Faculty in UCLA’s Department of Radiation Oncology are engaged in a variety of research strategies aiming to improve the ability of radiation therapy to kill cancer cells while sparing healthy tissues.

One of the key approaches involves learning more about the effects of radiation on the immune system and using that knowledge to

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Leading the Way Toward Better Cancer Outcomes

It’s hard to find anyone who hasn’t been intimately touched by cancer. If we haven’t had the disease ourselves, we’ve gone through it with a close friend or family member. Sadly, many of us have lost loved ones. This year, according to the World Health Organization, cancer will overtake heart disease as the world’s leading killer.

But more than ever before, we are poised to make rapid progress in cancer treatment. At leading research institutions, scientists are unraveling the biology involved in the cancer process — and using that understanding to apply the ever-more-powerful arsenal of diagnostic and therapeutic technologies to cancer treatment.

Nowhere is this better exemplified than at UCLA. In the Department of Radiation Oncology, we are an integral part of a world-class clinical, translational and basic scientific research infrastructure that enables our faculty to rapidly integrate advances in molecular biology, radiation biology and medical imaging of cancer with the new and highly precise techniques in radiation delivery, improving patient care and treatment outcomes. That is the UCLA advantage.

Within our department, an extraordinary team of physicians, medical physicists and research scientists work together to deliver state-of-the-art patient care. But as important as this is to our mission, it’s not enough. We are also determined to press the UCLA advantage to advance the state of the art in treating cancer with radiation therapy. And we are doing just that — through the development and testing of new treatments and technologies, the training of the next generation of outstanding physicians and scientists, and the outreach efforts designed to bring our knowledge to the community and improve the safety and efficacy of radiation therapy.

As you will read, we have significantly strengthened our department with the recruitment of pioneers and innovators of cutting-edge radiation oncology treatments. In the exciting area of stereotactic body radiation therapy (SBRT), which shortens treatment time while reducing side effects, we are applying this technology in new ways, such as in the treatment of prostate, kidney, pancreas, and recurrent head and neck cancer. Our new fully dedicated brachytherapy suite houses a team headed by nationally known Dr. Jeffrey Demanes that is performing complex interstitial implants and high dose rate brachytherapy procedures. We have a new chief in our Division of Medical Physics, Dr. Daniel Low, who brings a strong vision and a history of NIH-supported research and collaborations with companies to develop more powerful technologies. Dr. Patrick Kupelian, professor and vice chair of the Department of Radiation Oncology and a
pioneer in the development of image-guidance technologies, is heading exciting new clinical research initiatives.

Driving our excellence in clinical care and teaching is our research — in the laboratory, in the clinic and in the translation from one to the other. Our department brings in more than $6 million a year in grants — among the highest funding per faculty member at UCLA’s David Geffen School of Medicine. This includes a large award to establish the UCLA Center for Medical Countermeasures against Radiation, which is studying agents that could protect the population from radiation exposure resulting from a terrorist attack or a radiologic accident. Our basic-science faculty are leaders in the fields of cancer immunology, cancer stem cells and cancer signaling pathways, contributing knowledge that has led to new treatment strategies, which are having a major impact around the world. We are also developing the infrastructure to track patient outcomes longitudinally and in real time so that we can make better-informed treatment decisions.

The patient registry, including data from our community partners, will also facilitate studies of comparative treatment approaches and cost analyses.

The department’s mission is multifaceted, but characterized by a common thread: our dedication to providing compassionate care and advancing radiation treatment so that people diagnosed with the world’s leading killer can be returned to good health. After reading in this newsletter about some of the exciting developments underway, I hope you will agree we are making great progress.

— Michael Steinberg, M.D., Chair
UCLA Department of Radiation Oncology

Community Collaborations

The Department of Radiation Oncology has initiated an effort to actively engage its surrounding community. “Our simple aim is to improve the lives of our patients and the health of the community,” says Dr. Michael Steinberg, department chair. The department has been working with extramural clinics, filling their professional staffing needs with premier UCLA faculty physicians while responding to community needs for clinical expertise and access to cutting-edge clinical trials. In addition, through collaborations with community physicians across the greater Southern California area, the department is expanding participation in important clinical research that will allow for the development of new and better treatments for cancer.

Associate Professor Steve Lee M.D., Ph.D., is the department’s new director of extramural affairs and community engagement. In that role, Dr. Lee is coordinating the department’s clinical outreach efforts and sharing best practices with the community. In addition to these efforts, the department is employing telemedicine to link external physicians to UCLA’s main campus in Westwood, facilitating improved communication and physician involvement for complex cases.

Dr. Kenneth Wong, assistant clinical professor in the department, currently practices at Children’s Hospital Los Angeles, extending the department’s expertise, quality, teaching and residency program. Dr. Phil Beron, assistant clinical professor, and Dr. Terrence Roberts, assistant clinical professor, extend the UCLA faculty reach to Providence Holy Cross Cancer Center sites in Mission Hills in the San Fernando Valley and in Santa Clarita, just north of Los Angeles.

Locations Professionally Staffed by UCLA Physicians:

Children’s Hospital Los Angeles
4650 Sunset Blvd., MS #54
Los Angeles, CA 90027
Tel: (323) 361-2417
Fax: (323) 361-7977

Providence Holy Cross Cancer Center — Mission Hills
15031 Rinaldi Street
Mission Hills, CA 91345
Tel: (818) 898-4410
Fax: (818) 496-4758

Providence Holy Cross Cancer Center — Santa Clarita
26357 McBean Parkway, Suite 150
Santa Clarita, CA 91355
Tel: (661) 288-5965
Fax: (661) 288-5988
Laboratory Discoveries Advance Patient Care

(continued from cover)

strengthen the effect of the therapy. “The goal is for radiation of the cancer to be able to enhance the immune response by translating radiation-induced cell death into systemic immunity,” explains William H. McBride, D.Sc., the department’s vice chair of basic science research. Dr. McBride, chief of the Division of Molecular and Cellular Oncology within the department, is a world leader in immunology as it relates to radiation.

In related work, Nick Cacalano, Ph.D., associate professor in the department, is focusing on suppressors of cytokine signaling (SOCS) proteins. Cytokines are molecules involved in regulating the immune response. Dr. Cacalano has found that in certain cancers, SOCS proteins are abnormally expressed — either silenced or activated. He is investigating the signaling mechanism by which this occurs, information that could contribute to an immunotherapy strategy.

To improve the results of radiation therapy, enhancing the dose to the tumor while sparing normal tissue is the goal. Keisuke Iwamoto, Ph.D., adjunct associate professor, is studying ways to do that through the use of high-density materials used in diagnostic radiology to enhance dose absorption by the tumor.

One of the most exciting research initiatives in the department is taking place in the lab of Frank Pajonk, M.D., Ph.D., associate professor. Dr. Pajonk’s focus is on how to detect and target cancer stem cells in prostate, breast and brain tumors. Radiation oncologists have known for some time that a small number of cells within tumors are able to re-grow tumors when the therapy fails. These cancer stem cells are so rare that they often don’t appear in laboratory models, explaining why certain experimental drugs that have been effective in the lab have not worked in patients.

Between 2001 and 2004, landmark studies prospectively identified cancer stem cells in solid tumors for the first time. Dr. Pajonk and his colleagues have developed a tool to image these cells in the lab, enabling the testing of new drugs that can attack these cells. His lab is also looking into what makes the cells radiation-resistant. “If we can find effective ways to target these cells directly, we will be able to treat cancer more effectively,” Dr. Pajonk says.

Dr. McBride also is the principal investigator for a major federal grant that funds the UCLA Center for Medical Countermeasures against Radiation (CMCR), one of seven such centers in the country funded to conduct research into agents with the potential to provide protection in the event of a nuclear radiologic accident or terrorist attack. “The recently recognized imminent threat from radiation dispersal devices operated by terrorists has led to a reassessment of the nation’s preparedness for handling the effects of radiation exposure on the general population and on emergency workers who have to deal with radiological events,” Dr. McBride notes.

As far back as 1996, Dr. McBride’s lab was among the first to show that certain growth factors and immune cell regulators could be manipulated to protect against radiation’s effects. The CMCR center is part of an effort to apply this knowledge to the study of agents that could mitigate against radiation injury, with a view toward stockpiling them for emergency use. This research also has significant applications in the care of patients with cancer.
SBRT:  Shortened Treatment Time, Fewer Side Effects with Potent Therapy

UCLA’s Department of Radiation Oncology is leading the way in the growth of an exciting new approach to radiotherapy — one that significantly reduces both the length of treatment and the side effects from it, while improving the ability to target tumors.

Using state-of-the-art technology, UCLA is now taking an approach that was once used only for brain tumors and applying it to certain lung, liver, pancreatic, kidney and prostate tumors. Compared with conventional radiation treatment, Stereotactic Body Radiation Therapy (SBRT) delivers a larger equivalent dose of radiation over the course of far fewer treatments.

“Traditionally, we have given a small amount of radiation each day to allow the normal tissue to heal,” explains Percy Lee, M.D., assistant professor in the Department of Radiation Oncology and medical director of the UCLA SBRT Center of Excellence. “SBRT technology allows us to be more precise in targeting the tumor, so that we exclude the normal tissue and can deliver larger doses.” Because SBRT treats a smaller area of the body over a shorter treatment course, Dr. Lee adds, side effects such as skin reddening and severe fatigue are rare.

“For many patients, daily treatments for 8–9 weeks represent a huge investment of time, and some live too far away to go to a top medical center on a daily basis,” notes Christopher King, M.D., Ph.D., associate professor in the department and a pioneer in the use of SBRT in prostate cancer. “This makes the treatment much more accessible.”

Comfort and convenience represent only part of the equation: studies also show that in certain cancers, the approach can lead to equal or better results when compared with conventional treatment. In early-stage lung tumors where surgery is an option, Dr. Lee notes, research indicates that SBRT may be as effective as surgery. For inoperable early-stage lung tumors, conventional radiotherapy involves 6–7 weeks of daily radiation doses with a success rate (defined as whether the cancer returns to the treated site) of 50 percent. Studies have shown SBRT has a 90 percent success rate in the same patients with only three treatment sessions. Equally encouraging results have been obtained for pancreatic and liver cancers.

Through Dr. King’s efforts, UCLA is pioneering the use of SBRT in prostate cancer. As part of a clinical trial, patients with low and intermediate risk, localized tumors are offered SBRT as an alternative to surgery or conventional radiation therapy. Treatment is completed in five sessions over the course of 10 days, as opposed to standard radiotherapy techniques, which are typically five days a week for 8–9 weeks. Dr. King has been using SBRT for prostate cancer patients since 2004, giving him the longest continuous experience with the treatment. “Our results are outstanding compared to the standard treatment, both in terms of success rate and in minimizing side effects,” he says.

The proper delivery of high-precision, high-dose treatments requires both state-of-the-art technology and expertise, and the UCLA SBRT Center of Excellence has both. Sophisticated imaging systems have enhanced the ability of the team of radiation oncologists and medical physicists to detect the cancer in advance. The use of image-guidance techniques — including four-dimensional CT and PET scans — enables the team to account for movement of the cancer during breathing, ensuring that the state-of-the-art radiation machines hit their target. The clinical expertise is unmatched, led by Dr. Lee, who has treated more than 200 patients with SBRT since coming to UCLA in 2008.

“SBRT technology allows us to be more precise in targeting the tumor, so that we exclude the normal tissue and can deliver larger doses.”

— Percy Lee, M.D.
In the last year, the UCLA Department of Radiation Oncology has successfully recruited three renowned faculty members, bringing the department to an unprecedented level of excellence. They are:

**D. Jeffrey Demanes, M.D.**
A pioneer in the field of high dose rate (HDR) brachytherapy, Dr. Demanes founded the California Endocurietherapy Cancer Center in 1981—the first brachytherapy-only center in the United States. Since 1991, he has done more than 25,000 HDR treatments.

In brachytherapy, radioactive sources are placed directly in or near the tumor, enabling delivery of a high radiation dose while reducing exposure to the surrounding healthy tissues. Dr. Demanes and his team use a computerized robotic-delivery device to insert the tiny radiation sources on or into the tumor with millimeter precision. The HDR brachytherapy procedure delivers the radioactive material through hollow straw-like applicators the size of intravenous lines that can be placed in virtually any part of the body. Working with a powerful treatment-planning computer program, the team captures a 3D image of the implant and surrounding anatomy to customize the dose distribution. Electronic instructions for positioning the radioactive source are then sent to a robotic “afterloader” to deliver the radiation based on the patient’s anatomy. Unlike older forms of brachytherapy, HDR can often be done on an outpatient basis, with the entire treatment process typically taking only 1–2 weeks.

“By treating the tumor from the inside out, we can rapidly deliver higher doses of radiation to the tumor, with relatively few side effects,” says Dr. Demanes, who moved his center from Northern California to UCLA early in 2010 and is now chief of the Division of Brachytherapy. Dr. Demanes has successfully used HDR—either alone or in combination with surgery, external-beam radiation therapy or chemotherapy—in treating many types of cancer, including prostate, breast, head and neck, gynecologic, gastrointestinal, skin and soft-tissue sarcomas.

Now led by Dr. Demanes, UCLA houses one of the nation’s only fellowship programs training physicians to do brachytherapy procedures. A dedicated brachytherapy suite opening this year features a team of specialists, including radiation oncologists, physicists, nurses and physician assistants.

**Patrick Kupelian, M.D.**
An internationally known expert in the development and evaluation of cutting-edge technologies for radiation oncology, Dr. Kupelian has initiated a number of image-guidance technologies and has pioneered the use of high-dose radiation therapy for prostate cancer. At UCLA, he is professor of radiation oncology and vice chair of clinical operations and clinical research for the department.

“In the past, we did imaging studies on patients before, but not during the treatment,” Dr. Kupelian explains. “As a result, we couldn’t see what was happening inside the patient when we were delivering the radiation.” A little more than a decade ago, Dr. Kupelian collaborated with industry to track the position of the prostate and the prostate tumor during the radiation therapy process. Dr. Kupelian also helped to introduce the use of CT scan image guidance during the radiation treatment itself. These image-guidance approaches have become the standard of care in radiation oncology, enabling more precise targeting with less irradiation of normal tissues.

**Daniel Low, Ph.D.**
With extensive experience in physics research and educational outreach, Dr. Low was the co-founder and director of the Center for Image-Guided Radiotherapy and Therapy at M. D. Anderson Cancer Center. Now at UCLA, he is designing image-guided therapy to improve the precision of cancer treatment.

**NEW FACULTY**

**Prestigious Faculty Strengthen Department**
Dr. Kupelian, who comes to UCLA from M.D. Anderson Cancer Center in Orlando, Florida, is coordinating with colleagues in the department’s medical physics group to foster collaborations that will help to develop and evaluate new technologies, bringing the most promising ones to UCLA in their early stages.

Dr. Kupelian is currently working with industry on advancing image-guidance approaches, including the use of magnetic resonance imaging (MRI) — with its promise of higher-quality real-time images — to increase the precision of treatments. He is also collaborating with the department’s medical physicists and computer scientists in an effort to improve the way images are processed and utilized in patient care. In addition, Dr. Kupelian continues to explore ways to reduce overall time it takes to complete a course of treatment — and potentially increase the efficacy of the therapy by targeting higher radiation doses to particularly resistant areas within tumors.

Daniel Low, Ph.D.

Dr. Low arrived in August to serve as vice chair of the department and chief of the Division of Medical Physics. He heads a group whose goal is to maximize the therapeutic impact of radiation therapy by refining existing technologies and developing new ones.

His team’s clinical focus includes ensuring that devices put out the proper and precise radiation doses according to manufacturer specifications, as well as directing the radiation therapy team in developing treatment plans that make the most effective use of the devices.

“We need to do more to take advantage of the quality of the imaging devices that are now available, which have gone well beyond applications of the technology,” Dr. Low asserts. He notes that many current radiation therapy protocols were developed in the era of slower imaging devices.

In addition to working with existing tools, Dr. Low is involved in developing new approaches to radiation treatment. One of his major research interests is in gaining a better understanding of the impact of human breathing motion on radiation therapy delivery and the quality of imaging, and developing techniques to reduce the impact of breathing during treatment.

“Breathing motion has a profound impact on the quality of radiation therapy and of nuclear medicine imaging,” says Dr. Low, who came to UCLA from Washington University School of Medicine, where he served as chief of medical physics. “We are developing techniques to quantify and mitigate those impacts,” he adds. Dr. Low is also a leading proponent for improving the safety of radiation therapy for patients — applying the latest research tools to better understand the causes of human errors and machine malfunctions, and developing precautions to reduce and eliminate such errors.

Renowned Brachytherapy Team Comes to UCLA

The new Division of Brachytherapy was launched in early 2010 with the recruitment of D. Jeffrey Demanes, M.D., who serves as chief of the division. Dr. Demanes is one of the most experienced brachytherapy physicians in the country, having performed more than 25,000 of the procedures, with superior published outcomes, results and national acclaim. Dr. Demanes is the founder of the California Endocurietherapy Cancer Center (CET), which was the first dedicated brachytherapy center in the United States. His extraordinary patient care team at UCLA, consisting of innovative physicians, medical physicists, nurses and radiation therapists as well as state-of-the-art technology, creates the highest probability of successful treatment outcomes.

Under the expert direction of Dr. Demanes, the Department of Radiation has designed a new state-of-the-art brachytherapy procedure suite that will accommodate both high dose rate (HDR) brachytherapy and electronic brachytherapy. The suite was designed to enable the brachytherapy program to coordinate and achieve the highest-quality patient care possible. It will offer a way for patients to be treated completely within the department on an outpatient basis for most diagnoses, allow for shorter treatment time frames, and result in fewer side effects.

In addition to the new treatment suite, the department has established a fellowship program in brachytherapy. The year-long fellowship is designed to train physicians who have completed their residency in radiation oncology and who are interested in further developing their skills and knowledge in brachytherapy as a subspecialty.
Clinical Trials Update

Choosing to participate in a clinical trial is an important decision. Investigator-initiated trials at UCLA are for patients with defined diagnoses with specific characteristics. Information obtained from these trials enables the development of better treatments and cures for cancer. In addition, patients may benefit from receiving specialized cutting-edge treatments not otherwise available.

The UCLA Department of Radiation Oncology is leading the way in clinical research and is committed to an ongoing quest to develop new treatments and cures for cancer. Areas currently under investigation include:

- Prostate Cancer: SBRT for complete course in five sessions
- Lung Cancer: SBRT with RFA in lung cancer to improve tumor control and decrease side effects
- Lymph-Node-Positive Lung Cancer: precision high-dose adaptive therapy
- Liver Cancer: SBRT for cholangiocarcinoma as a bridge to liver transplant
- Cancer Immunity Trial: following patients’ immunologic response to treatment

Featured Clinical Trial

Hypo-fractionated stereotactic body radiotherapy for newly diagnosed prostate patients

UCLA’s Department of Radiation Oncology is conducting a study of the effect of hypo fractionated radiotherapy, also known as stereotactic body radiotherapy (SBRT), for newly diagnosed prostate cancer with no suspicion that the disease has spread outside of the prostate. This type of radiotherapy divides the total prescribed dose of radiation into fewer but larger doses as compared with conventional external beam radiotherapy.

The aim of the study is to determine whether delivering higher but more accurately targeted doses of radiation will be more effective and better tolerated than concurrent standard methods when used in the treatment of patients.

The investigator will design a treatment plan consisting of five radiation treatment sessions, each taking less than half an hour, delivered in less than two weeks.

For more information about eligibility requirements and participation in these or other UCLA Radiation Oncology clinical trials, please contact Anne E. Wagner, R.N., B.C., clinical trials coordinator, at (310) 825-6577, or go to www.radonc.ucla.edu and click on the Clinical Trials link.

Give Now

For more information about making a gift to the Department of Radiation Oncology, please call Valerie Amador, associate director of development, at (310) 794-4746, or visit our website: www.radonc.ucla.edu.