



LOMA LINDA UNIVERSITY

Cancer Center

CANCER PROGRAM

ANNUAL REPORT



INTRODUCTION



Historically, research has been one of the founding elements at Loma Linda University and Loma Linda University Medical Center. This report is not intended to be an exhaustive reference or to elevate any individual's work. It is intended to share some of the amazing research being conducted by researchers on campus. Our goal is to feature a small part of the ongoing research which we hope will inform, inspire, and honor the legacy of the many researchers who are asking questions, solving problems, and uncovering new ideas to understand and treat cancer.

This first, research focused Cancer Program Annual Report is dedicated with gratitude to James M. Slater, M.D., F.A.C.R., Director, Radiation Research Laboratories.

PIONEER OF HOSPITAL-BASED PROTON THERAPY

Loma Linda University Medical Center was the first hospital in the world to offer proton radiation therapy treatment in a hospital based facility expressly designed for that purpose. The growth of the Proton Therapy treatment and the Radiation Research program are inseparably linked to the man whose vision and work helped them become a reality.

Beginning in the 1970's through the mid-1980's as radiation medicine technology was evolving, Dr. James Slater consulted with his colleagues at the National Cancer Institute to help design the feasibility study and recommendations that formed the foundation of the Proton Therapy Program here at LLUMC. The initial consensus of the group at that time was that it was still too early to accomplish the project due to technological deficiencies in several key areas. To overcome these would require:

1. More Sophisticated Imaging Systems
2. More Powerful (Super) Computers
3. The Development of the Hardware and Software used in Treatment Planning

The first meeting to plan and design the proton facility was held in 1984 and included 93 physicists from East and West Europe, Asia, and North America. Each physicist not only donated their time but also paid their own travel expenses to participate in this first-ever Proton Planning Conference. Later, this same group would lead to the development of the Proton Therapy Oncology Group (PTCOG). In addition to physicists, the Proton Planning group included a consortium of structural engineers, physicians, and computer engineers. At each step in the development of what we now know as Proton therapy, there were countless research projects to develop the initial equipment, computers, software, tools, and procedures necessary to run the systems. At Loma Linda University we developed the first technology capable of computer assisted planning for radiation treatments.

As further advancements were made in better imaging and more powerful and faster computers were created, the ability to design the control systems for the entire facility became feasible. The construction phase for the facility we have today began in 1986 but the first patient to be treated with protons would not occur until October 1990. Upgrades have continued over the last 18 years, including most recently, the new Robotic Patient Alignment System and upgrade construction in 2008.

As a pioneer in the design and development of the technology and delivery of proton radiation, Dr. Slater's achievements now span close to four decades. His expertise and vision continue to inspire others daily in this expanding field. His focus however, remains constant, to look ahead for better ways of harnessing proton radiation to treat patients. Taken as a whole, Radiation Research and Proton Therapy under the Radiation Medicine Department at LLUMC serve as a dynamic model for living our Mission, Vision, and Values and remains a significant Center of Excellence.



MISSION

The Medical Center’s mission is to continue the healing ministry of Jesus Christ, “to make man whole,” in a setting of advancing medical science and to provide a stimulating clinical and research environment for the education of physicians, nurses, and other health professionals.

VISION

Our vision, “innovating excellence in Christ-centered healthcare,” reflects the goals and aspirations of all who share in a common desire to make the Medical Center the first choice of employees, physicians, and community.

LIVING OUR VALUES

The hospitals of Loma Linda University have many strengths, skilled and compassionate staff, renowned physicians, advanced technology, world-class facilities, but only one mission: to make man whole. This vision has lead to the development of the “innovating excellence in Christ-centered care,,” which embraces five core values of patient centered care:

- COMPASSION – Reflecting the love of God through caring, respect, and empathy.
- INTEGRITY – Ensuring our actions are consistent with our values.
- EXCELLENCE – Providing care that is safe, reliable, and patient centered.
- TEAMWORK – Collaborating to achieve a shared purpose.
- WHOLENESS – Embracing a balanced life that integrates mind, body, and spirit.

HISTORY OF LOMA LINDA UNIVERSITY MEDICAL CENTER

Loma Linda University Medical Center (LLUMC) is an academic institution dedicated to provide comprehensive cancer patient care, research, and education to adults and pediatric patients seen on campus or at one of the various satellite facilities located throughout the Riverside and San Bernardino County areas. The Cancer Program received accreditation by the American College of Surgeons and commendations in six of the standards evaluated in 2006 with the next survey scheduled for May, 2009. In addition to its capabilities in the clinical area, LLUMC also serves as a regional health center in the Inland Empire community sponsoring and hosting many cancer prevention, detection, and educational programs annually. To meet the increasing need for healthcare in the region, Loma Linda University Medical Center celebrated the groundbreaking for a new medical facility in the Beaumont/Banning area and construction on the Highland Springs facility continued through 2008 with the opening in early 2009.



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CANCER COMMITTEE MEMBERS

PHYSICIAN MEMBERS

Chairman Mark Reeves, MD, PhD Director, Cancer Center Sharmilla Roy-Chowdhury, MD ACOS Liaison Physician	Pain Management Gina Mohr, MD Monica Neumann, MD
Breast Surgery Sharon Lum, MD Jan Wong, MD	Pathology G. William Saukel, MD Kevin Thompson, MD
Chair, Department of Surgery Carlos Garberoglio, MD	Pediatric Oncology Blood & Marrow Transplant Program Chris Morris, MD, PhD
Colorectal Surgery Kevork Kazanjian, MD*	Pediatric Hematology/Oncology Liesel Mathias, MD
Dermatology Abel Torres, MD	Pediatric Surgery Joanne Baerg, MD
Genitourinary Paul Lui, MD Herbert Ruckle, MD Kristin Sanderson, MD*	Pulmonary/Critical Care/ Thoracic Surgery Gregory Cheek, MD Salman Zaheer, MD
GYN Oncology Angela Caffrey, MD	Radiation Medicine David Bush, MD Lilia Loreda, MD Jerry Slater, MD
Head & Neck Surgery Alfred Simental, MD	Radiology Richard Tully, MD Jason Smith, MD
Medical Oncology C.S. Chen, MD, PhD Thomas Godfrey, MD Steve Hardin, MD* Chung-Tsen Hsueh, PhD, MD Hamid Mirshahidi, MD Walter Quan, MD* Yuan Yuan, MD, PhD*	Resident Physicians Michael Kyle, MD* Windy Olaya, MD* Naveen Soloman, MD
	Transplant Institute Pedro Baron, MD Arputharaj Kore, MD* Okechukwu Ojogho, MD

*New Member 2009

NON-PHYSICIAN MEMBERS

Administration
Brenda Bruneau, Chief Patient Executive
James Pappas, MD, MBA, VP Quality

American Cancer Society
Alyson Henson Merrill

Cancer Call Center
Tamie Vasquez, Supervisor

Cancer Center Administration
Judy Chatigny, RN, MSN
Executive Director
Becky Cassady, RHIA, CTR
Director, Research
Linda Fine, CTR, Manager
Outcomes & Quality
Mariana Gonzalez, BS, BA
Administrative Assistant*
Brandon Zinke, MBA, LCSW
Clinical Director

Chaplain Program
Saul Sandoval
Leigh Averling

Desert Sierra Cancer Surveillance Program
John Morgan, DrPH, Epidemiologist

Dietitian, Adult Oncology
Andrew Woodward, MS, RD *

Oncology Nursing Inpatient Oncology Units
Terri Gasche, RN, Clinical Educator
Becky Yartzoff, BSN, Director

Outpatient Oncology Clinic
Terry Bonilla, RN, Clinical Educator
Lexine Thall, RN, MN, BC, AOCN,
Nurse Manager

Nurse Navigator Program
Karen Contreras, RN, BSN, OCN
Lung Navigator
Connie Haglund, RN, BSN
Breast Navigator
Vicky Ramirez, Navigator Assistant

Surgical Oncology
Pam Esquivel, RN, MSN, NP-C
Breast Center

Palliative Care
Lisa Bolla, APN, Nurse Practitioner

Pediatric Oncology
Dina Rincon, RN, Nurse Manager

Pharmacy Inpatient Pediatric Oncology Pharmacy
William Brown, PharmD

Outpatient Oncology Pharmacy
Mohammed Ghonim, PharmD, Director

Inpatient Adult Oncology
Michelle, Spencer, PharmD

Psychology
Jason Owen, PhD
M'Liss Doman, MD, Psyche Intern*

Quality Management Patient Safety & Reliability
Virginia Mullen, RHIA, Director

Radiation Medicine
Julihanna Madison, RN, Nurse Manager
Yoly Magana, RN, BSN, MBA
Clinical Director
Sandra Teichman, RN, BA, BSN
Publication & Protocol Development

Rehabilitation
Sarah Clark, MOTR/L, CLT*

Research Biospecimen Lab
Saied Mirshahidi, MSc, PhD,
Research Scientist

Center for Health Disparities Research
Marino DeLeon, PhD, Director
Nathan Wall, PhD, MBA
Molecular Medicine

Oncology Clinical Research
Teresa Gross, RN, BSN, OCN
Adult Team Lead
Susan Nottmeier, RN, MSN, CNS
Adult Team Lead
Candy Turner
Manager, Special Projects

Radiobiology Research
Daila Gridley, PhD, Radiobiology Research

Sponsored Research, IRB
Linda Halstead, IRB Administrator

Translational Research
Larry Sowers, PhD, Director

Social Work
Talolo Lepale, MSW
Oncology Social Worker

*New Member 2009

CANCER COMMITTEE REPORT

Mark Reeves, MD, PhD, Cancer Committee Chair

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Loma Linda University Medical Center’s Oncology programs and services are designed to meet the needs of patients and their families for comprehensive, innovative cancer care. Our work includes prevention, early detection, state-of-the-art treatment, long-term support, and lifetime follow-up of our cancer patients.

Members of the Loma Linda University “Cancer Care Team” include physicians, nurses, allied health professionals, chaplains, social workers, dieticians, clinical researchers, and hospital administrators who work together to provide optimum care for our patients. LLUMC offers eleven different disease specific tumor boards, multiple division level grand rounds, pre-treatment conferences, and physician education symposiums to provide the highest level of care, to teach, to explore treatment options, to maximize technological advances, and to encourage new ways of finding solutions.

Providing high quality care for our oncology patients and their families in a caring environment continues to be our primary focus and ongoing privilege. The Cancer Committee at LLUMC is committed to maintaining and improving the systems that support our Mission, Vision, Values, and Goals.

During 2008, the Cancer Committee and Cancer Data Center worked diligently to review, assess, and compile the documentation needed to demonstrate compliance with the standards of the American College of Surgeons (ACOS), in preparation for our May 2009 survey. This re-accreditation process which happens every three years, offers us an important opportunity to evaluate our cancer program to ensure that we not only meet but also exceed the industry standards with regard to cancer care.

Part of our commitment to quality and meeting the ACOS standards, involves completing a minimum of two improvement projects and two cancer outcomes quality of care studies annually. In 2008, the patient care and patient satisfaction studies completed include Stem Cell Mortality Study, Newly Diagnosed Lung Cancer Supportive Care – Needs Assessment Study, Lung Cancer Patient Gender Coping Study, and a Pathology Case Finding Completeness Audit.

At the end of 2008, a series of five data years including 2007, 2002, 1997, 1992, and 1987 were submitted to the National Cancer Data Base (NCDB) error free in compliance with our ACOS accreditation.

Reaching out to our patients and local community to provide cancer education and prevention programs is an important part of Loma Linda University Medical Center’s focus. The Cancer Committee, the Loma Linda University Cancer Center, and each of the other units and departments throughout the healthcare system, work in

collaboration to provide the “best practice” principles of cancer care and education to our patients. Together with other community agencies such as the American Cancer Society, we are able to bring programs and services to a rapidly growing Inland Empire Region. In 2008, we facilitated two new support groups, participated in local community events, gave six education talks, staffed four health fairs, and grew from an outreach of 11,000 in 2007 to over 13,000 in 2008.

One of the Standards of the ACOS for our Cancer Program Accreditation is to review and set annual goals. The Cancer Committee reviews and sets annual quality improvement goals to meet the criteria set forth by the College of Surgeons. There are four Taskforce subcommittees that contribute additional goals in several categories targeted for improvement. These Taskforce subcommittees and their facilitators include:

- I. Quality – Alfred Simental, MD, Chair
- II. Cancer Conference – Mark Reeves, MD, PhD, Chair
- III. Cancer Data Quality – Paul Lui, MD
- IV. Community Outreach – Sharmilla Roy-Chowdhury, MD, Chair (ACOS Liaison)

In 2008, the Cancer Program Goals focused on improvements in patient-centered care, and community outreach. These improvements included processes, programs, and services offered to our cancer patients across the various disciplines and allowed us to evaluate and improve the level of care offered at LLUMC. Goals accomplished in 2008 include:

CANCER CARE

- Opening of the New Oncology Clinic
- New Symptom Management Team & Program (Palliative Care)
- New Breast Cancer Survivors Clinic
- Two dedicated inpatient Palliative Care rooms were completed

CANCER DATA CENTER

- Tracked compliance of NCCN/COC Breast Cancer Treatment Guidelines
- Prepared for ACOS Accreditation Survey in May 2009
- Completed COC/AJCC Studies on Staging for Breast & Rectal Cancer

CANCER PATIENT SUPPORT SERVICES AND RESOURCES

- ♦ New Breast Cancer Survivors Clinic
- ♦ Developed a Care Journey Patient Resource Binder for each new patient
- ♦ Cancer Center Nurses gave cancer education talks at local businesses
- ♦ Started two Support Groups, one for Caregivers and one for Men
- ♦ Lung patient chemotherapy educations classes taught by nurse navigator
- ♦ Developed a psychosocial assessment tool to measure cancer patient distress levels
- ♦ Expand and improve the Cancer Center web site

COMMUNITY OUTREACH

- ♦ My Journey, My Health – 18th Celebration of Life Event for cancer survivors, their families, caregivers, and friends
- ♦ 1st Annual Inland Women Fighting Cancer “Believe & Walk for the Cure” 5k/10k Walk/Run benefiting the Loma Linda University Cancer Center
- ♦ Participated in four local health fairs to promote cancer awareness and education
- ♦ Provided four cancer education talks to community groups
- ♦ Provided sponsorship and participated in Relay for Life Loma Linda

RESEARCH

- ♦ Participated in Office of Sponsored Research Accreditation Project to improve community awareness of clinical trials available at LLUMC
- ♦ Screened all pediatric patients for potential protocol participation
- ♦ Completion of the new Biospecimen Tumor Tissue Bank
- ♦ Started planning for Chan Shun build-out of clinical and basic cancer research space

NEW MEDICAL ONCOLOGY SPACE FOR CANCER CENTER

In April 2008, the new Medical Oncology Clinic opened. This new comprehensive cancer treatment facility expands and significantly improves our ability to provide quality cancer care in state-of-the-art, esthetically designed infusion areas, procedure rooms, and examination rooms. This new facility, together with the recruitment of additional oncology physicians and nurses, has significantly changed the way that cancer care is delivered at Loma Linda University Medical Center. With our new members in place, the cancer team has achieved our goal to: “Provide service excellence in quality, efficiency, and profitability through an integrated cancer care delivery model that includes medical oncology, surgery, and radiation medicine.” Each day, the team identifies new ways to create seamless clinically integrated cancer patient care.

With the opening of the new Oncology Clinic, we have witnessed many goals and plans became a reality. This was demonstrated not only by the continually escalating numbers of patients seen, but by our improved patient satisfaction scores.

These new quarters enable the staff to deliver patient-centered care in a patient oriented environment. The new space tripled the size of the space available to treat our patients and encompasses over 10,000 square feet of renovated space. The space has been re-designed to accommodate medical oncology exam areas, an infusion suite, laboratory specimen collection, pharmacy, conference room, patient resource center, consultation rooms for psychosocial assessment, and nutritional consults. Another great feature is the healing gardens that offer patients and staff a place to think, talk, and reflect among a serene and lush garden setting.

Chemotherapy in the form of biologic response modifiers and all classifications of agents, blood products, antibiotics, and other services will now be administered in a specially designed infusion suite that holds a combination of 18 lounge-style chairs equipped with remote control ceiling mounted warming units to individualize the temperature for each patient with two additional private rooms with beds. Other services provided will include central line care, dressing changes, and injections. The patient and the nurse have the opportunity to select the best option for a comfortable clinical experience. Private beds, single lounge chair alcoves, and group rooms will be available to the patient to select from based upon their clinical condition and choice.

The examination area of the cancer center provides a state-of-the-art clinical setting to accommodate the physician in diagnosing, developing a comprehensive treatment plan, for consultations, second opinions, follow-up care, and in performing bone marrow biopsies. Thirteen examination rooms grouped in pods of three to five rooms can easily adjust to the medical oncologist’s style of practice. Special procedure rooms are equipped with all the tools necessary to perform bone marrow biopsies and aspirations without the patient leaving the comfortable and familiar surrounding of the exam area.

With Phase I of the new Oncology Clinic now completed, subsequent phases of the project will include additional examination rooms, consult rooms for psychosocial and nutrition assessments, a patient resource center, and clinical research space. A patient library, an image and appearance center, and clinical space to facilitate the practice of multidisciplinary disease specific clinics are all part of the different phases of the grand plan to change the delivery of cancer care in the future. In addition, the Biospecimen lab is nearing completion and is scheduled to open in early 2009. In Phase II of the Cancer Center expansion, additional research laboratory space and surgical oncology clinical space will be added. With Radiation Medicine located adjacent to the new Oncology Clinic, patients will soon find their support and care all in one convenient location.

We are continually grateful for the contributions of all those who helped plan, build, and especially to those who continue to work behind the scenes each day, to translate our goals into a higher level of oncology care for our patients. We appreciate not only the incredible work that has been done but, also the ongoing prayerful support of our staff, our physicians, our patients, and administration. We look forward with great anticipation to the next phases of development and many other significant improvements planned for our Cancer Program.

New Oncology Clinic Overview



CLINICAL CENTERS OF EXCELLENCE

Breast

Our approach to breast cancer treatment and research is comprehensive, multidisciplinary, and patient-centered. Members of the team include dedicated breast surgeons, pathologists, radiologists, social workers, advanced practice nurses, and others who are experts in breast cancer. This health care delivery team works collaboratively to assess the patient, plan the care, and then follows the patient through the process. In addition to the team, the patient has access to a nurse navigator, advanced practice nurse, clinical psychology intern, and Reach to Recovery volunteer. The coordinator helps the patient navigate through the system of appointments, schedules, and doctors appointments.

Gastrointestinal

LLUMC offers highly skilled surgeons who specialize in treating upper and lower GI cancers. In addition to surgery, they also offer a multidisciplinary approach to treating peritoneal carcinomatosis through Hyperthermic Intraperitoneal Chemothapy (HIPEC). This procedure offers hope to patients with peritoneal surface malignancies which can result from seeding of gastrointestinal cancer or abdominopelvic sarcoma, breast cancer, ovarian malignancy, and can also occur as a primary disease, for example with peritoneal mesothelioma.

HIPEC is a procedure which offers cytoreductive surgery to relieve the obstruction and remove macroscopic disease followed by Intra-peritoneal chemotherapy infusion. Because this chemotherapy is given at the time of surgery, directly into the abdomen, it targets any remaining microscopic disease which may remain following surgery. This provides the pharmacokinetic advantage of attaining high local concentrations of the chemotherapeutic agents that are 12 to 15 fold greater than the maximum tolerated plasma concentration.

Genitourinary

Genitourinary tract cancers are treated with multiple modalities, including surgery, radiation therapy, and chemotherapy alone or in combination, using a multidisciplinary approach to aggressively treat urological malignancies. Depending on the site and extent of disease, treatment for some GI cancers may require a collaborative surgical approach between GI and Urology surgeons to ensure optimal surgical debulking and the best long term management and quality of life possible for each patient.

The department is staffed with highly trained specialists for adult and child urological problems. The scope of procedures being offered also includes the use of robotic assisted laparoscopic surgery. The hospital system now owns two da Vinci Surgical Robots which were moved to the new Heart and Surgical Hospital in the Fall of 2008.

They are utilized to perform minimally invasive procedures by genitourinary and other services. Minimally invasive procedures with the da Vinci Surgical System provide improved clinical patient outcomes including a shorter hospital stay, faster recovery, and return to normal daily activities with markedly decreased post-operative discomfort and pain. The use of this innovative equipment has the added benefit of reduced strain to the body, reduced risk of blood loss and transfusions, a decreased risk of infections, a shorter hospital stay, less scarring, and improved cosmesis.

Gynecologic Oncology

The gynecologic department has three physicians with advanced training in the treatment and care of oncology patients. These gynecologic oncologists work closely with other oncologists to provide a multi-disciplinary approach to treatment by performing the surgery and the chemotherapy. These specialists collaborate to evaluate the disease status of new patients, plan their treatment, and assess the appropriate state-of-the-art treatment and combined approach for successfully fighting both GYN malignancies that spread to GI sites and GI malignancies that may spread to other GYN sites. When this type of spread occurs, the GYN and GI surgeons work together as a team to give each patient both optimal debulking, and the maximum functionality.

Otolaryngology - Head & Neck Surgery

State-of-the art surgical approaches offer unsurpassed outcomes in head and neck tumor surgery. A multidisciplinary tumor board with colleagues in radiation, medical oncology, pathology, radiology, and social work consult to offer the optimal treatment for each patient. A dedicated head and neck surgeon specializing in microsurgical plastic reconstruction treats patients with major head and neck defects. All services are coordinated to expedite patient care and scheduling. Our multidisciplinary care approach includes colleagues from Endocrinology, Nuclear Medicine, and the Head & Neck Surgery Team working together for thyroid and parathyroid diseases. The demonstrated excellence of the LLUMC Head & Neck Surgery Team have made them the regional referral center for tumors of the oral cavity, base of tongue, laryngeal cancer, endoscopic anterior skull base surgery, subcranial anterior skull base surgery, salivary gland tumors, thyroid cancer, and head and neck cancer reconstruction.

Minimally Invasive Video Assisted Thyroid surgery (MIVAT) is available to perform minimally invasive thyroidectomies with incisions as small as 1.5 cm instead of the 6-8 cm incisions from conventional thyroidectomies. This surgery, takes only 1.5 hours and is done with the assistance of magnified endoscopic cameras with dissection through mini incisions. Patients recover well with minimal blood loss which allows almost all of them to go home the next day and some the same day.

The newly opened Sinus and Allergy Center specializes in the medical and surgical treatment for tumors of the nose and sinuses and other ailments. This center allows for patients to be screened and treated for simple allergic disorders all the way up to skull

base tumors. The center has on site basic imaging which allows patients to be screened at the time of visit if necessary, providing an expeditious and convenient pathway to final diagnosis.

Neuro-Oncology

The department of neurosurgery is dedicated to innovation and research. Patients are treated by surgeons at multiple clinic sites in the Inland Empire. Our skilled clinical staff and neurosurgical specialists ensure that patients receive the highest level of integrated care. In 2008, the Neuro-Oncology Tumor Board moved to the new Cancer Center where it meets the first and the third Wednesday of each month. The Neurosurgery has a fully accredited Residency Training Program with five full-time clinical faculty and nine residents.

In 2008, LLUMC started the Gliadel Implantation Program. It was approved by the Pharmacy and Therapeutics Committee and the first patient was treated on November 7, 2008. From November 2008 to November 2009, a total of 11 patients have been treated.

Skin and Melanoma - Dermatology Oncology

It is estimated there will be more than 6,585 new cases of melanoma of the skin in California in 2008. At LLUMC there were 57 cases of melanoma in 2008. Among the innovative treatment interventions offered at LLUMC, the special micrographic surgery procedure conducted by a Mohs surgeon provides the highest potential recovery for many types of skin cancer even if the skin cancer has been previously treated. In this procedure, the physician serves as surgeon, pathologist, and reconstructive surgeon. It relies on the accuracy of a microscope to trace and ensure removal of skin cancer down to its roots. This procedure allows dermatologists trained in Mohs Surgery, to see beyond the visible disease, and to precisely identify and remove the intact tumor, leaving healthy tissue untouched. This technique is most often used as treatment for two of the most common forms of skin cancer: basal cell carcinoma and squamous cell carcinoma. While superficial in nature, they can behave aggressively. These frequently occur on the face which presents significant challenges in function and cosmesis. Mohs procedure is an extremely valuable surgical tool as it offers the benefit of tissue sparing. Ongoing vigilance through skin screening and education in sun protection techniques are an important part of ongoing patient education provided by dermatology at LLUMC.

Thoracic - Pulmonary Medicine

Lung cancer is the leading cancer killer in men and women in the United States. The weekly multidisciplinary Thoracic Tumor Board reviews new cases of lung cancer and other tumors of the chest and chest wall that are seen at LLUMC and at the Jerry L. Pettis Veterans Administration Medical Center. Specialists from both institutions engage in thoughtful and provocative discussions regarding the most effective diagnosis and treatment for each individual patient. The latest surgical and chemotherapy regimens and national treatment guidelines are discussed.

Pathology and Laboratory Medicine

The pathology and laboratory medicine provides a wide range of laboratory tests and services for inpatients and outpatients who have cancer and supports a variety of cancer research programs. Pathologists employ state-of-the-art immunohistochemical and electron microscope analysis to diagnose, classify, and determine the extent of cancers.

Radiology Department

The department offers comprehensive diagnostic imaging services and participates in each of the multidisciplinary cancer conferences (Tumor Boards) held at LLUMC. The department offers state-of-the-art 8, 16, and 64 channel multi-detector computed tomography (CT) scanners, three magnetic resonance imaging (MRI) magnets, and full-service diagnostic ultrasound (US) laboratory complement three conventional fluoroscopic angio-interventional suites. The radiology department supports the various multispecialty clinics and weekly tumor boards with state-of-the-art equipment such as computerized tomography, ultrasound, PET, and magnetic resonance imaging. They also offer nuclear medicine services to treat patients with I-131, Strontium.

Interventional Radiology

The interventional radiology section supports the cancer center by providing a full breadth of minimally invasive, image-guided (CT, US, and fluoro) oncologic procedures. The vast majority of these procedures are done with intra-venous sedation, with minimal recovery time. This includes percutaneous biopsies of deep visceral and lymphatic tumors, as well as other extra-cardiac and extra-CNS lesions. A robust ancillary central venous access service provides PICC lines and port-a-catheter placements for administration of chemotherapy and other medications.

Therapeutic procedures routinely provided are trans-arterial chemoembolizations (TACE) of liver tumors not amenable to surgical resection or curative chemotherapeutic or radiation treatments. Interventional radiology is currently involved in a prospective, randomized trial of proton therapy versus TACE in patients with limited hepatomas.

Recent years have seen the emergence of a growing practice of using percutaneous thermal based ablative technologies (radiofrequency, microwave, and cryo) for the treatment of visceral malignancies (mostly hepatic, renal, and pulmonary); these are performed in the CT-suite under mostly conscious sedation, and most patients have a short, overnight hospital stay. In both primary and metastatic hepatic and pulmonary lesions, these treatments are generally considered palliative and/or temporizing, with a goal of local control. With renal carcinomas however, a collaborative effort by interventional radiology and urology have led to these ablative techniques in many instances replacing surgery as the definitive oncologic treatment.

Radiation Medicine

The LLUMC department of radiation medicine was the first in the country to offer proton therapy in a clinical setting. The first patient was treated in October 1990, and through October 2009, a total of 14,062 patients have been treated for various types of tumors. The tumor sites most commonly treated include, prostate, CNS, breast, thoracic, pituitary, head and neck, chondromas, pelvic, and paraspinal neoplasms. Other benign conditions treated include macular degeneration and AVM's. Proton therapy through the Bragg Peak effect allows the radiation oncologist to increase the dose to the tumor while reducing the dose to surrounding normal tissue. In addition to proton therapy, conventional radiation services include external beam therapy and brachytherapy are given to patients with a wide range of malignancies and non-malignant conditions.

Surgical Oncology

The division of surgical oncology includes surgeons that are highly trained in the surgical treatment of cancer. This includes breast cancer, GI cancers, such as esophageal, gastric, pancreatic, colorectal, small bowel, liver and gallbladder; sarcomas; neuroendocrine tumors, such as carcinoids; skin cancers, such as melanoma. In addition, they specialize in the surgical treatment of metastatic lesions, such as liver resections for metastatic colon cancer. Our surgeons also treat other diseases, such as performing splenectomies, for those with ITP, not responding to medical management. The department performs a large volume of venous access device (porta-catheter) placements for those patients needing chemotherapy, or frequent IV hydration and have poor venous access. They work in conjunction with other departments, including other surgery specialties such as plastic surgery and urology on the combined procedures in the operating room to provide the most optimal outcomes for our patients.

PATIENT SUPPORT/OUTREACH

Oncology Nursing

LLUMC provides care for adult and pediatric oncology patients in both inpatient units and outpatient clinics in satellite offices located in Loma Linda and in the surrounding communities. All adult and pediatric patients are treated by oncology nurses who specialize in cancer treatment regimens and must meet competency standards annually. All oncology nurses are chemotherapy certified, and ONS Chemotherapy Certification classes are offered twice a year.

In the pediatric hematology and oncology nursing division, technological advances have effected dramatic improvements in the survival rates of children with cancer. Pediatric nursing care demands an advanced range of skills, from expertise in intensive care management to family counseling. Pediatric oncology nurses through training and experience possess a unique understanding for challenges families face when their child has been diagnosed with cancer. Their specialized training helps them not only treat the patient but identify needs for individualized supportive care throughout the treatment process for both the patient and their family as a unit. This Family-Centered Care Culture encourages and provides for inclusion of the parent(s) or primary caretakers in the decision-making process relating to the care interventions for their child. The Child Life department is actively involved in this Family-Centered Care model with patients and their families.

Nurse Navigator Program

Both lung and breast nurse navigators are available to provide concierge quality service for cancer inpatients and outpatients from point of referral through surveillance. LLUMC nurse navigators assist patients with:

- ♦ Access to cancer care services
- ♦ Resolution of appointment issues
- ♦ Oncology education for patients and caregivers
- ♦ Referral to community resources
- ♦ Scheduling to diagnostic testing

Navigators assist patients with scheduling of tests, presentation to tumor boards, questions, and provide infusion therapy education classes.

Nutrition Services

The clinical dietitian provides cancer patients with vitally essential support service that assesses each patient’s nutritional status and develops a nutritional care plan. The patient, dietitian, and physician can devise a nutritional plan adequate in calories and protein to meet the increased needs that may occur during treatment.

Psycho-Oncology Counseling

Patients of all ages and at all stages of diagnosis and treatment can have access to psychosocial support. Oncology social workers are available to assist patients with their psychosocial needs relating to diagnosis, treatment, and survival issues.

Breast Health Center

The Breast Health Center offers patients a comprehensive medical evaluation by one of our breast surgeons. These services include the added option of Oncoplastic reconstructive surgery performed by the plastic surgery team in conjunction with the surgical oncologist at the time of or directly following the primary surgical treatment. A multidisciplinary committee reviews the imaging and pathology as well as each patient’s medical information as recommended by the American College of Surgeons and in accordance with the NCCN breast cancer treatment guidelines. The Center offers supportive services that include a nurse navigator and a health psychology intern. Education on genetic testing, breast cancer diagnosis, and surgical postoperative care are provided to each patient.

Complete imaging studies are available including a dedicated breast MRI machine with a radiologist whose expertise provides excellent diagnostic recommendations. Follow-up studies can easily be compared with previous imaging to provide even better evaluation.

Our surgical oncology nurse practitioner is a valuable asset to the Breast Health Center. She works closely with the physicians during the work-up and surgical treatment phase and manages the survivorship clinic to provide long term follow-up care. LLUMC is blessed to have an experienced nurse practitioner whose many years of dedicated service have developed her skills to a high degree.

American Cancer Society

The country’s largest community-based volunteer organization dedicated to eliminating cancer by supporting research, prevention, education, and providing patient services. The ACS contributes to preventing cancer, saving lives from cancer, and diminishing suffering from the disease. From August 2007 to September 2008, a total of 199 LLUMC patients received services from our local Inland Empire ACS office through the use of physician referral forms. The ACS has also given LLUMC researchers thousands of dollars in grant funding over the years. Our local ACS partners with LLUMC each fall at our Family Health Fair to promote prevention and early detection programs.

Cancer Call Center

The new cancer call center assists cancer patients desiring an appointment with the Oncology Clinic, Breast Health Center, or other clinics by streamlining the referral process. When patients contact the call center, they receive concierge services to advise them on gathering all of their medical records including slides, reports, and films to ensure that their experience from their first consultation through each subsequent appointment will be informative and complete.

Loma Linda University Cancer Resource Center

Loma Linda University Cancer Center’s Patient Resource Center provides education and support for cancer patients, their families, and health care professionals. A large selection of cancer related literature is available to the patients and the public. Cancer support programs and groups include: “Look Good Feel Better,” “New Dimensions,” and “Transitions.” The Lebed Method, an effective therapeutic exercise and movement to music program, is offered twice a week. In collaboration with the American Cancer Society, we team up to offer a cancer resource library stocked with educational materials and other resources. Additionally, all patients have the opportunity to avail themselves of free wig fitting services.

Lebed Method Therapeutic Exercise Program

The philosophy of the Lebed Method is to focus on body’s restorative capacity through movement and dance as a way to improve the physical and emotional well-being of cancer survivors. The Cancer Center has a trained instructor and holds free weekly sessions throughout the year. This therapeutic exercise program is available for women with a history of breast surgery, node dissection, radiation, chemotherapy, lymphedema, or those who suffer with chronic fatigue. The program was created by two physicians and a dance movement specialist as a way to address many of the side-effects patients experience related to cancer treatment. The benefits of the program include:

- ♦ Regain range of motion
- ♦ Increase flexibility in frozen shoulder
- ♦ Work with balance issues both physically and emotionally
- ♦ Reduce swelling from lymphedema
- ♦ Minimize the risk of lymphedema
- ♦ Minimize depression
- ♦ Increase sense of femininity
- ♦ Enhance positive self image and joy
- ♦ Improve weight stabilization
- ♦ Increase fun
- ♦ Easy-no special physical abilities required.

The most important advantage of this program is that it encourages exercise through gentle movement, in a social environment with other individuals who have a common experience. It has been shown to improve mobility and decrease many of the debilitating problems cancer survivors face whether their treatment was completed recently or 30 years ago.

Look Good Feel Better

The Look Good Feel Better program is a community-based, free, national service designed to teach female cancer patients beauty techniques to help restore their appearance and self-image during chemotherapy and radiation treatments. Volunteer beauty professionals lead small groups, usually consisting of 6 to 10 women, through practical, hands-on experience. Women learn about makeup techniques, skincare, nail care, and options related to hair loss such as wigs, turbans, and scarves. Each program participant receives a free kit of cosmetics for use during and after the workshop.

Community Outreach Events

Throughout the year, the Cancer Center provides nurses to staff booths at many local health fairs, to serve as speakers at professional and lay audience presentations on cancer education topics to local organizations. The Cancer Center also sponsors special community events like: “Speaking of Women’s Health,” “Relay For Life Loma Linda,” and “Celebration of Life.” Combined, these support groups and events served an audience of over 1,372 people in our community in 2008.

Candlelighters Childhood Cancer Foundation Childhood Cancer Foundation of Southern California

The Inland Empire chapter is part of the national nonprofit organization that provides support for families who have or have had children with cancer. They provide emotional, social, educational, and emergency assistance to children and their families.

Family Care and Home Health

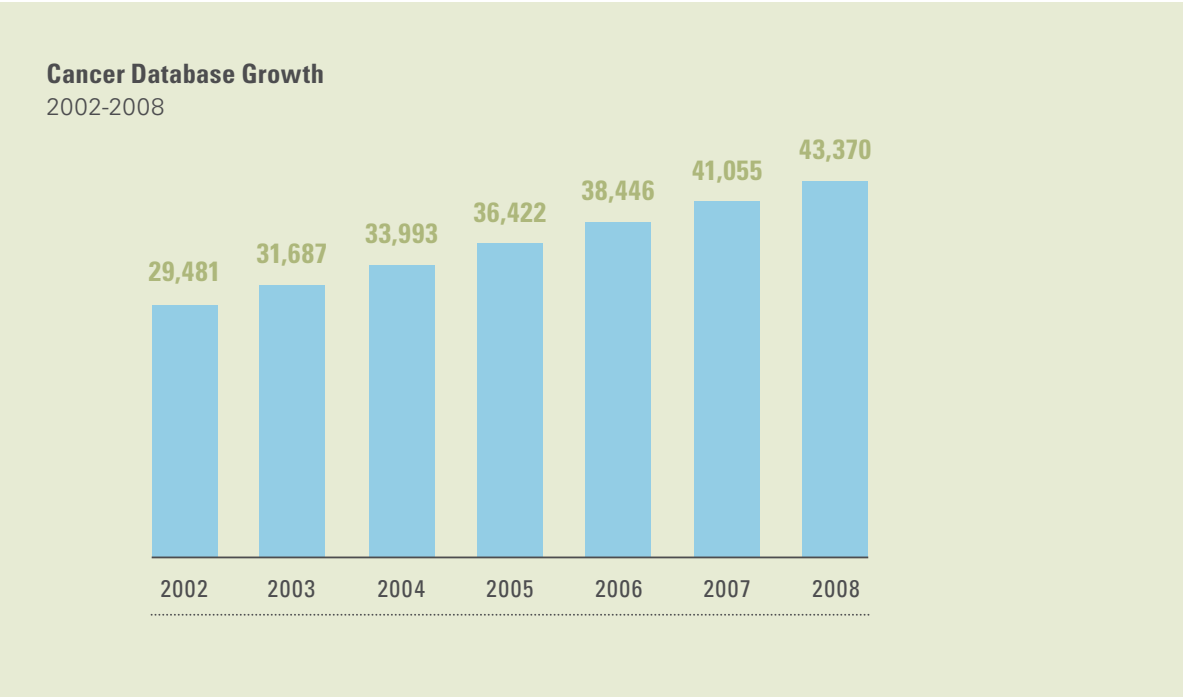
The Medicare-certified program provides holistic, and total shift care to cancer patients in their home, as well as, intermittent nursing, home health aides, homemaker, and ancillary services. Hospice care is referred to community organizations.

Ronald McDonald House

Serves as a low-cost, home-like site for families battling the stress of having a child with a critical illness.

CANCER OUTCOME AND QUALITY REPORT

Loma Linda University Medical Center has been a leader in treating cancer patients since 1905 and is one of only a handful of institutions throughout California with such a long history of collecting cancer. The Loma Linda Tumor Registry began collecting cases in 1947, long before reporting cancer became a law. This original data base now in archival status, contains over 33,000 cases through the year 1986. Beginning with cases from 1987, the active database by year-end 2008, contained over 43,000 cases. In 2008, the total number of living patients under active follow-up rose to a total of 17,670. At this current rate of growth, the Cancer Registry Database will grow to over 45,000 cases by 2009.



The cancer outcomes section collects specific cancer related information on each reportable cancer patient diagnosed or treated within the LLUMC system and continues to perform annual lifetime follow-up on each of these patients. The information collected is reported both to the California Cancer Registry in Sacramento as mandated by law and to the National Cancer Data Base, in conjunction with LLUMC’s American College of Surgeons (ACOS) accreditation requirements. Physicians and researchers at LLUMC utilize the data to identify ways to improve the quality of the services and care given to our patients. The database serves as an important resource for feasibility

studies, for grant proposals, and as the source data for many ongoing studies approved by the LLUMC/LLU Internal Review Board (IRB). Throughout this process, the confidentiality of each individual and their right to privacy is strictly protected.

In 2008, the cancer outcomes staffing included three Abstractors, one Tumor Board Coordinator, one Casefinder, one full-time and one part-time follow-up staff. The four Certified Tumor Registrars collected a total of 2,315 cases with 2,087 of those being newly diagnosed and treated. (See site table, page 33)

Multidisciplinary Tumor Boards

The Medical Center now offers nine weekly multidisciplinary tumor board conferences, coordinated by cancer data personnel. Tumor Board Conferences offer physicians an opportunity to present newly diagnosed cancer cases for a multidisciplinary review. Based on the type of cancer, cases are presented at one of the following cancer-specific conferences: breast, pediatric, ENT, GYN, thoracic, urology, melanoma, liver tumor conference, or the general tumor which covers all other types of cancer. In 2008, a new Neuro-Oncology Conference and in 2009, the Multidisciplinary GU Conference was added bringing the total tumor boards cancer conferences to 11.

At each of the tumor board cancer conferences, physicians present prospective cases for consideration. The patient’s history, scans, and pathology are reviewed. The findings are then discussed with further diagnostic and treatment options proposed. In 2008, a total of 1,272 prospective cases were presented among these weekly Cancer Conferences.

Cancer Conference – Tumor Boards Totals For 2008

*ACOS Standard 2.8 Requirements

Tumor Boards	Total Held	Total Cases	Prospective	Retrospective	Follow-Up	Physicians	House Staff	Allied Health
Breast	35	238	238	0	0	202	37	174
Pediatric	33	222	222	0	0	412	349	195
ENT	48	258	256	0	2	348	396	70
General	34	105	105	0	0	326	119	36
Gynecology	11	111	111	0	0	82	15	26
Thoracic	29	103	103	0	0	225	23	14
Urology	11	80	80	0	0	123	68	28
Melanoma	8	12	12	0	0	60	65	9
Neuro-Oncology	4	13	13	0	0	26	27	11
Liver Tumor	19	132	132	0	0	126	20	49
TOTAL	232	1272	1272	0	0	1930	1119	612
Total Analytic Cases			2087					
% Prospective To Analytic Cases			61%					

The Cancer outcomes section also completes audits, patient care evaluations studies, quality control on the data collected, and submits the selected data years annually to the National Cancer Data Base of the ACOS for comparison and benchmarking with other national data. In 2008, a total of 7,597 selected cases were submitted for the years 1987, 1992, 1997, 2002, and 2007.

In addition to collecting all cancer cases seen at LLUMC, each cancer patient is followed for life. Over the past three years, we have tracked a steady increase in the number of patients currently being followed. The trend appears to be about 1,000 patients a year or roughly half the patients that are diagnosed at LLUMC annually. Not surprisingly, this increase comes at a time when access to information via the internet is growing geometrically. The computer now provides anyone with a a basic knowledge of the internet access to whole libraries of information, medical texts, journals, and other publications. Patients are encouraged by medical facilities like Loma Linda University Medical Center, our community healthcare partners, the American Cancer Society, and other cancer related groups to participate in early detection, to understand all the treatment options and become their own health care advocates. The goal is to encourage earlier detection and diagnosis. The result of this greater patient awareness is reflected in an increasing demand and utilization of healthcare services.

Primary Site	*LLUMC	San Bernardino	California
Years	2008	2008	2008
Prostate	698	885	22,600
Breast	203	880	21,160
Lung/Bronchus	107	800	16,915
Colon & Rectum	66	630	14,080
Melanoma	62	265	6,585

*Many LLUMC cases come from other states and other counties in California.

On a national level, cancer outcomes data confirms that cancer patients are not only living longer with stable disease but in many cases without any detectable disease. As this trend continues, it is reasonable to expect that the number of patients under follow-up will also grow at an even higher rate. Our own follow-up also tells us that these patients do not come to us just for cancer care, in many cases they look to LLUMC for their overall healthcare needs. When you consider this, together with the sharp increase in the population density in the Inland Empire, these increasing patient numbers become an alarming signal of the demands we should expect on our healthcare systems in the coming years.

2008 COMPARISON OF MAJOR SITE DISTRIBUTIONS

The American Cancer Society’s publication “California Cancer Facts and Figures 2008” estimates there will be 142,085 new cancer cases diagnosed and 53,710 deaths from cancer. In 2008, the Cancer Registry recorded a total of 2,315 cases of cancer seen at LLUMC. Of these, 2,087 were newly diagnosed and/or received all or part of their first course of treatment at LLUMC. The top five cancers seen at LLUMC were compared with statistics from California and the United States in the table below.

The statistics for LLUMC are actual recorded new cancer cases collected from the medical record by registry staff and entered into the Cancer Registry Database. The figures for San Bernardino County and California are taken from estimated new cases by the American Cancer Society “California Cancer Facts and Figures 2008,” which is based on data from the California Cancer Registry.

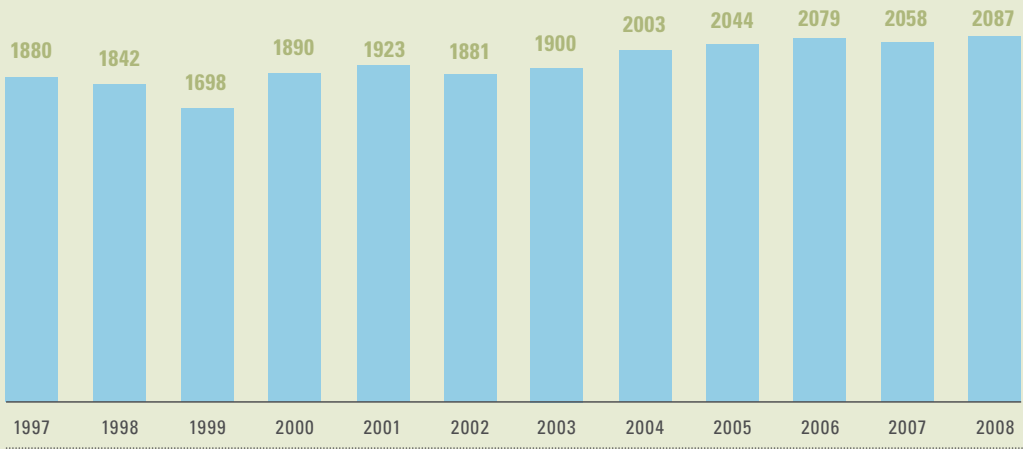
Market Share LLUMC Top Five Site In San Bernardino County

*LLUMC site numbers below include only San Bernardino County residents.

Site	San Bernardino	LLUMC*	Percentage
Prostate	885	144	16%
Breast	880	102	12%
Lung	800	48	6%
Colorectal	630	42	7%
Melanoma	265	37	14%
TOTAL	3,460	343	10%

Analytic Cases per Year

1997-2008



Loma Linda University Medical Center
New Cancer Cases by Year

Primary Site	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008
Oral Cavity	60	64	49	66	60	42	58	60	78	76	73	75
Nasal Cavity/ Sinus/Ear								10	11	11	9	
Esophagus	16	16	19	15	21	9	5	10	7	13	12	13
Stomach	14	13	13	24	14	14	8	20	21	19	18	13
Colon	64	56	59	50	34	53	41	36	47	57	37	39
Rectum	42	33	26	19	29	30	37	24	27	27	34	27
Liver	22	31	39	48	22	34	28	32	19	38	17	23
Pancreas	19	30	29	23	30	27	22	25	22	44	29	35
Other GI	14	21	19	13	23	15	18	21	19	25	19	36
Larynx	16	17	13	16	15	12	9	10	14	15	14	21
Lung/Bronchus	129	132	159	174	143	124	106	134	108	114	88	107
Other Respiratory	9	11	8	21	15	8	17	11	3	2	3	3
Soft Tissue	19	20	20	24	27	22	17	33	21	8	16	12
Bone	24	44	42	31	33	35	31	21	41	29	30	28
Melanoma	45	38	41	43	49	45	41	71	77	56	52	57
Other Skin	7	8	9	4	4	7	10	6	8	5	6	11
Breast	188	154	154	170	187	159	160	150	140	180	166	202
Cervix	131	73	49	42	29	26	21	36	41	30	34	46
Uterus	69	58	50	55	52	39	54	59	77	93	81	87
Ovary	27	35	30	40	40	34	40	44	29	56	38	61
Female Genital	25	19	17	12	14	20	20	24	26	18	22	43
Prostate	576	617	520	543	652	727	742	752	738	713	835	696
Male Genital	6	11	2	6	15	8	9	8	8	6	11	11
Bladder	28	40	23	33	31	34	33	28	25	27	38	42
Kidney & Other Urinary	38	25	39	42	40	45	37	45	51	40	51	67
Brain/CNS/Eye	111	94	78	124	130	113	131	130	134	118	103	109
Thyroid	12	30	36	45	25	19	31	32	59	58	53	53
Endocrine	16	9	6	27	23	13	20	21	18	24	4	16
Leukemia	63	44	52	67	61	60	64	65	68	69	54	55
Multiple Myeloma	6	12	9	18	9	15	8	12	11	16	2	8
Hematopoietic, NOS	1	4	3	2	2	5	7	3	6	1	8	0
Hodgkin's*/ Lymphoma	52	56	57	51	60	60	45	48	71	54	67	63
Unknown/Other	31	27	28	42	34	27	30	32	20	37	32	19

*Includes lymphoma cases coded to nodal and extranodal sites

Loma Linda University Medical Center
New Cancer Cases 2008 Residents

						AJCC TNM Stage Group						
Primary Site	Total Cases	Analytic	Non-Analytic	Male	Female	0	I	II	III	IV	Unknown	
Oral Cavity/Pharynx												
Tongue	27	24	3	18	9	1	6	2	3	10	2	
Other Mouth	20	18	2	8	12	0	7	0	1	10	0	
Parotid/Salivary Glands	19	17	2	13	6	0	3	3	3	6	2	
Tonsil	7	6	1	7	0	0	1	1	1	2	1	
Pharynx (Oropharynx, Hypopharynx, Nasopharynx)	10	10	0	9	1	0	1	1	1	5	2	
Digestive												
Esophagus	14	13	1	9	5	1	2	3	2	3	2	
Stomach	16	13	3	9	7	0	2	2	3	5	1	
Small Intestine	1	1	0	1	0	0	0	0	0	1	0	
Colon	51	39	12	25	26	0	7	4	10	13	5	
Rectosigmoid/Rectum	30	27	3	19	11	1	7	2	12	4	1	
Anus/Anal Canal/Anorectal	9	9	0	1	8	0	2	4	2	0	1	
Liver	24	23	1	13	11	0	7	4	6	2	4	
Gallbladder/Bile Ducts	17	17	0	7	10	1	3	7	3	2	1	
Pancreas	37	35	2	12	25	0	3	7	11	7	7	
Other GI	9	9	0	5	4	0	1	2	0	1	5	
Respiratory & Thoracic												
Sinuses/Nasal Cavity/Ear	12	9	3	7	5	0	0	1	2	1	5	
Larynx	30	21	9	23	7	3	5	1	6	6	0	
Lung and Bronchus	120	107	13	64	56	0	24	10	19	45	9	
Pleura/Other Thoracic	4	3	1	2	2	0	0	1	0	0	2	
Endocrine/Thyroid	77	69	8	33	44	0	20	6	15	9	19	
Blood and Bone Marrow												
Leukemia	61	55	6	32	29	0	0	0	0	0	55	
Multiple Myeloma	12	8	4	7	5	0	0	0	0	0	8	
Other Hematopoetic	1	0	1	1	0	0	0	0	0	1	0	
Bone and Joints	34	28	6	24	10	0	17	6	0	2	3	
Soft Tissue	14	12	2	10	4	0	2	1	3	2	4	
Skin												
Melanoma	61	57	4	36	25	18	20	6	6	4	3	
Other Skin	14	11	3	9	5	1	3	0	1	0	6	
Breast	228	202	26	6	222	57	52	54	20	13	6	
Female Genital												
Cervix Uteri	47	46	1	0	47	2	21	7	8	5	3	
Corpus Uteri	90	87	3	0	90	2	45	16	14	4	6	
Ovary/Fallopian Tubes	62	61	1	0	62	0	15	6	14	21	5	
Vagina	9	8	1	0	9	4	0	0	1	0	3	
Vulva	36	35	1	0	36	16	7	3	2	3	4	
Male Genital												
Prostate	760	696	64	760	0	0	5	649	31	8	3	
Penis	1	1	0	1	0	0	0	0	0	1	0	
Testis	11	10	1	11	0	0	4	3	2	0	1	
Urinary												
Bladder	53	42	11	43	10	12	11	8	0	9	2	
Kidney/Renal Pelvis	69	63	6	50	19	0	30	9	12	9	3	
Ureter/Other Urinary	4	4	0	3	1	1	2	1	0	0	0	
Brain/CNS/Eye												
Brain	85	79	6	52	33	0	0	0	0	0	79	
Other Nervous System	24	18	6	9	15	0	0	0	0	0	18	
Eye	13	12	1	9	4	0	0	3	1	0	8	
Lymphatic System												
Hodgkins Disease	15	15	0	7	8	0	0	8	4	0	3	
Non-Hodgkins Lymphoma	54	48	6	28	26	0	6	8	6	15	13	
Other/Unknown Primary	23	19	4	13	10	0	0	0	0	0	19	
TOTAL		2315	2087	228	1396	919	120	341	849	225	229	324

LOMA LINDA UNIVERSITY RESEARCH

Blood and Marrow Program and Research

Bone marrow transplantation is an established therapy for a variety of malignant and non-malignant pediatric diseases. Approximately 10% of pediatric ALL, nearly all cases of pediatric AML and neuroblastoma, recurrent pediatric non-Hodgkins and Hodgkins lymphoma, and many types of brain tumors or metastatic sarcomas are conditions for which blood or marrow transplant are the recommended therapy. In addition, non-malignant conditions such as: aplastic anemia, severe immune deficiencies, and a variety of inborn errors of metabolism can be cured with bone marrow transplantation. The pediatric oncology program at LLUMC generates about 35-40 referrals for transplant per year.

The pediatric blood and marrow transplant program is under the direction of Christopher Morris MD, PhD, and Joan Morris, MD. In 2008, a total of 23 pediatric transplants were performed. This brings the total of transplants performed for both adult and pediatric since the program's inception in June of 2002 through 2008 to 207. The pediatric transplant team currently includes two pediatric oncologists (CCS paneled) with extensive experience in autologous and allogeneic transplants.

Adult Blood and Marrow Program

Stem Cell Transplants 2002 - 2008

	Autologous	*Allogeneic
2002	16	0
2003	10	1
2004	7	3
2005	10	6
2006	4	1
2007	1	0
2008	0	0

Pediatric Blood and Marrow Program

Stem Cell Transplants 2002 - 2008

	Autologous	*Allogeneic
2002	1	3
2003	3	14
2004	5	15
2005	11	13
2006	5	7
2007	5	13
2008	5	18

*Matched related donor

Pediatric Hematology/Oncology

The inpatient pediatric oncology unit 4800 is a 33 bed Intensive/Intermediate and Acute care nursing unit providing comprehensive 24-hour nursing care to infants through adolescents with problems related to neoplastic diseases such as leukemia, blood diseases and disorders such as sickle cell disease, and aplastic anemia. The unit performs blood and marrow transplants to infants through age 21 years, provides inpatient chemotherapy, high dose chemotherapy, treats the complications associated with neoplastic disease and provides post operative care.

Matched related	45	Adult	59
Cord blood	6	Pediatric	118
Matched unrelated	32	TOTAL	177

Adult Hematology/Oncology Research

Medical oncologists provide personalized, multidisciplinary, diagnosis, and treatment for all cancer diagnoses on the outpatient and inpatient units. Areas of emphasis include adult acute leukemia, prostate, breast, lung, and colon cancer. Patients with colon cancer often benefit from both pre and post surgical systemic therapy. Many GI protocols now utilize the newest targeted therapies and drugs. In addition, eligible patients can participate in industry-sponsored trials and in National Cancer Institute sponsored clinical trials through the Southwest Oncology Group, the National Surgical Adjuvant Breast and Bowel Projects, and the Radiation Therapy Oncology Group.

Inpatient adult oncology care is provided on our dedicated 26 bed unit. The unit supports an intermediate and acute level of nursing care to a patient population ranging in age from adolescent to the geriatric patient. These patients are under the care of the following services: hematology/oncology, surgical oncology, gynecology oncology, radiation oncology, and palliative care. On the oncology unit, the inpatients receive chemotherapy, radiation therapy, post-operative care, and palliative care by nurses who have received additional training to provide this specialized care. The unit staff provide a patient-centered care experience that is safe, compassionate, and timely for patients and their families. Chemotherapy nurses at LLUMC receive specialized training and credentialing to be certified to administer infusion treatments safely. The new oncology clinic's infusion unit, provides a comfortable state-of-the-art equipped facility to administer outpatient chemotherapy to adult oncology patients.

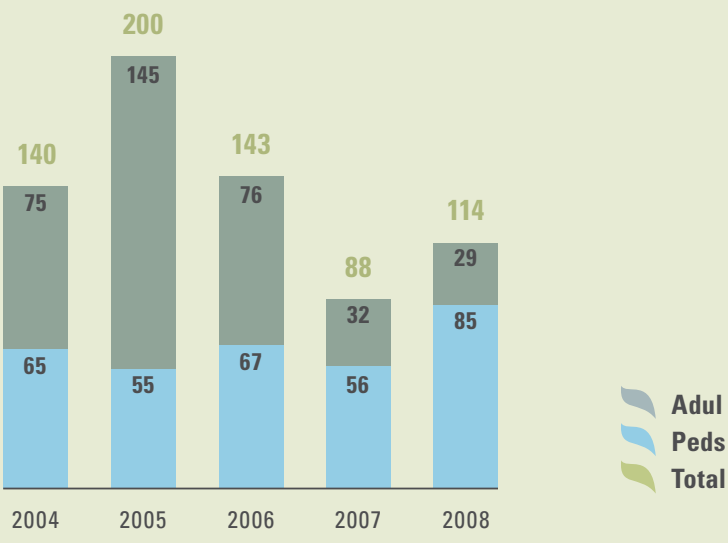
Clinical Oncology Research

The ongoing mission is to help educate our patients and the community on the newest treatment options and those available through clinical research at LLUMC. To achieve this, oncology clinical research works in cooperation with the departments of medical oncology, surgical oncology, pediatric oncology, radiation medicine, palliative care, and home health services to provide patients with up-to-date information on the various protocol treatments along with other options in palliative and supportive care services available to help them achieve optimal recovery and the best quality of life possible. Loma Linda University Medical Center and Loma Linda University Children’s Hospital maintain their commitment to offer clinical trial participation to any eligible patient seen at these facilities or any of the other LLUMC outpatient clinics and satellite offices.

Clinical research at LLUMC is designed to reach out to community physicians in the surrounding region to foster better communication on treatment protocols. Working together, physicians in both the local and university setting can offer their patients the newest and best care that research has to offer. Future goals are to continue participation in pharmaceutical trials, develop additional physician initiated trials and empower all physicians to collaborate in achieving a World Class Center of Excellence in clinical research.

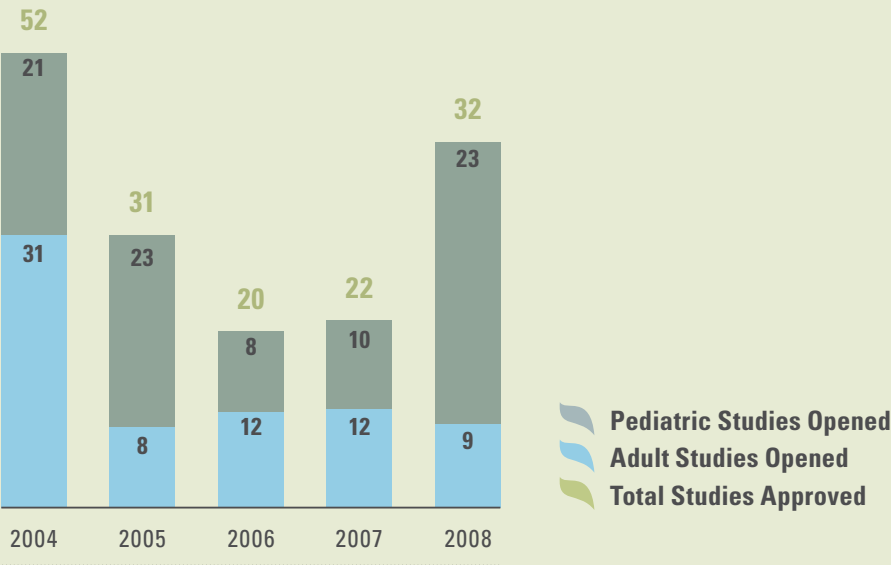
In 2008, a total of 114 patients both adult and pediatric were accrued on clinical oncology research protocols, plus an additional 31 patients were accrued on radiation medicine oncology protocols. Pediatric trials are performed in cooperation with the Children’s Oncology Group and other industry sponsored pharmaceutical studies. Adult trials are implemented in cooperation with various national cooperative groups including SWOG, NSABP, and other industry sponsored pharmaceutical studies.

Oncology Clinical Research
Adult and Pediatric Enrollments 2004-2008



In 2008, we added nine new pediatric treatment studies. A total of 85 new pediatric patients were enrolled on protocols through 2008.

Oncology Clinical Research
Studies Opened 2004-2008



In 2008, we opened 23 new adult studies and enrolled an additional 29 adults on protocol studies.

Center for Health Disparities Research

Eliminating Health Disparities through research, education, diversity, and community outreach and partnership is the goal of the LLU Center for Health Disparities and Molecular Medicine (CHDMM). The CHDMM is a National Center on Minority Health and Health Disparities (NCMHD) Research Center of Excellence, funded by awards from the NCMHD and NIGMS, NIH. The CHDMM is located at the School of Medicine and includes a collaborative transdisciplinary partnership with the LLU School of Public Health. The CHDMM team includes 17 leading faculty members engaged in the education, research, and community outreach components of the center. The main objectives are as follow:

EDUCATION: To increase the number of biomedical and physician scientists from underrepresented groups and medically underserved backgrounds. Educate the physicians and scientists through dialogue on emerging solutions in health disparities.

RESEARCH: To create a multidisciplinary team of biomedical scientists focused on studying the role of oxidative stress and other cellular stressors that contribute to health disparities in cancer, diabetes, and stroke. To evaluate the Center’s efforts to translate emerging research results and evaluate subsequent community-based interventions to test the relevance of clinical findings in “real life.”

COMMUNITY: To establish strategic partnerships with community organizations in the Inland Empire. Only if the community is part of the solution can new insights be translated from the laboratory to effective interventions. To share these findings in ways that are both understandable and accessible with interested partners in the Inland Empire.

MARINO DE LEON, PhD: Serves as the director of the CHDMM. His focus is in the effects of fatty acids and fatty acid proteins in cellular growth and oxidative stress. This research has specific implications for cancer, diabetes, and stroke.

Other team members that are principal investigators in the NIH center award are:

CARLOS A. CASIANO, PhD: His focus is the relationship between prostate cancer, oxidative stress, and TCP75 (LEDGF) and their relationship to the increased incidence and mortality rates among African-American men.

DAISY D. DE LEON, PhD: Her research studies demonstrate how IGF-II, cathepsin D (CD), and FABP are associated with the disparity in survival among African American cancer patients.

NATHAN R. WALL, PhD: His focus is on potential genetic based therapies, specifically, the inhibitor of apoptosis protein “Survivin” as a therapeutic target.

SUSANNE B. MONTGOMERY, PhD: Her focus is to strengthen and expand the already formed community partnerships and form new relationships to create a strong outreach core in the Inland Empire.

Nursing Research

Nursing research seeks to understand the patient knowledge and response to their diagnosis and treatment of cancer. Through the collaboration with healthcare practitioners at Loma Linda University Medical Center, Loma Linda University Faculty Medical Offices, Loma Linda University Cancer Center, and other universities and Cancer Centers within our region, we hope to build a greater understanding of the care and treatment of patients diagnosed with cancer.

Over the past year we have built our network with the City of Hope, UCLA School of Nursing, and Azusa Pacific University School of Nursing. Students completing their Ph.D. in nursing have studied breast cancer in Hispanic women over 70 years of age. We have also provided insight into the use of navigators in assisting patients traverse the health care system when diagnosed with cancer. Future studies include evaluating spirituality in the cancer patient and use of the simulation lab in development and assessment of communication skills.





Jason E. Owen, PhD

TITLE: Supportive Care Needs In Patients With Lung Cancer
AUTHORS: Jason E. Owen, PhD, MPH, Erin O. Bantum, PhD, Sharon Sanders, MA, Andrea Thornton, PhD and Annette Stanton PhD

PURPOSE: We sought to characterize unmet supportive care needs in individuals with lung cancer and to identify correlates of these unmet supportive care needs.

METHODS: Fifty-six participants from Loma Linda University and City of Hope Medical Center were recruited to complete a questionnaire assessing demographic characteristics, supportive care needs, interest in psychosocial services, and a range of other psychosocial constructs.

RESULTS: Across the 4 supportive care needs domains, participants reported the greatest level of need for help with coping with physical symptoms (=3.1), followed by psychological needs (=2.6), health system/informational needs (=2.4), and physical and emotional needs related to healthcare (=2.1). In multivariate regression models, demographic and medical characteristics were not associated with greater intrusiveness of cancer-related thoughts/feelings, distress, total mood disturbance, and depressive symptoms, as well as more physical symptoms and both avoidance and problem-focused coping. Additionally, having more supportive care needs was significantly associated with lower levels of satisfaction with healthcare providers. Regarding interest in services, 94.4% of participants reported interest in at least 1 of 13 possible supportive care services, and the mean number of desired services was 4.2 (sd=3.0). 50% of participants endorsed interest in receiving at least one psychological service. Greater symptoms burden, mood disturbance, and cancer-related trauma symptoms were also positively associated with interest in a number of psychosocial services.

CONCLUSIONS: Those with lung cancer experience a variety of unmet supportive care needs that appear to be strongly linked with psychosocial symptoms, suggesting that patients are interested in and could potentially benefit from a number of services that might improve quality of life.

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Translational Research

Translational research seeks to bridge the gap between the basic science laboratory and the clinic for the purpose of improving the quality of patient care. Benefits to the clinic can involve more selective and targeted therapy options and more accurate methods for diagnosing disease. At Loma Linda, several laboratories are performing state of the art research in many fields relevant to cancer, including cell biology, biochemistry, and pharmacology. The investment in shared equipment and resources at Loma Linda have placed the most current technology in the hands of our scientists and have facilitated studies impossible only a few years ago. Translational projects formed between clinicians and laboratory-based scientists can increase the rate at which scientific discoveries are “translated” into better patient treatment. Conversely, by interacting with clinicians, the laboratory-based scientists can more finely tune their investigations toward meaningful and clinically significant questions.

In 2008, five groups in the basic sciences were actively involved in Translational Cancer Research, producing peer-reviewed papers. Several of these projects are funded by the National Institutes of Health and National Cancer Institute.

One of our younger investigators, **Dr. Eileen Brantley** is actively involved in the development of novel chemotherapy agents and in particular, developing agents that are active against estrogen-receptor negative breast tumors which currently represent a formidable clinical challenge.

McLean, L., Soto, U., Agama, K., Francis, J., Jimenez, R., Pommier, Y., Sowers, L. and Brantley, E. (2008) Aminoflavone induced oxidative DNA damage and reactive oxygen species-mediated apoptosis in breast cancer cells. *Int J Cancer*. Apr 1;122(7):1665-74. http://www.ncbi.nlm.nih.gov/pubmed/18059023?ordinalpos=5&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_DefaultReportPanel.Pubmed_RVDocSum

Dr. Daisy DeLeon’s group has also been studying breast cancer. Dr. DeLeon’s group has been very active in studies aimed at understanding signaling pathways in breast cancer and how these pathways, when inappropriately activated, provide an unwanted selective advantage to the cancer cells.

Singh K.S., Moretta, D., Almaguel, F., De Leon, M. and De Leon, D. (2008) Precursor IGF-II (ProIGF-II) and Mature IGF-II (mIGF-II) Induce Bcl-2 And Bcl-x(l) Expression through different signaling pathways in breast cancer cells. *Growth Factors*. 26(2): 92-103. http://www.ncbi.nlm.nih.gov/pubmed/18428028?ordinalpos=28&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_DefaultReportPanel.Pubmed_RVDocSum

The Laboratory of **Dr. Penny Duerksen-Hughes** has been studying the mechanisms by which particularly virulent form of the human papillomavirus (HPV) interfere with signaling pathways in susceptible cells, resulting in several types of cervical and head and neck cancers. Dr. Duerksen-Hughes has also initiated an ambitious drug discovery program to identify agents that could potentially reverse the effects of HPV infection and render infected tumor cells susceptible to standard forms of cancer chemotherapy.

Filippov, V., Schmidt, E.L., Filippova, M. and Duerksen-Hughes, P.J. (2008) Splicing and splice factor SRp55 participate in the response to DNA damage by changing isoform ratios of target genes. *Gene*. 420:34-41. http://www.ncbi.nlm.nih.gov/pubmed/18571879?ordinalpos=3&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_DefaultReportPanel.Pubmed_RVDocSum

Tungteakkhun, S., Filippova, M., Neidigh, J.W., Fodor, N. and Duerksen-Hughes, P.J. (2008) The interaction between HPV 16 E6 and FADD is mediated by a novel E6 binding domain. *J Virol*. 82:9600-9614. http://www.ncbi.nlm.nih.gov/pubmed/18632871?ordinalpos=4&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_DefaultReportPanel.Pubmed_RVDocSum

Dr. Jonathan Neidigh has been investigating how reactive chemicals from activated inflammatory cells (neutrophils) can cause damage to the proteins that surround DNA, potentially resulting in cancer-causing damage.

Kang J.I. and Neidigh, J.W. (2008) Hypochlorous acid damages histone proteins forming 3-chlorotyrosine and 3,5-dichlorotyrosine. *Chem Res Toxicol*. 21, 1028 – 1038. http://www.ncbi.nlm.nih.gov/pubmed/18452314?ordinalpos=5&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_DefaultReportPanel.Pubmed_RVDocSum

Dr. Lawrence Sowers has been conducting studies into how damage to DNA can result in cancer-causing mutations. Studies are also underway to understand how this damage is repaired. These studies will allow us to understand more fully how cancer is caused, why certain people are more prone to developing cancer, and how cancer chemotherapy agents can be modified so they are more selective in killing tumor cells with fewer side-effects.

Liu, P., Theruvathu, J.A., Darwanto, A., Lao, V.V., Pascal, T., Goddard, W 3rd and Sowers, L.C. (2008) Mechanisms of base selection by the Escherichia coli mispaired uracil glycosylase. *J Biol Chem*. 283, 8829-8836. http://www.ncbi.nlm.nih.gov/pubmed/18208817?ordinalpos=12&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_DefaultReportPanel.Pubmed_RVDocSum

Kang, J. and Sowers, L.C. (2008) Examination of hypochlorous acid-induced damage to cytosine residues in a CpG dinucleotide in DNA. *Chem Res Toxicol*. 21, 1211-1218. http://www.ncbi.nlm.nih.gov/pubmed/18826175?ordinalpos=8&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_DefaultReportPanel.Pubmed_RVDocSum

Cui, Z., Theruvathu, J., Farrel, A. and Sowers, L.C. (2008) Characterization of synthetic oligonucleotides containing biologically important modified bases by MALDI-TOF mass spectrometry. *Anal Biochem*. 379, 196-207. http://www.ncbi.nlm.nih.gov/pubmed/18485883?ordinalpos=10&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_DefaultReportPanel.Pubmed_RVDocSum

Translational Research - Mass Spectrometry

The Loma Linda University Mass Spectorometry Facility, established in the summer of 2007, is located on the second floor of Mortensen Hall (room 230). It currently houses nine mass spectrometers including three Agilent GC/MS, on Waters Ultima GCT, two Waters Ultima QTOFs, and one Thermo-Scientific LCQ-Deca, one Agilent Triple-Quadruple, and one Bruker's Atofex MALDI-TOF. Collectively, these instruments provide a unique and complementary mass spectrometry capability to investigators in the Loma Linda University and Loma Linda University Medical Center for identification, structure elucidation, and identification of protein post-translational modification sites. A more complete description of each instruments capabilities is listed below.

AGILENT GC-MSD

The mass spectrometry facility has two identical Agilent CG (6890N)-(MSD (5973 inert) systems-GCMS 2 (top) set with the EI (electron ionization) mode and GCMS 3 (middle) set with the CI (chemical ionization) mode, and one old Agilent GC (5890) –MSD (5970) system, GCMS 1 (bottom) which is set with the EI (electron ionization) mode, and a manual injection port for routine GC/MS analysis of small organic compounds.

The Agilent GC-MSD series is a single quadruple mass spectrometer with unit resolution. This instrument is dedicated to separation (by MIM scan modes) of non-polar small organic mixtures. Polar compounds are derivatized with TMS or other types of derivatization reagents before introduction to the GCMS system.



WATERS GCT

The Waters GCT (gas chromatography/time-of-flight mass spectrometer) is linked with an Agilent 6890plus Gc. The TOF analyzer of this instrument has a resolving power (resolution) of 5000 in FWHM providing exact mass measurement (<10 ppm) of small non-polar organic compounds.



WATERS QTOF ULTIMA

The Waters Q-TOF is applied to the identification of proteins and post-translational modifications, de novo peptide sequencing, intact protein analysis (<20K, MW), as well as to exact mass determination (HRMS – 10000 FWHM) for small molecules. Currently, the facility houses two QTOFs, one linked with Waters capillary HPLC and dedicated to proteomics research by nanoLC/MS/MS; another linked with Waters 2795 HPLC and dedicated for small molecule mass measurement and for students training.



LCQ DECA XP

The LCQ Deca XP is used primarily for proteomic applications, including protein identification, detailed peptide mapping; long column capillary chromatography is used for peptide mapping. Identification of proteins is performed on proteolytic digests by means of nanoflow LC-MS/MS with subsequent database searches using software packages such as Mascot and Sequest.



AGILENT 6410 TRIPLE QUADRUPE

The Agilent 6410 Triple Quadrupole Mass Spectrometer is linked with the Agilent 1200 HPLC and PAL autosampler housing six 96 well plates. It has the capability of performing electrospray (ESI in both positive and negative mode) mass analysis and has the features of Product-Ion scan, precursor-Ion scan, selective-Ion scan (SIM), and multiple-Ion scan (MRM). The MRM mode is very specific and highly sensitive for quantification of polar small organic molecules or peptides. For small molecules, the sensitivity (LOD is about one pico-gram on a HPLC column).



BRUKER AUTOFLEX MALDI-TOF

The Bruker AutoFlex (MALDI-TOF) mass spectrometer uses UV nitrogen laser to perform linear-(low resolution for higher molecular weight compounds such as intact proteins) or reflectron mode (higher resolution for lower molecular weight compounds such as protein digests, oligoDNAs) with delayed extraction mass analysis. Typical analysis performed at the uM (micromolar) concentration range, depending on sample type.



Medical Oncology

BIOSPECIMEN LABORATORY

The LLUCC Biospecimen Laboratory located in the Chan Shun Pavilion was completed in 2008 and the collection of tumor tissue samples began in January 2009.

Cancer research studies frequently rely on tissue specimens to investigate the causes of cancer, how to treat it and how to prevent it. Obtaining the specific types and quantities needed to do these type of investigational researches can be challenging.

Biospecimen laboratory at LLUCC is providing high-quality human tissues and correlating demographic and medical information, including age, gender, race, diagnosis, stage of disease, and treatment, for the conduct of molecular genetic and proteomic research in cancer to the investigator.

The biospecimen laboratory, a 1,200 square foot facility, contains high-quality specimens obtained from cancer patients, such as fresh frozen tumor and matching normal tissues, blood products such as blood cells, plasma, serum, bone marrow, also DNA, RNA, and protein isolated from tumor tissues.

The biospecimen laboratory utilizes a specialized software program caTissue for inventory, storage, and entering basic clinical data for each specimen collected. It provides a summary page which indicates the number and types of available specimens which can help to facilitate collaborative research. The software program caTissue is part of the National Cancer Institute Biomedical Informatics Grid (caBIG).

The biospecimen laboratory is designed to host visiting scientists and graduate students working on different research studies. The biospecimen laboratory will collaborate with other cancer research institutes and researchers to explore new types of therapies.

Physicians and scientists are encouraged to visit the summary page for the biospecimen lab located on the LLUMC VIP Web site, ancillary desktop under Cancer Center, caTissue. This summary page tracks the current number and types of available specimens and can facilitate cooperative research between Loma Linda University Cancer Center and other departments on campus. <https://gcatisue.mc.ad.lluahsc.org/catissuecore/RedirectHome.do>



Saied Mirshahidi, MSc, PhD
Research Scientist

Chien-Shing Chen, MD, PhD

MEDICAL ONCOLOGY RESEARCH

TITLE: In Vivo Activity of ABT-869, A Multitargeted Kinase Inhibitor, Against Acute Myeloid Leukemia With Wild-Type FLT3 Receptor



IN VIVO ACTIVITY OF ABT-869, A MULTITARGETED KINASE INHIBITOR, AGAINST ACUTE MYELOID LEUKEMIA WITH WILD-TYPE FLT3 RECEPTOR

Zhou J, Janakakumara, JV, Bi C, Neo S, Pan M, Poon L-F, Xie Z, Yu H, Yeoh E-J, Lu Y, Glaser K, Albert D, Davidsen S, Chen CS. In vivo activity of ABT-869, a multitarget kinase inhibitor, against acute myeloid leukemia with wild-type FLT3 receptor, Leukemia Research 32:1091–1100, 2008.

ABSTRACT

Neoangiogenesis plays an important role in leukemogenesis. We investigated the In Vivo anti-leukemic effect of ABT-869 against AML with wild-type FLT3 using RFP transfected HL60 cells with In Vivo imaging technology on both the subcutaneous and systemic leukemia xenograft models. ABT – 869 showed a five-fold inhibition of tumor growth in comparison with vehicle control. IHC analysis revealed that ABT-869 decreased p-VEGFR1, Ki-67 labeling index, VEGF and remarkably increased apoptotic cells in the xenograft models. ABT-869 also reduced the leukemia burden and prolonged survival. Our study supports the rationale for clinically testing an anti-angiogenesis agent in AML with wild-type FLT3.



Chung-Tsen Hsueh, MD, PhD

MEDICAL ONCOLOGY RESEARCH - METABOLIC APPROACHES TO CANCER

TITLE: Mechanism of decreased cell viability in prostate cancer cell lines following arginine depletion. – April 15, 2008

LOCATION: 2008 AACR Annual Meeting, San Diego Convention Center

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AUTHOR BLOCK: Eddy C. Hsueh, Stephanie M. Knebel, Chung-tsen Hsueh, Yun-chung Leung, Wai-hung Lo, Paul N. Cheng, St. Louis University, St. Louis, MO, Loma Linda University, Loma Linda, CA, Hong Kong Polytechnic University, Hong Kong, China

We have previously reported the sensitivity of prostate cancer cell lines to arginine depletion. To elucidate the mechanisms causing decreased cell viability following arginine depletion, we investigated mTOR pathway proteins and levels of nitric oxide synthase (NOS) following arginine depletion.

Recombinant human arginase (BCT-100) was manufactured by fermentation of a recombinant B. Subtilis strain LLC 101 encoded with human arginase gene. Urea cycle integrity was evaluated by co-culture of 0.5 U BCT-100 and increasing concentrations of citrulline or ornithine. Cell viability was determined using tetrazolium salt conversion method after 72h treatment at 37 degrees Celceus. Levels of DNA fragmentation were detected using ApoDirect TUNEL assay following 24h and 36h treatment with BCT-100. Western blot analysis for 4EBP1 and S6K1 phosphorylation were performed following 48h co-culture with BCT-100 with and without citrulline supplementation. To determine whether addition of rapamycin further affects cell viability, prostate cancer cells were co-cultured with 0.5 U BCT-100 and 0nM, 10nM or 100nM rapamycin. To determine the effect of BCT-100 on NOS level, prostate cancer cells were cultured with increasing concentrations of BCT-100 for 72h. NOS levels were detected using Ultrasensitive Colorimetric NOS Assay Kit.

Ornithine supplementation following arginine depletion failed to rescue prostate cells from cytotoxicity. Addition of citrulline diminished the cytotoxic effects of arginine depletion. TUNEL analysis at 24h and 36h demonstrated that BCT-100 mediated cell death due to non-apoptotic events. Western blot analysis revealed that arginine depletion with or without citrulline supplementation caused changes in phosphorylation of mTOR signaling pathway proteins, 4EBP1 and S6K1. However, addition of rapamycin did not enhance cytotoxicity in prostate cancer cell lines following arginine depletion. Increasing levels of BCT-100 did not affect NOS levels in prostate cancer cell lysates.

BCT-100 mediated cell death in prostate cancer cell lines were not due to cytotoxicity via the apoptotic pathway. Arginine depletion with BCT-100 affects the mTOR pathway, but does not affect NOS concentration.

Walter D.Y. Quan, Jr., MD, PhD

MEDICAL ONCOLOGY RESEARCH

TITLE: High-dose Intensity Pulse Interleukin-2 with Famotidine in Metastatic Kidney Cancer

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Lymphokine-activated killer cell (LAK) activity against tumor cell lines may be induced by intravenous (i.v.) interleukin-2 (IL-2). Daily short infusions (pulses) have been developed to decrease toxicity while maintaining the anticancer activity of this agent against kidney cancer. The antihistamine, famotidine, may increase IL-2 uptake by the IL-2 receptor on lymphocytes. We have treated 12 patients with metastatic kidney cancer, using pulse IL-2 (18 million IU/M2 i.v.) over 15-30 minutues, preceded by famotidine (20 mg. I.V. daily for 5 days) on an oncology inpatient unit. Cycles were repeated every three weeks until decease progression. Patient characteristics were as follows: nine males with median age of 66 years (range, 48-74), and median Eastern Cooperative Oncology Group performance status of one; common metastatic sites included in lungs nine, and lymph nodes three. Median number of cycles received was 2two (range, 1-5). The most common toxicities were fever, rigors, and hypomagnesemia. Two (2) patients had partial responses (17% response rate). Responses occurred in the liver (1115 months) and lung, pleura, and lymph nodes (3 months). Pulse IL-2 with famotidine shows activity in kidney cancer.



D. Duane Baldwin, MD

SURGICAL ONCOLOGY RESEARCH

TITLE: Mechanisms of Hemostatic Failure During Laparoscopic Nephrectomy: Review of Food and Drug Administration Database

AUTHORS: Yan S. His, Daniel T. Saint-Elle, Grenith J. Zimmerman, and D. Duane Baldwin

OBJECTIVES: To compare the complications with endovascular stapling devices, nonlocking titanium clips, and nonabsorbable polymer ligating (Hem-o-lok) clips during laparoscopic nephrectomy.

METHODS: The Food and Drug Administration Manufacturer and User Facility Device Experience Database, was retrospectively reviewed for reports dated from January 1992 to March 2006 using the key words “nephrectomy” and “kidney.” All episodes of pure and hand-assisted laparoscopic nephrectomy were evaluated.

RESULTS: Of 2172 total nephrectomy or kidney-related reports, 352 reported failure using the laparoscopic hemostatic devices to secure the renal vasculature, and 223 complications (63%) resulted during the use of endovascular stapling devices, 111 (33%) from nonlocking titanium clips and 18 (5%) from locking clips. The leading causes of failure reported in stapling devices were staple line malformation (47%) and locking up (29%). In titanium clips, jamming/feeding difficulties (27%) and trouble closing or “scissoring” clips (26%) were the most common. In locking clips, dislodgement (44%) was most frequently reported. Three, one, and three deaths were reported after the use of the stapling device, titanium clip, and locking clip device, respectively.

CONCLUSIONS: All three methods used to secure the renal hilum in laparoscopic nephrectomy can result in malfunction. Because the overall denominator of use is not known, it would be inappropriate to conclude that one device is safer than another. When they occurred, these device malfunctions were potentially serious. Knowledge of the possible mechanisms of failure seen with each device could allow surgeons to anticipate potential complications and, therefore, perform laparoscopic surgery more safely.

UROLOGY 70: 888-892, 2007. © 2007 Elsevier Inc.

James M. Slater, MD

RADIATION RESEARCH

TITLE: Developing and Understanding a Hospital-based Proton Facility: Bringing Physics into Medicine



From October 18 to 20, 2006, a symposium, Developing and Understanding a Hospital-based Proton Facility: Bringing Physics Into Medicine, was held at the Renaissance Esmeralda Resort and Spa, Indian Wells, California. The event was offered by the department of radiation medicine at Loma Linda University (LLU), supported by the Telemedicine and Advanced Technology Research Center (TATRC) and the United States Army Medical Research and Material Command (USAMRMC). The meeting was intended to discuss factors involved in planning, developing, and operating a hospital-based proton treatment center. It brought together some of the most distinguished physicists, radiation biologists, and radiation oncologists in the world, and more than 100 individuals participated in the three-day educational offering. This overview reports on the event and introduces several papers written by many of the speakers from their presentations, for publication in this issue of “Technology in Cancer Research and Treatment.” Both the symposium and the papers are appropriate for this journal: exploitation of technology was one of the underlying themes of the symposium.

Technology in Cancer Research and Treatment 6(4 Suppl):1-7, 2007



David A. Bush, MD; Jerry Slater, MD; Carlos Garberoglio, MD; and James Slater, MD

RADIATION RESEARCH

TITLE: A Technique of Partial Breast Irradiation Utilizing Proton Beam Radiotherapy: Comparison with Conformal X-ray Therapy

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PURPOSE: To develop a breast immobilization system and clinical technique to deliver partial breast irradiation with a proton beam and compare dose distributions using proton therapy and conformal x-rays.

METHODS: A clinical technique to provide reproducible breast immobilization was developed. Breast immobilization begins by fitting each patient with a treatment brassiere. Patients are placed prone in a cylindrical polyvinyl chloride shell with the upper and lower body being supported and immobilized with Vac-Lok foam bead cushions. The upper chest and breast areas are immobilized with two-part expandable foam. After a treatment planning computed tomography scan, the lumpectomy cavity is outlined, and a clinical target volume is generated by adding 1cm in all dimensions. A three-dimensional treatment plan is developed with treatment typically given with two to four separate proton beams. The dose administered is 40 cobalt Gray equivalents (CGE) delivered in 10 daily fractions of four CGE with multiple fields treated each day. Proton and conformal x-ray plans were compared using dose-volume histogram analysis to determine volumes of normal breast tissue and skin treated with each technique.

RESULTS: An institutional review board-approved clinical trial was developed using this technique, and 20 patients have completed treatment. All subjects were able to undergo the immobilization procedure and daily treatments without significant discomfort, and no treatment interruptions were encountered. There was no evidence of respiratory motion identified on treatment planning CT images or on daily set-up radiographs. Acute toxicity has been limited to occasional radiation dermatitis (Radiation Therapy Oncology Group grade 1-2). Proton plans were compared with two methods of photon partial breast irradiation, including reduced tangential fields and five-field conformal techniques. Ten treatment plans with dose-volume histogram analysis revealed that the use of proton beams provided a significant reduction in doses to the ipsilateral breast and skin while eliminating doses to the heart and lung tissues.

CONCLUSIONS: A simple immobilization procedure provides accurate and reproducible breast positioning while simultaneously eliminating respiratory motion. The procedure has been well tolerated by the first 20 patients. Protons can provide substantial normal tissue protection compared with the use of conformal x-rays when used for partial breast treatment. We plan to continue enrollment and analyze long-term toxicity, local control, and survival.

Cancer Journal 13(2):114-118, 2007

Lilia Loreda, MD; Jerry Slater, MD

RADIATION RESEARCH

TITLE: Surgery and Radiotherapy: Complementary Tools in the Management of Benign Intracranial Tumors

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AUTHORS: Johnson WD, Loreda LN, and Slater JD

Historically, radiation therapy has been used extensively in the treatment of malignant and aggressive intracranial tumors, and the importance of its role has been repeatedly verified by prolonged patient survival rates and increased tumor control. As more modern capabilities are employed in surgery and radiotherapy, attention is being directed to the utility of radiation as either primary or secondary treatment of benign tumors. Specifically, primary treatment encompasses irradiation of small benign tumors without biopsy confirmation of tumor type; secondary treatment involves postoperative radiation therapy, with the possibility that less-aggressive tumor resection may be performed in areas that have a higher probability of resultant neurological deficit. Current literature suggests that this is not only a possible treatment strategy, but that it may be superior to more radical resection in some cases, for example, in vestibular schwannomas and meningiomas. This article provides an overview of factors to consider in the use of radiation therapy and reviews the relationships between radiation and surgery, notably the unique complementary role each plays in the treatment of benign intracranial tumors.

Neurosurgery Focus 24(5):E2, 2008





Lora M. Green, MD

RADIATION RESEARCH

TITLE: Alterations in Glutamate Uptake in NT2-Derived Neurons and Astrocytes after Exposure to Gamma Radiation.

AUTHORS: Sanchez, MC, Benitez, A, Ortloff, LS, Green, LM

Currently, the cellular and molecular mechanisms that underlie radiation-induced damage in the CNS are unclear. The present study seeks to begin investigating the underlying mechanism for radiation-induced neurotoxicity by characterizing glutamate transport expression and function in neurons and astrocytes after exposure to gamma-rays. NTera2-derived neurons and astrocytes, isolated as pure cultures, were exposed to doses of 10, 50, and 200 cGy gamma rays and transporter expression and function were assessed 3 hours, 2 days, and 7days post-exposure. In neurons, at 7 days post-exposure, significant increases were detected in EAAT3 after 50 cGy (p<0.05), as well as a dose-dependent increase in GLT-1 expression between doses of 10cGy and 50cGy (p<0.05). Functional assays of glutamate uptake revealed that neurons and astrocytes respond in a reciprocal manner after irradiation. Neurons responded to radiation exposure by increased glutamate uptake; an effect still evident at our last time point (7 days) post-exposure (p<0.05). The astrocyte response to gamma irradiation was an initial decrease in uptake and recovery to baseline levels at 2 days post-exposure (p<0.05). The observations made in this study demonstrate that neurons and astrocytes, while part of the same multifunctional unit, have distinct functional and reciprocal responses. The response in neurons seems to indicate a protracted response with potential long term effects after irradiation.

Radiation Research 171:41-52 (2009)

Daila Gridley, PhD; Michael J. Pecaut, PhD

RADIATION RESEARCH

TITLE: Spaceflight Effects on T Lymphocyte Distribution, Function and Gene Expression

AUTHORS: Gridley DS, Slater JM, Luo-Owen X, Rizvi A, Chapes SK, Stodieck LS, Ferguson VL, and Pecaut MJ

The immune system is highly sensitive to stressors present during spaceflight. The major emphasis of this study was on the T lymphocytes in C57BL/6NTac mice after return from a 13-day space shuttle mission (STS-118). Spleens and thymuses from flight animals (FLT) and ground controls similarly housed in animal enclosure modules (AEM) were evaluated within 3-6 h after landing. Phytohemagglutinin-induced splenocyte DNA synthesis was significantly reduced in FLT mice when based on both counts per minute and stimulation indexes (P < 0.05). Flow cytometry showed that CD3(+) T and CD19(+) B cell counts were low in spleens from the FLT group, whereas the number of NK1.1(+) natural killer (NK) cells was increased (P < 0.01 for all three populations vs. AEM). The numerical changes resulted in a low percentage of T cells and high percentage of NK cells in FLT animals (P < 0.05). After activation of spleen cells with anti-CD3 monoclonal antibody, interleukin-2 (IL-2) was decreased, but IL-10, interferon-gamma, and macrophage inflammatory protein-1alpha were increased in FLT mice (P < 0.05). Analysis of cancer-related genes in the thymus showed that the expression of 30 of 84 genes was significantly affected by flight (P < 0.05). Genes that differed from AEM controls by at least 1.5-fold were Birc5, Figf, Grb2, and Tert (upregulated) and Fos, Ifnb1, Itgb3, Mmp9, Myc, Pdgfb, S100a4, Thbs, and Tnf (downregulated). Collectively, the data show that T cell distribution, function, and gene expression are significantly modified shortly after return from the spaceflight environment.

Journal of Applied Physiology 106(1):194-202, 2009





Reinhard W. Schulte, MD

RADIATION RESEARCH

TITLE: Nanodosimetry-based Quality Factors for Radiation Protection in Space.

AUTHORS: Shulte RW, Wroe AJ, Bashkirov VA, Garty GY, Beskin A, Chechik R, Shchemelinin S, Gargioni E, Grosswendt B, and Rosenfeld AB

Evaluation and monitoring of the cancer risk from space radiation exposure is a crucial requirement for the success of long-term space missions. One important task in the risk calculation is to properly weigh the various components of space radiation dose according to their assumed contribution to the cancer risk relative to the risk associated with radiation of low ionization density. Currently, quality factors of radiation both on the ground and in space are defined by national and international commissions based on existing radiobiological data and presumed knowledge of the ionization density distribution of the radiation field at a given point of interest. This approach makes the determination of the average quality factor of a given radiation field a rather complex task. In this contribution, we investigate the possibility to define quality factors of space radiation exposure based on nanodosimetric data. The underlying formalism of the determination of quality factors on the basis of nanodosimetric data is described, and quality factors for protons and ions (helium and carbon) of different energies based on simulated nanodosimetric data are presented. The value and limitations of this approach are discussed.

Medical Physics 18(4):286-296, 2008

John F. Dicello, PhD

RADIATION RESEARCH

TITLE: Cytomorphologic Differentiation of Benign and Malignant Mammary Tumor in Fine Needle Aspirate Specimens from Irradiated Female Sprague-Dawley Rats



AUTHORS: Baktiar O. Karim, Syed S. Ali, Jennifer A. Landolfi, Jill F. Mann, Guosheng Liu, Archie Christian, John F. Dicello, Dorothy L. Rosenthal, David L. Huso

BACKGROUND: Find needle aspiration (FNA) offers a rapid and minimally invasive means to distinguish malignant from benign neoplasms. However, few studies have been published regarding the cytopathology of mammary tumors in rats despite widespread use of the rat model for breast cancer formation and inhibition.

OBJECTIVE: The purpose of this study was to determine the diagnostic accuracy of FNA cytology and to develop distinguishing cytologic criteria for the diagnosis of radiation-induced benign and malignant mammary tumors in rats.

METHODS: In a study of radiation-induced mammary carcinogenesis, 100 Sprague-Dawley rats with cutaneous masses were randomly chosen for FNA. The aspirates were smeared, fixed, and stained with a modified Papanicolaou procedure for diagnostic evaluation. Cytologic and histologic diagnoses (benign vs. malignant) were compared, and diagnostic accuracy was calculated using the histologic diagnosis as the criterion standard. FNA smears were scored semiquantitatively on a scale of 1-4 for cellularity, atypia nuclear size, chromatin pattern, nuclear membrane thickness, nucleoli, and mitoses. The background was evaluated for necrosis, hemorrhage, inflammation, and mucosecretory material. Cytomorphologic features were compared statistically between benign and malignant tumors, based on the histologic diagnosis.

RESULTS: The sensitivity of FNA was 92.3% and specificity was 89.4% for the detection of malignancy. However, 14% of specimens, all fibroadenomas by histology, had insufficient cells for cytologic evaluation, for an overall accuracy rate of 78.0%. Malignant tumors had significantly higher scores for all cytomorphologic features, and were significantly more likely to contain cell clusters and necrotic debris.

CONCLUSIONS: FNA is an accurate method for differentiating benign and malignant rat mammary tumors.

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