabama, Georgetown University, Memorial Sloan-Kettering Cancer Center, University of Texas Southwestern and University of Washington, Seattle.

For more information, contact Nneka Emenyonu at 415/353-7606.

Tamoxifen v. letrozole in patients with DCIS

One of the challenges in breast cancer care is determining how aggressively to treat ductal carcinoma in situ (DCIS), the earliest form of the disease. A current BCC trial under the direction of Shelley Hwang, MD, is studying the effects of tamoxifen and the aromatase inhibitor letrozole administered prior to lumpectomy on patients with DCIS, with the goal of identifying non-surgical treatments that may prevent the progression of DCIS to invasive cancer. Patients accepted into the trial are placed on tamoxifen or letrozole for three months prior to surgery and are examined with a breast MRI before and after treatment to determine the effect of these medications on DCIS. This trial uses the neoadjuvant approach to examine how to best prevent or treat progression from DCIS.

National randomized trials have shown that tamoxifen reduces the risk of breast cancer recurrence, including recurrence of DCIS, after initial treatment with lumpectomy and radiation. Aromatase inhibitors are a new class of drugs found to be effective in reducing the risk of breast cancer recurrence in postmenopausal women. They have few adverse effects, and, unlike tamoxifen, do not lead to an increased risk of endometrial cancer. Studies such as this one may identify a role for these medications as an alternative to surgery for patients with DCIS.

For more information, contact Alex Herrera at 415/885-3849.

Immunotherapy for breast cancer

A dendritic cell vaccine directed against HER-2/neu, a genetic mutation associated with certain breast cancers, is currently being tested in patients with advanced disease. The concept of a HER-2 vaccine is based on studies by Michael Campbell, PhD, and Laura Esserman, MD, showing that vaccines have the potential to prevent HER-2 tumors in transgenic mice.

The current patient trial, under the direction of John Park, MD, and Michelle Melisko, MD, is a collaboration with Dendreon Corp. Dendritic cells are removed from the patient’s blood, altered in the laboratory, and then infused back into the body. Clinical trials at UCSF and elsewhere have shown excellent T-cell responses following a dendritic cell vaccine in prostate cancer.

For more information, contact Jennafer Carlin at 415/885-7643.
TARGET radiotherapy trial

Regional radiotherapy techniques are being studied around the world. UCSF has joined an international effort to test a single intra-operative dose of radiation as a replacement for a six-week course of external radiotherapy. This study, scheduled to begin before the end of 2003, will be open to women over 50 with stage I and II cancers.

Researchers led by surgeons Karen Lane, MD, and Shelley Hwang, MD, and radiation oncologists Alison Bevan, MD, and Catherine Park, MD, will examine which biological characteristics predict a good response to this treatment.

For more information, contact the clinical trials manager at 415/353-7213.

Preventing disease in high-risk women

The Prevention Program at the UCSF Breast Care Center provides educational services and clinical trials for women at high risk for breast cancer. Women eligible for preventive programs include those with a family history of breast and/or ovarian cancer or BRCA 1/2 mutation, personal history of breast cancer or atypical hyperplasia, or other reproductive risk factors such as late or no childbearing or early menarche. At the Center’s weekly Prevention Clinic, patients receive breast cancer education, a thorough breast exam and breast mapping, a personalized risk assessment and follow-up plan, an introduction to breast cancer prevention clinical trials and genetic counseling as needed. Providers are drawn from an expert team of breast surgeons, gynecologists and internists, nurse practitioners, genetic counselors and researchers.

Tamoxifen is currently the only preventive medical therapy approved for high-risk women, but many women are reluctant to take it because of potential side effects. Additional tests can be performed in these women to assess both risk of breast cancer and likelihood of benefit from tamoxifen. These include testing for atypia with fine needle aspirations or ductal lavage. Serum-estradiol levels can also be measured in postmenopausal women.

Breast density is also being studied as a potential marker for breast cancer risk. Dense breast tissue has been linked to an increased risk of developing breast cancer. Tamoxifen has been shown to reduce breast density, but again, many women may be unwilling to take this drug. A BCC pilot study (PREVENT), under the direction of Jeffrey Tice, MD, is examining whether soy protein may be useful in reducing breast density in high-risk, premenopausal women. Women who are at high risk for breast cancer, based on a Gail Risk Factor >1.67% and breast density >50%, are eligible to participate in the study, in which they are randomly assigned to receive soy protein or placebo. Participants are monitored over a six-month period with digital mammography and blood tests for serum biomarkers.

For more information, contact Nicole Guthrie at 415/353-9739.

Postmenopausal high-risk women also have the opportunity to participate in a multicenter clinical trial, the Study of Tamoxifen and Raloxifene (STAR). For more information, contact Rowena Mah at 415/476-4082, x156.

For more information about the Prevention Program or to schedule an appointment, contact Caroline Annis at 415/353-7029.
Thyroid tumors
Thyroid cancer, which is more common in women than in men, accounts for 1% of all cancers diagnosed in the United States. Most thyroid cancers grow slowly, but certain types can be highly aggressive, making thyroid cancer second only to ovarian cancer as a leading cause of death from endocrine cancers. UCSF offers the full range of treatment options for thyroid cancer, including videoassisted and open operation via small incisions, radioiodine treatment, external beam radiation and chemotherapy. Most patients can be cured of their disease with some combination of these treatments.

Thyroidectomy is recommended in thyroid cancer patients, with total removal of the gland preferred for tumors greater than 1.5 cm, when the procedure can be performed safely. Total thyroidectomy is associated with a lower recurrence rate and, in many reports, improved survival. Serious complications such as hypoparathyroidism or recurrent laryngeal nerve injuries occur in less than 0.5% of UCSF patients undergoing thyroid operations.

In an effort to explore alternatives to thyroidectomy, UCSF surgeons will soon begin a study of the effectiveness of radiofrequency (RF) ablation for some patients with either low-risk thyroid cancers or clinically benign thyroid nodules. In the first stage of the study, patients will be treated initially with RF ablation, then undergo thyroidectomy to establish treatment response.

The UCSF group offers special expertise in treating inherited forms of thyroid cancer. These include familial medullary thyroid cancer, a rare malignancy of the parafollicular cells that secrete calcitonin, and familial papillary and Hurthle cell cancers. Medullary thyroid cancers are commonly invasive, and both a total thyroidectomy and meticulous, prophylactic bilateral central neck operation are necessary in these patients to maximize the chance of a cure. Genetic testing for RET point mutations is available to identify patients with the familial
form of the disease, which may also be associated with adrenal and parathyroid tumors. Total thyroidectomy is recommended prior to age six in children with a history of familial medullary thyroid cancer who are found to have a RET germ line mutation. Familial papillary and Hurthle cell cancer is less aggressive than medullary thyroid cancer, but is more aggressive than sporadic forms of the disease. Identifying the gene(s) responsible for this form of familial thyroid cancer is a particular research interest of the UCSF endocrine surgical team.

Parathyroid tumors
Most studies, including substantial research performed at UCSF, show that treating patients with primary hyperparathyroidism with parathyroidectomy relieves symptoms, resolves most related metabolic problems and improves survival rates. UCSF has special expertise in initial and reoperative parathyroid surgery as well as in parathyroid cryopreservation and autotransplantation. The latter technique can prevent permanent hypoparathyroidism in the small number of patients who are hypocalcemic following subtotal or total parathyroidectomy or after parathyroid reoperations.

For patients with primary sporadic hyperparathyroidism, the UCSF team uses sestamibi scans and ultrasound to localize parathyroid tumors preoperatively so that a minimally invasive surgical approach can be used. UCSF surgeons also routinely employ an intraoperative blood test to measure parathyroid hormone (PTH), which helps determine if the operation is complete. When the PTH level falls at least 50% from the highest pre-removal level 10 minutes after excision of the tumor, the operation is usually (>98%) successful, and the other parathyroid glands do not have to be identified. Use of this simple blood test has made it possible to perform many parathyroid operations through a small (2.5 cm) incision. The standard 4 cm incision is now needed only when the localization studies do not identify a single parathyroid tumor or the patient has familial hyperparathyroidism.

In a UCSF series of more than 1,000 patients undergoing initial operations for primary hyperparathyroidism using either a bilateral or focused approach, there were no patients with permanent hypoparathyroidism or recurrent laryngeal nerve injury. These complications occur in about 1.5% of patients undergoing reoperations at UCSF, a rate lower than that reported at other medical centers.

Adrenal tumors
Treatment of patients with adrenal tumors has changed markedly due to improved diagnosis, more precise localization and less invasive operative procedures. Laparoscopic removal has become the treatment of choice for most adrenal tumors less than 6 cm in size. Because few centers have expertise in laparoscopic endocrine surgery, UCSF is a major referral site, performing 40 operations annually for these rare tumors. Laparoscopic removal of adrenal tumors has shortened hospital stays, decreased postoperative pain and reduced recovery times.

Endocrine surgical oncology research
The endocrine surgery team is involved in several research projects exploring the pathogenesis and treatment of thyroid cancers. The group includes principal investigators Drs. Clark, Duh and Kebebew, laboratory director Mariwil G. Wong, as well as one clinical science and two basic science research fellows.

Redifferentiation therapy
Compared to well-differentiated tumors, poorly differentiated cancers are more likely to invade and metastasize and are less responsive to radiodine therapy. Several UCSF studies attempting to redifferentiate thyroid cancers are currently under way. In vitro investigations have shown promising results inhibiting thyroid cancer growth with PPAR-gamma agonists, histone deacetylase inhibitors and Cox 2 inhibitors. Treatment with some of these agents produced a thousandfold increase in radioiodine uptake. Growth of the thyroid cancers also decreased with use of these agents, and cancer cell death (apoptosis) increased. Based on these results, UCSF endocrine surgeons and endocrinologists are beginning a clinical trial in which patients will be given the PPAR-gamma agonist, rosiglitazone. This drug, used to treat diabetes, resembles similar medications that have been shown by UCSF researchers to have redifferentiating effects on thyroid cancer cells. This treatment approach could help many patients who have unresectable metastatic disease by increasing tumor cells’ capacity to trap radioiodine, and perhaps, by other mechanisms.

Genetic regulation
The UCSF team is also investigating the genetics of familial nonmedullary thyroid cancer, using comparative genomic hybridization and linkage analysis. They have identified chromosomal sites that appear to be associated with familial, papillary and Hurthle cell thyroid cancer. Subsequent investigations will explore the specific genes that are responsible for these cancers.

CONSULTATIONS AND REFERRALS
For more information, please call 415/353-2161.
CAMPBELL TO OVERSEE SURGICAL EDUCATION

Andre Campbell, MD, one of UCSF’s most honored medical educators, has been named Chair of Surgical Education, an endowed position recently created by the UCSF Academy of Medical Educators in conjunction with the Department of Surgery. The Academy, one of only a few such programs in the United States, was established in 2001 to advance the teaching of medical students and provide moral and financial support to talented teachers at UCSF. In his new position, Campbell will represent teaching excellence in the Department of Surgery and work to promote the highest standards of medical education throughout UCSF.

Campbell, an Associate Professor in the Department of Surgery, has been repeatedly honored for distinction in the role of teacher and mentor. Earlier this year he was one of four recipients of the national Association for Surgical Education’s Outstanding Teacher Award, and he was nominated by UCSF medical students to receive the Henry J. Kaiser Excellence in Teaching Award. He previously received the 1998-99 Distinction in Teaching Award from the UCSF Academic Senate.

Dr. Campbell’s appointment comes at a challenging time for surgical education, as many students opt to specialize in other areas such as emergency medicine, radiology and anesthesia. “We have some of the best teachers in the School of Medicine in our Department and I would like to make sure UCSF students get exposure to us,” said Campbell. “I am optimistic that we can increase the numbers of students who are going into surgery in the future and inspire the next generation of surgeons,” he said.

The establishment of endowed chairs will allow faculty to reduce their obligations in other areas to focus more attention on teaching and mentoring students and creating top-notch educational programs. UCSF plans to create 30 such chairs within the next five years, eventually supporting up to 75 faculty members per year through a combination of chairs and program stipends.