

Current Clinical Trials at the USC/Norris Comprehensive Cancer Center and Hospital

The National Cancer Institute (NCI) has designated the USC/Norris Cancer Center as one of the nation's 41 comprehensive cancer centers. USC/Norris has held this designation since 1973, when it was named one of the first eight comprehensive cancer centers.

In its capacity as a comprehensive cancer center, USC/Norris engages in government- and industry-sponsored clinical trials. Trials currently accepting enrollment include:

Prospective Evaluation of TargetScan Guided Prostate Needle Biopsy by Creation of a Multi-Center Data Registry

This study is to evaluate the use of the TargetScan 3D Imaging and Targeted Biopsy System for the use of cancer detection and localization.

Entry criteria: Age > 18 years with elevated PSA or abnormal digital rectal examination.

A Randomized Comparison of the Studer Pouch vs. the T-Pouch Orthotopic Neobladder Urinary Diversion in Bladder Cancer Patients

Entry criteria: Age > 18 years with diagnosis of primary bladder cancer (any histology) undergoing radical cystectomy (cystoprostatectomy in men and anterior exenteration in women).

A Randomized Phase II Study with a Safety Lead-in of the Anti-IGF-1R Monoclonal Antibody IMC-A12 in Combination with Erlotinib, Compared with Erlotinib Alone in Patients with Advanced Non-Small Cell Lung Cancer (NSCLC) Who Have Failed at Least One Platinum-Containing Chemotherapy Regimen

In vitro and *in vivo* studies have implicated IGF-1R and IGF-1 signaling in the development, maintenance, and progression of cancer. Combining anti-IGF-1R antibody with Erlotinib provides dual inhibition of signalling pathways important to lung cancer cell survival.

Entry criteria: Age > 18 years with NSCLC who have failed 1 prior line of therapy.

An Open-Label, Randomized, Phase II Study of Efficacy and Tolerability of ABT-869 in Advanced or Metastatic Non-Small Cell Lung Cancer

ABT-869 is a novel, receptor tyrosine kinase (RTK) inhibitor of members of the vascular endothelial growth factor (VEGF) and platelet-de-

riated growth factor (PDGF) receptor families and exhibits potent antiproliferative and apoptotic effects on cancer cells.

Entry criteria: Age > 18 years with advanced NSCLC who have progressed disease after treatment with a platinum based doublet.

A Randomized, Double-Blind, Placebo-Controlled, Multi-Center, Phase II Study of Efficacy and Safety of Apricoxib in Combination with Erlotinib in Non-Small Cell Lung Cancer Patients

Apricoxib is a novel, potent inhibitor of COX-2 which is important for tumor angiogenesis and growth. Combining Apricoxib with Erlotinib provides dual inhibition of signalling pathways important to lung cancer cell survival.

Entry criteria: Age > 18 years with NSCLC who have failed 1 prior line of therapy.

A Phase Ib/ II Trial of AMG 479 or AMG 102 in Combination with Platinum-based Chemotherapy as First-Line Treatment for Extensive Stage Small Cell Lung Cancer

AMG 469 is a fully humanized antibody against the Insulin-like Growth Factor Receptor type I, and AMG 102 is a fully humanized monoclonal antibody against the Hepatocyte Growth Factor (HGF) that blocks binding to the c-MET receptor. There is strong rationale to combine these agents with chemotherapy to improve the outcomes of patients with small cell lung cancer (SCLC).

Entry criteria: Age > 18 years with untreated advanced SCLC.

Docetaxel (Taxotere) plus 6-Month Androgen Suppression and Radiation Therapy vs 6-month Androgen Suppression and Radiation Therapy for Patients with High-Risk Localized or Locally Advanced Prostate Cancer: A Randomized, Controlled Trial

The goal is to determine if adding docetaxel chemotherapy to standard treatment (radiation therapy and hormonal therapy) improves survival for patients with high risk prostate cancer.

Entry criteria: Age > 18 years with histologic confirmation of prostate cancer, no evidence of metastatic disease (-) bone scan and (-) lymph node assessment (CT, MR), adequate hematologic function.

A Phase I/II Trial of Adjuvant Radiation Therapy, Hormonal Therapy and Concurrent Chemotherapy for High Risk Pathologic T3 Prostate Cancer

The goal is to determine the safety and feasibility of combining weekly docetaxel with adjuvant 3-D conformal radiation therapy and hormonal therapy in men with high risk pathologic T2-3N0M0 prostate cancer after a radical prostatectomy.

Entry criteria: Age > 18 years with histologically confirmed adenocarcinoma of prostate, and Status Post Radical Prostatectomy and Lymph Nodal Sampling.

Randomized Phase III Trial to Evaluate Radio-Pharmaceuticals and Zoledronic Acid in the Palliation of Osteoblastic Metastases from Lung, Breast and Prostate Cancer

The goal is to determine if the addition of a radionuclide (Strontium-89 or Samarium 153) to bisphosphonates for patients with asymptomatic or stable symptomatic bone metastasis will delay the time to development of malignant skeletal related events.

Entry criteria: Age > 18 years, with history/physical examination, including bone scan, dental evaluation, etc.

Uterine Cancer: Molecular Staging Study of Endometrial Cancer (GOG-0210)

A randomized Phase III trial of Doxorubicin/Cisplatin/Paclitaxel/G-CSF versus Carboplatin/Paclitaxel in patients with stage III & IV or recurrent endometrial cancer.

Entry criteria: Age > 18 years, with history/physical examination, including bone scan, dental evaluation, bony metastatic disease.

Gynecologic Sarcomas (PHII-80)

A Phase II study of VEGF-TRAP in recurrent or metastatic gynecologic soft-tissue sarcomas.

Entry criteria: Age > 18 years with recurrent or metastatic soft-tissue sarcoma.

For more information on clinical trials, call 323-865-0451.

USC CONSULT

A Publication of The Doctors of USC, USC University Hospital and USC/Norris Cancer Hospital

Advances in the Treatment of Head and Neck Cancers

"The exciting developments in the treatment of head and neck cancers are really those that have improved the patients' quality of life," says Uttam K. Sinha, Chief and Residency Program Director, Department of Otolaryngology, Head and Neck Surgery and Associate Professor of Otolaryngology, Keck School of Medicine at the University of Southern California. "At USC, we are very aggressively pursuing the therapies that maintain a balance between survival and quality of life, focusing on the common functions that make us human beings, such as talking, chewing and swallowing."

"This is a true bench-to bedside-to community research project."

Uttam K. Sinha, MD

An example of this improvement in patients' quality of life can be seen in procedures such as tongue reconstruction following the resection of a tumor. In this operation, after removing a tumor from a patient's tongue, Dr. Sinha performs a microvascular free flap procedure that transplants skin, soft tissue and blood vessels from a patient's forearm to his or her tongue. This reconstruction of the diseased tongue provides enough bulk to help improve the vital processes of swallowing and speech. Without this tongue reconstruction, the patient's ability to swallow is reduced to the point where he

or she must be fed through a tube placed through their skin directly into the stomach, due to the fact that the patient is unable to take in enough food to maintain his or her caloric requirements.

Gene Silencing and Neuromuscular Electrical Stimulation

Another example would be gene therapy and a "gene silencing" approach that enables specialists to reduce the amount of radiation exposure in head and neck cancer treatment. It is not uncommon for head and neck cancer patients to be unable to eat after radiation treatment due to the amount of scarring in the throat. With gene silencing therapy, USC physicians render tumor cells more amenable to radiation so that patients typically need 8-10 times less radiation therapy.

USC physicians have identified and isolated a gene, known as the SPK gene, that is highly expressed in head and neck cancers. Gene-silencing therapy is a molecularly targeted therapy process by which the specialist blocks or "silences" this particular gene. This patented process benefits patients by doing less damage to the surrounding tissues, thereby increasing their quality of life. Additionally, if a tumor returns, physicians can administer additional radiation due to the original course of treatment involving such low dosage levels. According to Dr. Sinha, "This is a true bench-to bedside-to community research project."



Uttam K. Sinha, MD
Areas of Treatment: Head and Neck Cancer, Thyroid and Parathyroid Diseases, Plastic and Reconstructive Surgery, Microvascular Surgery, Skull Base Surgery, Facial Fractures, Tracheal Stenosis, Swallowing and Breathing Disorders, Snoring, Sleep Apnea, Voice Disorders and Clinical Trials

In addition to gene therapy and reconstructive surgery, USC is currently developing a process known as neuromuscular electrical stimulation with a new implantable medical device called BION® that can provide precise and inexpensive interfaces with an external electronic controller and may be used on a patient's muscles. Paralyzed muscles can be reanimated by electrical stimulation in order to prevent atrophy and restore functional movement. BION implants can be injected into

The Doctors of USC

The Doctors of USC is a group of more than 500 physicians and specialists who are full-time faculty members of the world-renowned Keck School of Medicine of the University of Southern California. The Doctors of USC see private patients at facilities all across Los Angeles, including USC University Hospital, one of "America's Best Hospitals"® in 2008, and USC/Norris Cancer Hospital, which provides patient care for the USC/Norris Comprehensive Cancer Center, one of only six institutions in California designated by the National Cancer Institute as a Comprehensive Cancer Center.

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USC University Hospital—888-700-5700 • USC/Norris Cancer Hospital—800-700-3956 • The Doctors of USC—800-872-2273

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To refer a patient to USC/Norris Cancer Hospital call 1-800-700-3956.

Head/Neck Cancers cont'd

various sites where they receive power and digital command data from a single external radiofrequency coil.

For example, Dr. Sinha or one of his colleagues may implant a BION close to the hypoglossal nerve. The patient will then electronically stimulate his or her tongue's movement by pressing the button on a remote device. He or she will do this exercise three times a day in order to strengthen the tongue for improved speech and swallowing abilities. As Dr. Sinha puts it, "The resulting benefit is that patients are able to eat a hamburger during radiation therapy instead of going on a liquid diet. The quality of life is greatly enhanced."

Though the Department of Otolaryngology's primary goal is to render its patients cancer-free, this is only the beginning of treating the whole patient. Dr. Sinha sums up the benefits of focusing on his patients' lives after surgery. "In the past, we were able to render these patients cancer-free, but they lived the rest of their lives with a tube in the stomach. Now we're able to restore some of their functioning through reconstructive surgery, gene therapy, and new implants." ■

REFERRAL NOTES

Tongue reconstructive surgery techniques may improve quality of life of head and neck cancer patients who have undergone tumor resection.

Gene therapy may prevent excessive scarring and improve outcomes from radiation therapy.

Electrical implants may improve patients' speech and swallowing abilities postoperatively.

To refer a patient, call the USC Head and Neck Group at 323-442-5790.

USC Houses Breakthrough Radiation Technology

USC has a legacy of radiosurgery expertise spanning more than 25 years. In fact, stereotactic radiosurgery was pioneered at USC in the mid-1980s concurrently and in collaboration with physician researchers at Harvard Medical School.

"We have all the tools under one roof," says Parvesh Kumar, M.D., Chair, USC Department of Radiation Oncology. He lists many capabilities: "At USC/Norris Cancer Hospital, we have a state-of-the-art Varian Trilogy linear accelerator. We have all of the armatorium: intensity-modulated radiation therapy (IMRT), image-guided radiation therapy (IGRT), stereotactic radiosurgery (SRS) and stereotactic radiation therapy (SRT). We have a large-bore GE CT simulator. We have high dose rate brachytherapy. We have hyperthermia. And of course, we have CyberKnife® and Gamma Knife®."

Dr. Kumar is quick to point out that simply having the latest technology is nothing without providing excellent patient care.



Parvesh Kumar, MD
Areas of Treatment: Prostate Cancer, Head & Neck Cancer, Lung Cancer and Cyberknife Stereotactic Radiotherapy

Kumar is also particularly excited about a recent \$1.3 million grant from the Department of Defense (DoD) to treat patients with prostate cancer, which is the largest in the history of the department by a single investigator. Of approximately 150 applications each year,

"We understand that all three entities involved – the patient, the referring physician and our department – are partners in the treatment process."

Parvesh Kumar, MD

"We see our patients very promptly. Our policy is to see an outpatient consult within five working days of when a referring physician calls and all inpatient consults within 24 hours. And we keep our referring physicians well informed regarding their patients. We understand that all three entities involved – the patient, the referring physician and our department – are partners in the treatment process."

The Department is also conducting state-of-the-art research for many disease sites, including head/neck, breast and prostate cancers.

the DoD typically awards funding for just three grants for the entire country. Focusing on patients with high-risk features after undergoing radical prostatectomy, this protocol involves radiation treatment with concurrent chemotherapy and hormone therapy. In addition, the study is looking at molecular markers in the radical prostatectomy specimen, as well as evaluating the patient's health-related quality of life. This grant involves a total of eight investigators from five different Keck School of Medicine departments.

To refer a patient, call the USC Department of Radiation Oncology at 323-865-3051. ■

To refer a patient to USC/Norris Cancer Hospital call 1-800-700-3956.

CyberKnife Used as Adjuvant Treatment for Musculoskeletal Tumors



Lawrence Menendez, MD
Areas of Treatment: Musculoskeletal Tumors, Joint Reconstruction and Musculoskeletal Infections

Patients referred to the USC Center for Orthopaedic Oncology may benefit from access to technologies and treatment modalities not available at other centers in the Los Angeles area.

Lawrence Menendez, M.D., Professor of Orthopaedic Surgery at the Keck School of Medicine of USC and Director of Orthopaedic Oncology at USC University Hospital, points to the use of the CyberKnife® stereotactic radiosurgery system at USC/Norris Cancer Hospital for musculoskeletal tumors as an example. "We offer a very progressive program here. We're the only center in the Los Angeles area with the CyberKnife system. In fact, we're one of just a few centers in the country – and the only center on the West Coast – to offer CyberKnife therapy as an adjuvant treatment for musculoskeletal tumors."

According to Accuray, the system's manufacturer, CyberKnife "is the world's first and only commercially available intelligent robotic radiosurgery system designed to treat tumors anywhere in the body with sub-millimeter accuracy." It is this high degree of accuracy that allows Dr. Menendez and his colleagues to use radiation therapy on tumors in more challenging areas of the body such as the sacrum and pelvis. Dr. Menendez elaborates. "We can treat select acetabular tumors with CyberKnife

that would not have otherwise been amenable to radiosurgery. This typically means the patient requires a lesser amount of traditional surgery."

He cites sacrectomy procedures as well. "The morbidity of sacrectomy is quite substantial. CyberKnife can spare the patient major surgical procedures in postoperative reconstruction," he says.

In addition to using CyberKnife as an adjuvant treatment for musculoskeletal tumors, the USC Center for Orthopaedic Oncology has also employed the Stryker Navigation System to assist in reconstruction for patients requiring oncological implants after undergoing tumor surgery.

Commonly used in traditional orthopaedic procedures such as hip and knee replacements, the Stryker Navigational System uses a highly specialized tracking technology to aid the surgeon in the accurate alignment of oncological implants. According to Dr. Menendez, "The more precise you make your cuts, the longer the implants will last. And I don't know of anyone else in the Los Angeles area utilizing surgical navigation to reconstruct defects after tumor resection. It's really taken a lot of the eyeball work out of it." ■

REFERRAL NOTES

USC/Norris Cancer Hospital is home to the only CyberKnife® stereotactic radiosurgery system on the West Coast being utilized as adjuvant therapy for the treatment of musculoskeletal tumors.

USC University Hospital is the only center in Los Angeles utilizing the Stryker Surgical Navigation System to reconstruct defects after tumor resection.

To refer a patient, call the USC Center for Orthopaedic Oncology at 323-442-5830.

CyberKnife Developed at USC

The original CyberKnife® was actually developed at USC with the help of Michael L.J. Apuzzo, M.D., the Edwin Todd/Trent H. Wells, Jr., Professor of Neurological Surgery and Radiation Oncology, Biology, and Physics at the Keck School of Medicine at the University of Southern California and Director of the Stereotactic and Radiosurgery Program for the Department of Neurology and Director of the Gamma Knife Unit at USC University Hospital.

According to its manufacturer, Accuray Incorporated, the CyberKnife Robotic Radiosurgery System is the world's first radiosurgery system designed to treat tumors anywhere in the body with sub-millimeter accuracy. Using image guidance technology and computer controlled robotics, the CyberKnife System is designed to continuously track the tumor, detect its location and correct for tumor and patient movement in real-time throughout the treatment. Because of its extreme precision, the CyberKnife System does not require invasive head or body frames to stabilize patient movement, vastly increasing the system's flexibility.

CyberKnife is being used by USC specialists to treat a variety of lesions throughout the body, including lung tumors, recurrent head and neck cancers and musculoskeletal malignancies. Paul G. Pagnini, M.D., Assistant Clinical Professor of Radiation Oncology, puts it simply, "Like the Gamma Knife, CyberKnife uses multiple convergent beams of radiation to treat tumors with sub-millimeter accuracy. What CyberKnife allows us to do is treat tumors virtually anywhere in the body, not just in the cranium. And thanks to its tracking system, we can deliver high doses of radiation to a small volume inside the body, even if it is moving in space, such as a lung lesion that moves as a patient breathes."

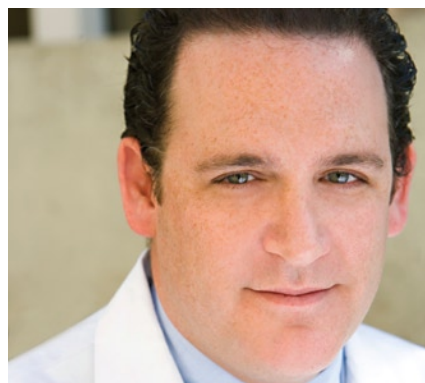
Prostate and Bladder Procedures Focus on Improved Diagnosis and Patients' Quality of Life

"Robotic surgery is great, but it's so 2005," says David Penson, M.D., Associate Professor of Urology at the Keck School of Medicine at the University of Southern California. "I want to be thinking more along the lines of 2015."

Though the USC Department of Urology utilizes two da Vinci® Surgical Systems at USC University Hospital for a variety of minimally invasive procedures, Dr. Penson's excitement is centered on focal therapy for selected patients suffering from prostate cancer. Similar in concept to a breast lumpectomy as an alternative to a radical mastectomy, this approach uses targeted cryosurgery to remove only part of the patient's prostate rather than treating the whole organ, as is common at other centers. According to Dr. Penson, this approach may offer the patient better continence and potency postoperatively.

In addition to focal therapy, Dr. Penson is overseeing advances in prostate diagnosis, too. "We're one of only four centers, along with the University of Michigan, Washington University in Saint Louis, Missouri, and New York University, studying the efficacy of the TargetScan® 3D Ultrasound System for use in prostate imaging and biopsy to see if it improves diagnosis – and we believe it does."

The TargetScan is a computer-guided hands-free diagnosis and treatment system that features a patented endorectal probe with a multiplane mechanical transducer with 3D solid volume imaging capability. The system also features a targeted biopsy system with single use needle and guide and multi-position probe carriage providing full sagittal and transverse access to the target site. According to Dr. Penson, "By creating a 3D ultrasonic map of the prostate, it takes the guesswork out of prostate biopsy." He continues, "Ultimately, it's my hope that it will lead to more accurate diagnosis of prostate cancer." The procedure is FDA-approved and is covered by most major insurance carriers.



David Penson, MD, MPH
Areas of Treatment: Prostate Cancer, Benign Prostatic Hyperplasia, Elevated Psa, Bladder Cancer, Erectile Dysfunction and Prostate Disease

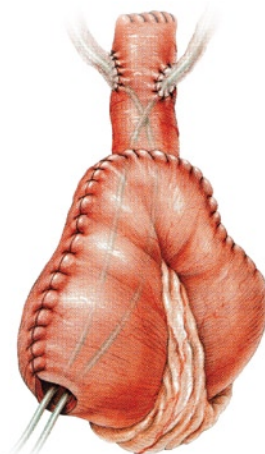


Donald G. Skinner, MD
Areas of Treatment: Bladder Cancer, Kidney Cancer, Prostate Cancer, Testis Cancer and Retroperitoneal Tumors

Quality of Life Improvements

Chair of the USC Department of Urology since 1980, Donald G. Skinner, M.D., has been instrumental in pioneering advances in bladder cancer treatment and procedures that improve the quality of life for patients who have undergone radical cystectomy. One of these advances, the "neobladder," an alternative to the traditional ileal conduit, has shown great promise for younger, more active patients in that it obviates the need for an external bag for the collection of voided urine.

According to Dr. Skinner, "We were the first center to develop the concept of continent urinary diversion, adapting the Koch pouch for the urinary tract in 1982." In 1986, the team developed the concept further, building the reservoir to bring urine back down to the urethra in what is known as an orthotopic bladder reconstruction. This breakthrough procedure allowed a man who had undergone radical cystectomy to void urine through the urethra by simply relaxing his pelvic floor muscle instead of having to use a catheter. A similar procedure for women followed in 1990.



The "T-Pouch" creates a low-pressure, high-capacity urinary reservoir.

After 26 years of his department performing the procedure, Skinner is confident in saying, "We've trained many residents and fellows at USC University Hospital who are scattered throughout the country, but we have the greatest experience with this particular operation."

"Bottom line – patients come here from all over the country because they don't want the bag on the outside, and we can build them a new bladder."

“Bottom line – patients come here from all over the country because they don't want the bag on the outside, and we can build them a new bladder.”

Donald G. Skinner, MD

Sixteen years ago, USC developed an adaptation of the neobladder called the "T-Pouch," which was designed to prevent the valvular stenosis that was noted to occur in about 10 percent of original Koch pouches, which obstructed the flow of urine from the kidneys. At the same time, Dr. Urs Studer in Bern, Switzerland, developed the

"Studer Modification," which allows reflux of urine to the kidneys but obviates the need for any antireflux valve. USC is currently conducting a clinical trial to study which method works best for patients. Physicians interested in enrolling patients in the trial should call 323-865-3700 for inclusion/exclusion criteria. ■

REFERRAL NOTES

Targeted cryotherapy may improve potency and continence in selected patients with prostate cancer.

Neobladder may improve the quality of life of patients who have undergone radical cystectomy by obviating the need for an external bag for the collection of urine.

To refer a patient, call the USC Department of Urology at 323-865-3700.

Update: Female Reproductive Cancers



Laila I. Muderspach, MD
Areas of Treatment: Gynecologic Malignancies and Complex Pelvic Surgery

being an academician brings certain benefits to her patients' bedsides.

"The students, residents and fellows are always asking new questions. It really forces us to keep up on all the latest developments in GYN oncology," she says. "We don't treat people in a cookie-cutter manner. We favor an individualized approach. For example, our department has pioneered new laparoscopic techniques that give us information that can't be obtained via imaging. This helps to plan and individualize cancer treatment." As director of the department's residency program, Dr. Muderspach has also seen the techniques they developed conveyed to institutions throughout California and the rest of the country by USC fellowship-trained GYN oncologists.

GYN oncology is a unique subspecialty for which physicians undergo a three-year fellowship program during which they study not only how to administer chemotherapy, but also how to utilize advanced surgical techniques to treat gynecologic cancers. One of only 35 such programs in the country, the USC GYN oncology fellowship program trains just a single fellow per year. In fact, there are fewer than 1,000 GYN board-certified oncologists in the United States, most of whom practice at academic medical centers.

For Laila Muderspach, M.D., Chair, Department of Obstetrics and Gynecology,

after only two weeks," says Muderspach.

In addition to treating gynecologic cancers, the department focuses on gynecologic cancer prevention. It was involved in early clinical trials for the human papillomavirus vaccine and offers genetic counseling and screening through the Cancer Genetics Program at the USC/Norris Comprehensive Cancer Center and Hospital. The program provides a certified genetic counselor trained in comprehensive risk assessment for hereditary cancer conditions. Genetic testing is available for familial cancers such as breast, ovarian, colorectal, uterine and other rare cancer syndromes. ■

REFERRAL NOTES

USC/Norris Cancer Hospital offers genetic counseling for breast, ovarian, colorectal, uterine and other rare cancers.

Advanced minimally invasive diagnostic and therapeutic procedures, including the fertility-sparing radical trachelectomy, were pioneered by the USC Department of Obstetrics and Gynecology.

To refer a patient, call the USC Department of Obstetrics and Gynecology at 323-226-3416.

Emerging Technologies and Advanced Techniques Improve Outcomes for Lung Cancer Patients

USC University Hospital and USC/Norris Cancer Hospital were the first hospitals in the Los Angeles area with a CyberKnife® Robotic Radiosurgery System. Much like the Gamma Knife® stereotactic radiosurgery system, which was developed to treat intracranial lesions, the CyberKnife delivers high doses of radiation to a target by converging multiple beams of low-dose radiation. This greatly reduces damage to the surrounding normal tissue. Unlike the Gamma Knife, which requires a head frame to keep the patient perfectly still during the procedure, the CyberKnife has the ability to track a moving lesion in three-dimensional space in real time. This makes it ideal for lung applications and gives USC physicians the ability to treat lung lesions previously considered untreatable with standard types of radiation therapy or for patients who are for some reason not amenable to surgery.



Jeffrey A. Hagen, MD

Areas of Treatment: **Lung Cancer, Esophageal Cancer, Barrett's Esophagus, High Grade Dysplasia, Tracheal Stenosis, Tracheal Tumors, Lung Metastases, Gastroesophageal Reflux Disease, Achalasia, Hyperhidrosis, Thoracoscopic Surgery and Minimally Invasive Surgery**



P. Michael McFadden, MD

Areas of Treatment: **Lung Transplantation, Lung Cancer, Tumors of Mediastinum and Chest Wall, Thoracoscopic Surgery, Endoscopic Bronchial Surgery, Surgical Treatment of Mesothelioma and Palomar Hyperhidrosis**

“For those who have had their limit of standard radiation therapy or where radiation isn't an option, this can mean new hope for many of those patients.”

Jeffrey A. Hagen, MD

Jeffrey A. Hagen, M.D., Associate Professor of Surgery, Chief of Thoracic/Foregut Surgery, is currently collaborating with USC radiation oncologists to develop techniques to allow CyberKnife to be used to treat more centrally located lesions, which can be difficult to distinguish from surrounding tissue and are therefore typically not amenable to treatment using standard CyberKnife techniques.

“To maximize the radiation dose to the tumor while minimizing the dose to the surrounding tissue, the CyberKnife must track the lesion in 3D space,” he says. “And for lesions in the mid-portion of the lung, the machine can differentiate between a tumor mass and the surrounding lung tissue. But when you get nearer to either the chest wall or to the central structures of the lung, this becomes more difficult.”

To help the machine “see” its target, Dr. Hagen uses tiny gold seeds called fiducial markers. Similar in size to brachytherapy seeds, because they exhibit a different density from anything else in the body – including surgical clips – they are easily distinguished by the CyberKnife's computer.

The use of fiducial markers to delineate lung lesions for radiation treatment is fairly common practice around the country in centers that perform such procedures. “Typically, the seeds are placed near the mass with a needle under CT guidance. But you run into problems the deeper you get into the lung,” says Hagen. “You have a much greater chance of a collapsed lung or bleeding, and then you have a much harder time telling what's a tumor and what's a hematoma in the lung.” To reduce the possibility of these complications, Dr. Hagen developed a technique to place fiducial markers via bronchoscopy. The bronchoscope and a catheter containing the seeds are fed into the lung via the trachea.

For Dr. Hagen, this new technique means certain patients who may have otherwise

been beyond the scope of radiation therapy may be treated successfully with targeted high-dose radiation. He says, “For those who have had their limit of standard radiation therapy or where radiation isn't an option, this can mean new hope for many of those patients.”

New Therapy Shows Promise for Patients With Mesothelioma

Treatment of mesothelioma using a novel “tri-modal” therapy is offering improved outcomes for patients suffering from this deadly disease.

As its name implies, tri-modal therapy for malignant mesothelioma involves three modalities consisting of surgery (extrapleural pneumonectomy), chemotherapy and radiation therapy. This multidisciplinary therapy requires interspecialty collaboration between thoracic surgeons, medical oncologists and radiation oncologists, something that occurs on a daily basis at USC/Norris Cancer Hospital during patient tumor conferences.

For P. Michael McFadden, M.D., Professor and Surgical Director of Lung Transplantation in the Department of Cardiothoracic Surgery at the Keck School of Medicine, the benefits of tri-modal therapy are significant.

“If a patient is a candidate for this tri-modal approach, I believe it can often be the best way to treat mesothelioma.” But he would like the procedure to be made available to more patients. He explains, “Many referring physicians, including some pulmonologists, aren't aware of tri-modal therapy. It's just not on their radar screens. So many will manage these cases with chemotherapy alone, almost in a palliative manner. For those selected patients and their physicians, tri-modal therapy – extrapleural pneumonectomy, chemotherapy and thoracic irradiation – offers a better alternative than chemotherapy alone.”

Targeted Therapies Personalize Treatment

“We're in a renaissance period for new cancer drugs,” says USC medical oncologist Barbara J. Gitlitz, M.D., when referring to targeted and genomic cancer therapies. “We don't want to waste someone's precious time giving him or her a drug that may be wonderful and exciting but that they won't respond to. So using molecular biology techniques, we're getting to the point where someday soon we'll be able to tailor which drugs will benefit them and which drugs won't benefit them – or may even be toxic to them.”

For Gitlitz, the advent of targeted therapies is the most exciting development in cancer research in the last four or five years. “It's being incorporated into all our clinical trials,” she says. She goes further, saying, “We're also treating people off of clinical trials, too, where we're striving to improve response rate and duration of response by using molecular techniques that are already available, such as excision repair gene testing and other genetic testing on tumors.”

The interspecialty approach to cancer care also benefits lung cancer patients. Gitlitz says, “For someone with lung cancer to come and in one day have the op-



Barbara J. Gitlitz, MD

Areas of Treatment: **Lung Cancer, Mesothelioma, Thymoma, Thyroid Cancer, Head and Neck Cancer, Clinical Trials and New Drug Development**

portunity to see all of us in a multidisciplinary thoracic tumor clinic means their care isn't scattered over many days and many locations.”

Having multiple specialists available to bring their expertise to a case highlights the importance of second opinions for Gitlitz. “I had a patient who presented three years ago with brain metastases, and her first opinion was, ‘Go home and get your affairs in order.’ We then saw her and treated her and she's still alive today because of it.” ■

REFERRAL NOTES

CyberKnife® Robotic Radiosurgery System can treat lung lesions previously considered untreatable by radiation therapy.

The placing of fiducial markers via bronchoscopy can prevent complications such as hematoma and pneumothorax.

Tri-modal therapy may provide better outcomes than chemotherapy alone for certain patients with malignant mesothelioma.

To refer a patient to the USC/Norris Lung Cancer program, call 323-865-3000.

USC Has L.A.'s Only New Gamma Knife®

As of this publication date, the Gamma Knife® Perfexion™ at USC University Hospital is the only such device in Los Angeles County.

The Gamma Knife Perfexion makes the entire procedure more efficient and user-friendly. Collimator changes can be made by the control program in a matter of seconds, optimizing workflow and significantly reducing treatment time and improving patient comfort. In the older versions, collimator changes had to be done manually, requiring up to 15 minutes to complete.

In addition, the new Perfexion model provides better dosimetry performance, better radiation protection for patient and staff, unlimited cranial reach, full automation and outstanding patient and staff comfort. According to Dr. Michael L. J. Apuzzo, “The Gamma Knife Perfexion gives us the ability to treat a larger spectrum of lesions in the intracranial space, and because of the fully automated nature of it, we can accomplish our treatment in a much more rapid time frame.” He continues, “There are more patients treated with the Gamma Knife; it is the ‘gold standard’ for treating patients.”

Dr. Apuzzo also notes, “USC is one of the few centers involving a radiation physicist in patient cases [Cheng Yu, PhD]. Any cases we do are performed with Dr. Yu, who does the physics and planning of the instruments.”