

Clinical Research

Newsletter for Colleagues in the Community

Stanford
Cancer Institute

A National Cancer Institute
Designated Cancer Center



Welcome to the Fall 2016 issue of the Stanford Cancer Institute Clinical Research Newsletter. This quarterly publication is designed to inform our colleagues in the medical community, and especially physicians who are considering treatment options for their patients with cancer, regarding current clinical trials available at the Stanford Cancer Institute, a National Cancer Institute Designated Comprehensive Cancer Center. Many of these trials provide access to novel therapies including new “targeted” agents, often not available in the community.

This newsletter edition focuses on the Department of Radiology and the Department of Radiation Oncology. Each department is renowned for leadership in its field, cutting edge treatments, research studies, and landmark scientific breakthroughs. Clinical trials are available across multiple disease sites and employ a variety of cutting edge techniques. In addition, this newsletter profiles the Developmental Therapeutics program, which concentrates on developing novel therapies for cancer.

The Stanford Radiology Department is a national leader with more than 100 years of contributions to the field. The department is renowned for translational research that advances early disease detection and personalized medicine using anatomical, functional, and molecular imaging. Stanford Radiology remains among the highest National Institutes of Health (NIH) funded radiology departments in the country. Our Radiology Department is also among the world’s leaders in creating imaging platforms for combined applications of CT, MR, PET, molecular imaging, nanotechnology, ultrasound, and bioinformatic technologies.

The Stanford Department of Radiation Oncology is an international leader in its field with a long history of research breakthroughs from employing the first medical linear accelerator in 1955, through its recent advances in stereotactic body radiotherapy. The department receives more per capita NIH funding than any other radiation oncology department in the United States. The department’s focus on translational and clinical research brings exciting discoveries from the laboratory to the clinic, directly impacting and improving patient care in an interdisciplinary setting.

The Developmental Therapeutics program conducts pharmacokinetic and pharmacodynamic driven first-in-human trials tailored to make early, informed decisions regarding the suitability of novel molecular agents for further clinical investigation.

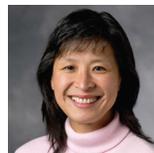
We hope that you will consider a Stanford Cancer Institute clinical trial when you deem it appropriate to refer a patient to an academic medical facility.

Sanjiv Sam Gambhir MD, PhD



*Virginia and D. K. Ludwig Professor of Cancer Research
Chair, Department of Radiology
Professor by courtesy, Departments of Bioengineering
and Materials Science & Engineering
Director, Molecular Imaging Program at Stanford (MIPS)
Director, Canary Center at Stanford for Cancer
Early Detection*

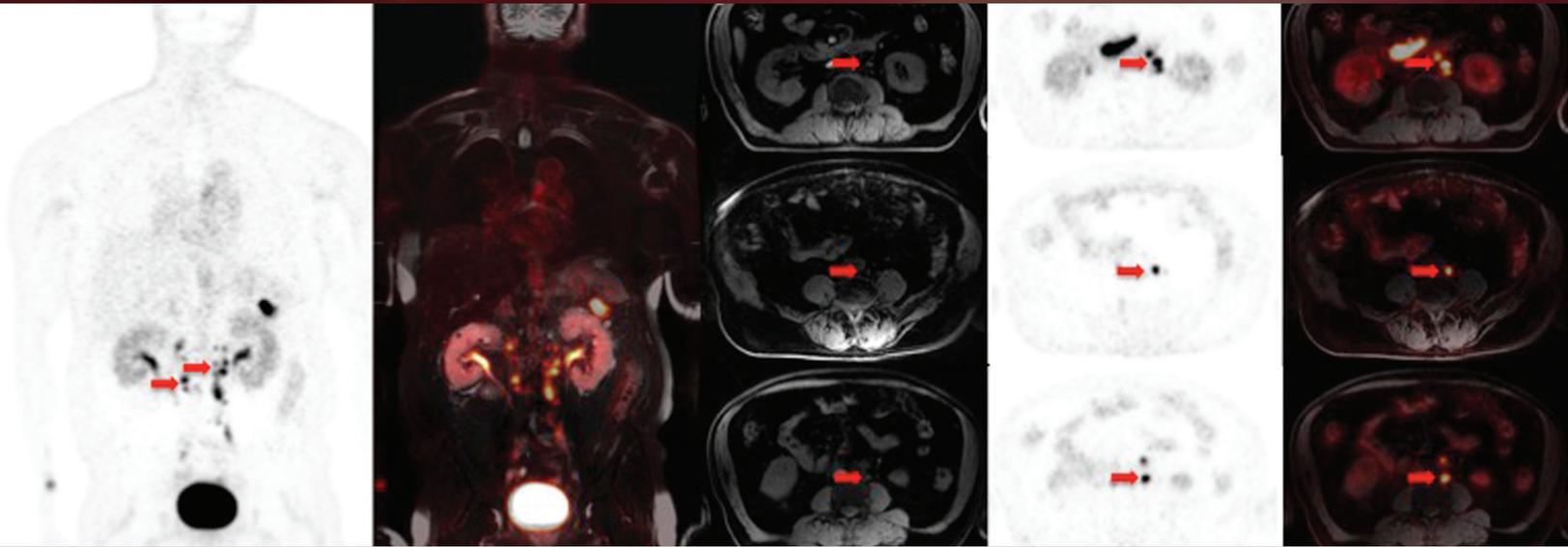
Quynh-Thu Le, MD, FACR



*Katharine Dexter McCormick & Stanley McCormick
Memorial Professor
Professor & Chair, Department of Radiation Oncology*

Stanford Radiology

National Leader in Research – Advancing Early Disease Detection and Personalized Medicine



⁶⁸Ga RM2 (⁶⁸Ga Bombesin) PET/MRI in a patient with prostate cancer shows lymph node metastases (arrows). Previously done conventional imaging (CT, MRI) did not identify disease. Images were acquired using a state-of-the-art time-of-flight enabled simultaneous PET/MRI scanner, first installed worldwide at Stanford University in December 2013.

The Stanford Radiology Department is a national leader in cutting edge translational research that advances early disease detection and personalized medicine using anatomical, functional, and molecular imaging.

With one of the highest National Institutes of Health (NIH) funding rankings in the country, Stanford Radiology is one of a very small number of Radiology departments in the US with multiple major NIH-funded Research Centers and is also among the world's leaders in creating imaging platforms for combined applications of CT, MR, PET, molecular imaging, nanotechnology, and bioinformatic technologies.

Led by Departmental Chair Sanjiv Sam Gambhir, MD, PhD, an international leader in the field of multimodality molecular imaging, Stanford Radiology focuses its research on a range of different disease groups including bone, breast, brain, pancreas, head & neck, liver, kidney, lung, non-Hodgkin's lymphoma, prostate, and others. Stanford Radiology research is highly translational and aims to provide benefit for both adults and children.

GOALS AND OBJECTIVES

Radiology research:

- Advances medical imaging through sophisticated physics and engineering approaches
- Develops molecular imaging techniques and probes for early detection, therapy, and disease monitoring
- Combines image processing techniques with biocomputational tools
- Develops strategies to marry in vitro diagnostics with in vivo imaging
- Investigates molecular mechanisms underlying cancer progression

A primary goal of Stanford Radiology's clinical and research activities is to detect and treat disease, especially cancer, at its earliest and most treatable stage.

RADIOLOGY RESEARCH HIGHLIGHTS: OVER 100 YEARS OF ACHIEVEMENT

For more than 100 years, Stanford's Department of Radiology has been making contributions to medical and surgical advances through pioneering research, innovations in image-based patient care, and education.

Since 1904, Stanford Radiology has made scientific breakthroughs by:

- Advancing imaging to cure Hodgkin's disease
- Establishing a program in MR technology development that is held in high regard internationally
- Developing CT angiography for the examination of blood vessels throughout the body
- Pioneering technical advances to enhance MRI and CT scanners
- Establishing one of the world's leading molecular imaging programs
- Cultivating innovative 3D imaging techniques to support more accurate diagnoses and improve communication of exam results to referring physicians and patients
- Pushing the technology and engineering envelope to develop increasingly sensitive and affordable imaging devices
- Developing computational and data integration solutions for the study of disease progression
- Developing strategies for the early detection of cancer including novel nanotechnologies

Stanford Radiology continues to make imaging discoveries. Department researchers have initiated 150 patents over the past five years.

NIH-FUNDED STANFORD RADIOLOGY RESEARCH CENTERS AND PROGRAMS

Major multidisciplinary NIH-funded Radiology Research Centers and Programs at the Stanford Department of Radiology include:

- Center for Advanced Magnetic Resonance Technology at Stanford (CAMRT, G Glover PI) The CAMRT, funded by NIH/ NIBIB, is located in the Richard M. Lucas Center for Imaging, and brings together the expertise and talent of individuals from the Radiology Department's Radiological Sciences Laboratory (RSL) and the Electrical Engineering Department's Magnetic Resonance Systems Research

Laboratory (MRSRL). This multidisciplinary group shares the common goals of developing innovative Magnetic Resonance Imaging and Spectroscopy (MRI/ MRS) techniques for fundamental anatomic, physiologic, and pathophysiologic studies. The CAMRT was awarded a 5-year funding cycle that began in 2015.

- In Vivo Cellular and Molecular Imaging Program at Stanford (ICMIC, SS Gambhir PI) The ICMIC, one of 7 NCI-funded Specialized Programs of Research Excellence (SPOREs), emphasizes the application and extension of molecular imaging to translational research and clinical applications. The ICMIC at Stanford integrates successful pre-clinical work into clinical applications that:
 - exploit molecular imaging by extracting information from animal models and pre-clinical studies.
 - provide new information on tumor diagnosis, initiation, progression, and responses to therapy.
 - develop new imaging technologies.
- Center for Cancer Nanotechnology Excellence and Translation (CCNE-T, SS Gambhir PI) The CCNE-T, one of 9 NCI-funded Centers of Cancer Nanotechnology Excellence (CCNEs), brings together scientists and physicians from Stanford University, University of California Berkeley/ Lawrence Berkeley National Lab, University of California Los Angeles, University of Southern California, and the Massachusetts Institute of Technology. Work of the CCNE-T expands on the concept that in vitro diagnostics, used in conjunction with in vivo diagnostics, can markedly impact cancer patient management. Utilizing nanotechnology, researchers aim to advance in vitro diagnostics through proteomic sensors, and in vivo diagnostics through nanotechnology for molecular imaging. The CCNE-T also brings together investigators in the Schools of Medicine, Engineering, and Humanities & Sciences.
- Center for Cancer Systems Biology (CCSB, S Plevritis PI) The CCSB, an NCI-funded Center for Cancer Systems

Biology, is a collaborative effort of faculty from the Schools of Medicine, Engineering, and Humanities & Sciences, with expertise ranging from molecular biology and oncology to mathematics, statistics, and computer science. CCSB focuses its research on the analysis of cancer as a complex system by merging experimental and computational methods. The group aims to discover molecular mechanisms underlying cancer progression by studying cancer as a complex biological system that is driven, in part, by impaired differentiation. CCSB's overarching goal is to provide a better understanding of the differentiation and self-renewal properties of cancer to help identify molecular therapeutic targets and strategies to eradicate this disease, or at least, maintain it in a nonlethal state.

- Early Detection Research Network (EDRN, SS Gambhir and J Brooks Co-PI's) The EDRN aims to improve current screening methods for prostate cancer by increasing the accuracy of detection and prognosis, and reducing the numbers of unnecessary surgeries. Prostate-specific antigen (PSA) testing currently serves as the test of choice to screen and manage prostate cancer. However, translating PSA scores is imperfect, frequently resulting in under or over-diagnosis. Better methods are needed for early and accurate detection and monitoring of prostate cancer. The EDRN, which leverages the CCNE and ICMIC, currently leads efforts to:
 - Adapt magneto-nanosensors for multiplex analysis of blood-based biomarkers for prostate cancer detection and prognosis. This platform is far more sensitive and specific than current techniques.
 - Adapt ultrasound technology using tumor angiogenesis-targeted microbubbles to image prostate cancer, an approach that will increase the accuracy of detection during the screening process.
 - The long-term goal is to combine these two approaches (blood-based biomarker and imaging) for accurate early detection and prognosis of prostate cancer.
- Magnetic Resonance Imaging-Guided Cancer Interventions (MRI-gCI, KB Pauly, PI) Through the MRI-gCI Program Project Grant (PPG), Stanford researchers are developing and testing controlled minimally invasive thermal ablation techniques

for the treatment of cancer. Utilizing precise imaging, feedback, and controlling the shape and size of thermal lesions, the aim is to improve treatment options for patients. The following five areas of pre-clinical and clinical research are conducted within the MRI-gCI program:

- MR-guided High Intensity Focused Ultrasound (HIFU) of soft tissue tumors
- Minimally Invasive MRI-Guided Management of Prostate Disease
- MR-Guided Precision Thermal Therapy of Retroperitoneal Tumors
- MRI Methods for Guiding Focused Ultrasound in the Brain
- MR-guided RF Ablation

The outcomes of this PPG will be:

- Improved minimally-invasive treatment options
- Increased understanding of tissue response to thermal treatments
- Advances in engineering, both hardware and software for the treatment of cancer

CURRENT STUDIES INCLUDE

Multiple Sites

- Development of Radiation Free Whole Body MR Imaging Technique for Staging of Children with Cancer (PEDSVAR0017)
- Detection of Serum Biomarkers for Patients with Suspicion of Cancer Undergoing 18F-FDG PET/CT Imaging (VAR0085) (SOON TO OPEN)
- Prospective Evaluation of Clinical and Quality-of-Life Outcomes in Patients with Intra-Peritoneal Catheters for Management of Refractory Malignant Ascites (VAR0131) (SOON TO OPEN)
- Evaluation of the Utility of the ePAD Tool for Cancer Lesion Assessment (VAR0135) (SOON TO OPEN)
- 18F FDG PET/CT vs. 18F FDG PET/MRI Comparison for Radiation Treatment Planning (VARIMG0007)
- 18F FPPRGD2 PET/CT or PET/MRI Imaging of $\alpha v \beta 3$ Integrins Expression as a Biomarker of Angiogenesis (VARIMG0002)

Bone

- A Post Approval Registry: ExAblate Treatment of Metastatic Bone Tumors for the Palliation of Pain (BONE0009)
- A Phase IV Post Approval Clinical Study of ExAblate Treatment of Metastatic Bone Tumors for the Palliation of Pain (BONE0008)
- Detection and Differentiation of Bone Lesions with Ferumoxytol-Enhanced MRI (PEDSBONE0006)
- Comparison of Magnetic Resonance Guided Focused Ultrasound and Re-irradiation for Persistent or Recurrent Pain from Osseous Metastases after Primary Treatment with Radiotherapy (BONE0011) (SOON TO OPEN)

Brain

- ¹⁸F FPPRGD2 PET/CT or PET/MRI Imaging of avb3 (alpha-v-beta-3) Integrins Expression as a Biomarker of Angiogenesis (VARIMG0002)
- MR Imaging of Inflammatory Responses in the Central Nervous System with Ferumoxytol-enhanced MRI (BRNCNS0007)

Breast

- A Feasibility Study of Radiofrequency Identification (RFID) Localization of Breast Lesions (BRS0053) (SOON TO OPEN)
- Contrast-Enhanced Digital Mammography (CEDM) vs Contrast-Enhanced Breast MRI (CE-MRI) in patients with Known Breast Cancer (BRS0031)
- Contrast-Enhanced Digital Mammography (CEDM) vs Mammography and Ultrasound in Patients with Suspicious Breast Abnormalities (BI-RADS 4/5) (BRS0028) (SOON TO OPEN)
- Magnetic Resonance Imaging of Breast Cancer (BRNSTU0004)

Liver, Kidney, Lung

- Perfusion CT in Evaluation of Renal Malignancies (RENAL0020) (SOON TO OPEN)
- Developing Non-Invasive Early Therapeutic Monitoring to Predict Treatment Efficacy in Renal Cell Carcinoma (RCC) (RENAL0026)
- US Elastography for Characterizing Focal Lesions in the Kidney (VAR0099)
- Phase 3 Prospective, Randomized, Blinded and Controlled

Investigation of Hepasphere/Quadraspera Microspheres for Delivery of Doxorubicin for the Treatment of Hepatocellular Cancer (HEP0038)

- Quantitative Ultrasound Spectroscopy to Detect HCC (GIIMG0007)
- Pilot Technical Feasibility Study on 3D Contrast-Enhanced Ultrasound Imaging and to Assess Whether Change in Ultrasound 3D Perfusion Pattern can Predict Treatment Response (HEP0043)
- Phase 3 Randomized, Open-Label Study Comparing Pexa-Vec (Vaccinia GM-CSF / Thymidine Kinase-Deactivated Virus) Followed by Sorafenib Versus Sorafenib in Patients with Advanced Hepatocellular Carcinoma (HCC) Without Prior Systemic Therapy (HEP0054) (SOON TO OPEN)
- Serum Biomarkers for FDG-PET Positive Lung Nodules (LUN0045)
- An Integrated Research Program for the Lung Stanford Nodule Assessment Program (Lung-SNAP) (LUN0060)
- Blood Biomarkers for Patients Undergoing Lung Cancer Screening by Computed Tomography (LUN0064)

Ovary

- Ultrasound and Photoacoustic Imaging of Surgically Removed Ovarian Tissue and Fallopian Tubes (GYNOPF0013) (SOON TO OPEN)
- Transvaginal Ultrasound and Photoacoustic Imaging of the Ovaries and the Fallopian Tubes: A Clinical Feasibility Study (GYNOPF0014) (SOON TO OPEN)
- ⁶⁴Cu-DOTA-B-Fab as a PET Tracer for Evaluating CA6 Expression in Tumors: a First in Human Study (GYNOVA0033) (SOON TO OPEN)

Pancreas

- Detection of Integrin Alpha-v-Beta 6 in Pancreatic Cancer with [¹⁸F]-R01-MG-F2: a First in Human Study (PANC0020)

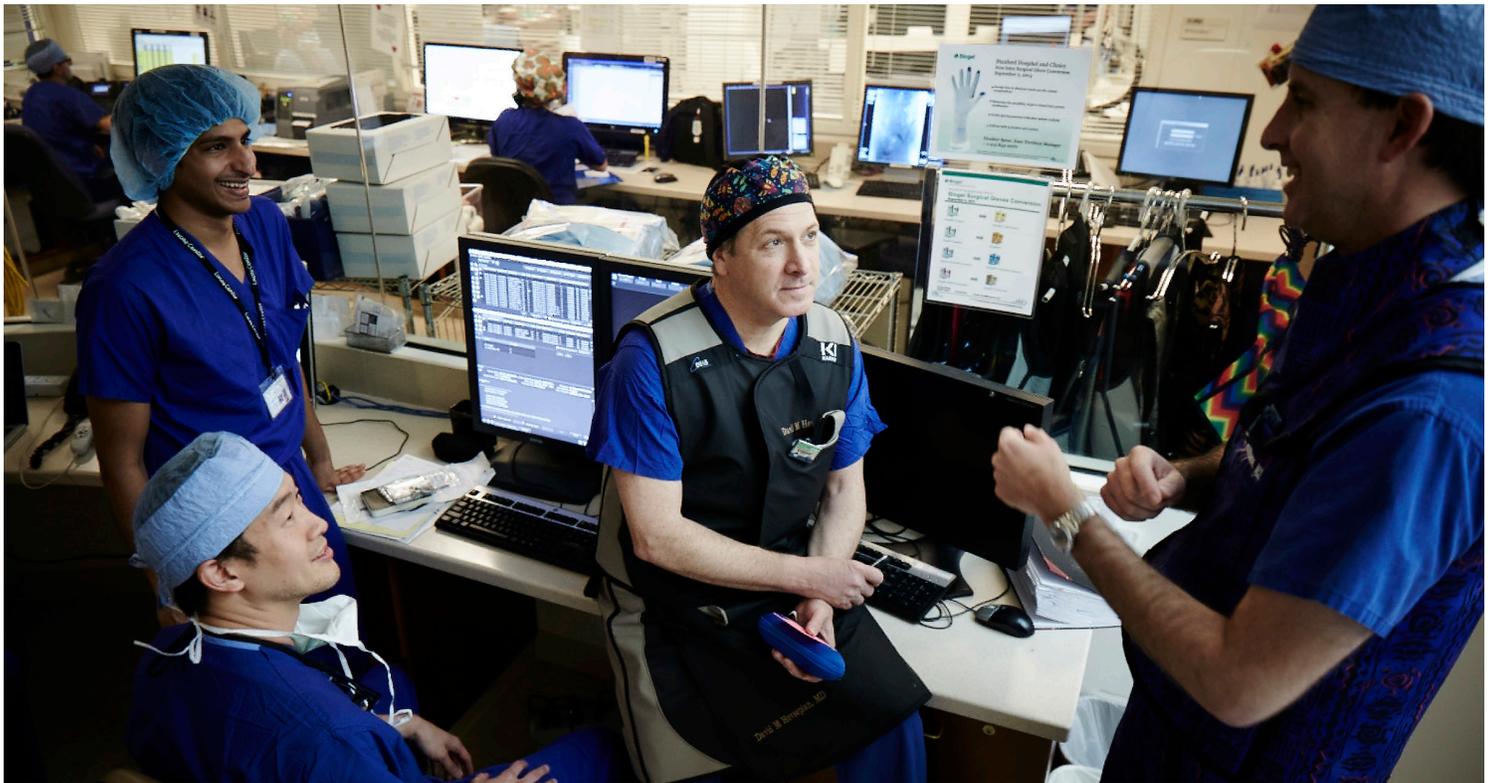
Prostate

- Transrectal Photoacoustic Imaging of the Prostate (PROS0044)
- Photoacoustic imaging (PAI) of the Prostate: A Clinical Feasibility Study (PROS0046)

• *highlighted studies are Stanford investigator initiated*

Stanford Interventional Radiology

Translational Research for Compassionate Treatment and Care



Stanford Interventional Radiology (IR), led by Division Chief Lawrence “Rusty” Hofmann, MD, is renowned for its translational research in developing methods for the delivery of safe, effective, and compassionate cancer care. Stanford is a world leader in IR, with research and clinical work recognized by peers and professional societies such as the Society of Interventional Radiology (SIR) and the Radiologic Society of North America (RSNA). Stanford IR has also been honored for its work with SIR-Spheres and TheraSphere, the only two radioembolization treatments currently available for the treatment of liver cancer.

ROUTINE CLINICAL CARE—VENOUS STENTING/THROMBOLYSIS

Stanford has pioneered treatment of acute and chronic deep venous thrombosis (DVT). Interventional radiology has techniques to treat cancer patients with acute DVT who present with significant pain and swelling in extremities. We have also developed techniques to treat patients with chronic DVT. Many of our patients have had venous occlusions for many years (up to 25 years), and we can successfully reopen the vein and return the patient to a normal lifestyle.

IR RESEARCH—“CANCER TREATMENT OF THE NEW MILLENNIUM”

Stanford interventional radiologists conduct clinical trials and basic laboratory research to discover new ways of treating cancer. Described as the ‘surgery’ of the new millennium, interventional procedures are developed and used to treat cancer with minimally invasive techniques, eliminating the need for open surgery, while decreasing risk, reducing pain, and promoting a speedier recovery time. Similarly, through interventional techniques, Stanford radiologists are able to deliver a localized therapeutic cytotoxic dose directly to the tumor site, reducing side effects including toxic dose to surrounding normal tissues.

Stanford IR investigates and provides image-guided tumor treatments that use:

- **Radioembolization:** A palliative therapy to treat both primary and metastatic tumors by injecting radioactive microspheres directly into the arteries that feed tumors allowing for a very high dose of radiation to be concentrated in tumors while limiting exposure to the surrounding normal tissues.



- Chemoembolization: A palliative, minimally invasive treatment for cancer involving the liver and other solid organs that is used for tumors not amenable to surgical intervention or radiofrequency ablation (RFA). Similar to radioembolization, chemoembolization delivers and traps a high dose of a chemotherapy drug directly in the tumor while depriving the tumor of its blood supply by blocking, or “embolizing,” the arteries feeding the tumor.
- Radiofrequency ablation (RFA): A procedure that offers a nonsurgical, localized treatment to kill tumor cells with heat while sparing the surrounding healthy tissue. RFA ablation is performed on inoperable tumors. With an RFA probe inserted into the tumor, radiofrequency waves (similar to microwaves) are transmitted through the probe to the surrounding tumor producing enough heat to destroy the tumor.
- Microwave ablation: A newer technique that kills tumor cells with high temperatures using a microwave-emitting probe that is placed directly into the tumor. Because it is capable of higher temperature induction within the tumor, and yields

faster ablation times, microwave ablation has the potential to treat larger tumors in the liver and may be the preferred approach for tumors situated near major blood vessels.

- Cryoablation: An alternative method of killing tumor cells also using extreme temperature. A needle probe is inserted into the tumor and applies extreme cold to destroy tumor cells by freezing. The freezing process stops blood flow and induces tumor cell death. Cryoablation may be used for tumors of the kidneys, lungs, and other body sites.

RESEARCH HIGHLIGHTS ENCOMPASS

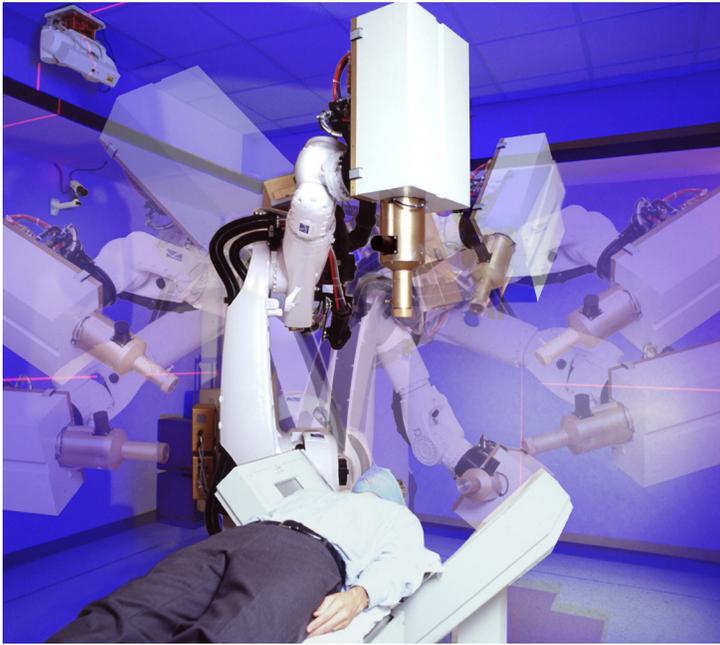
- Multicenter and Stanford-exclusive chemoembolization and radioembolization trials.
- Clinical trials that:
 - Study the treatment of liver tumors using viruses engineered to kill cancer.
 - Evaluate non-invasive pain palliation for cancer patients with metastases to bones.
 - Focus on the development of predictive models of vascular invasion in hepatocellular carcinoma through the integration of systemically extracted imaging characteristics and gene expression profiles.
 - Explore new methods of tumor ablation, such as microwave ablation and high-intensity focused ultrasound.
 - Conduct biomarker and imaging studies to detect pre-cursors to blood clot development in the cancer patient population.

CURRENT STUDIES INCLUDE

- A Phase IV Post Approval Clinical Study of ExAblate Treatment of Metastatic Bone Tumors for the Palliation of Pain (BONE0008)
- A Post Approval Registry: ExAblate Treatment of Metastatic Bone Tumors for the Palliation of Pain (BONE0009)
- Phase 3 Prospective, Randomized, Blinded and Controlled Investigation of Hepasphere/Quadrasphere Microspheres for Delivery of Doxorubicin for the Treatment of Hepatocellular Cancer (HEP0038)

Stanford Radiation Oncology

An International Leader in Translational Research



An international leader in its field, the Stanford Department of Radiation Oncology is comprised of three divisions: radiation therapy, radiation physics, and radiation and cancer biology. Led by Chair Quynh-Thu Le, MD, the Department receives more per capita NIH funding than any other radiation oncology department in the United States. Furthermore, the Department's focus on translational and clinical research brings exciting discoveries from the laboratory to the clinic, directly impacting and improving patient care in an interdisciplinary setting.

RESEARCH BREAKTHROUGHS

Stanford Radiation Oncology's laboratory and clinical research efforts have led to numerous scientific breakthroughs. Over the years, scientists and clinicians:

- Employed the first medical linear accelerator routinely used for radiotherapy in the Western hemisphere. Developed by Stanford in 1955, it was first used in the cure of a 7-month old boy with retinoblastoma.
- Initiated the first randomized, prospective studies on the treatment of Hodgkin's disease and other lymphomas, using high-energy radiation as part of an aggressive approach to treating these diseases, resulting in dramatic improvement in cure rates and decreased toxicity.

- Developed total skin electron beam therapy of mycosis fungoides reporting the first long-term disease-free survivors of this disease.
- The first that demonstrated the curative potential of external beam radiotherapy for the treatment of prostate cancer.
- Pioneered the arc-based radiotherapy technique for prostate cancer that is commonly used today.
- Pioneered stereotactic body radiotherapy for prostate cancer.
- Collaborated with the Stanford Department of Neurosurgery to develop the CyberKnife system and to apply it for stereotactic ablative treatment of brain, spine, and other extracranial tumors.
- Performed the first stereotactic ablative treatments for refractory bipolar depression and cardiac arrhythmia.
- Performed the first prospective single-fraction dose escalation studies investigating the use of stereotactic body radiotherapy (SBRT)/stereotactic ablative radiotherapy (SABR) for the treatment of lung, liver, and pancreatic tumors.
- Developed and initiated early trials of hypoxic cell radiation sensitizers and hypoxic cell cytotoxins.
- Identified several classes of small molecules that specifically kill VHL deficient renal cancer cells through a synthetic lethal screening approach and applied this technology to screen for novel therapeutics against other cancer targets.
- Discovered that the depletion of a protein called Perp could be an early indicator of skin cancer development and useful for staging and establishing prognoses.
- Discovered the first small molecule that targets the Ire1 signaling pathway in multiple myeloma and other cancers.
- Identified a potent anti-cancer therapy that starves cancer cells of glucose, their energy source, with minimal side effects and translated this discovery into clinical studies targeting tumor metabolism.

- Completed clinical trial to target connective tissue growth factor (CTGF) in pancreatic carcinoma. This is the first trial to target both pancreatic cancer cells and tumor stromal cells.
- Initiated the first randomized Multi-Center Phase III study investigating the efficacy of SBRT/SABR in locally advanced pancreatic cancer.
- Developed a novel technique to automatically track prostatic motion and reconstruct dose during VMAT treatment.

CURRENT RESEARCH HIGHLIGHTS

- Developing a comprehensive strategy for detecting and quantitating circulating tumor DNA in blood. The method, called CAPP-Seq (Cancer Personalized Profiling by deep Sequencing), is able to identify tumor mutations without the need for biopsy and can detect the presence of microscopic cancer deposits not visible on scans.
- Studying the effect of targeting several hypoxia induced proteins and pathways, including AXL, Galectin-1 and the unfolded protein response, in the management of solid cancers such as pancreas, breast, lung, head and neck, breast, and gynecologic tumors.
- Developing new technology to enable pediatric patients to undergo radiation therapy without anesthesia by allowing them to watch streaming video during radiation therapy, using the Audio-Visual Assisted Therapeutic Ambience in Radiotherapy (AVATAR) system.
- A prospective clinical trial studying the feasibility and efficacy of a tablet-based neurocognitive intervention program in pediatric patients treated with total body irradiation prior to stem cell transplant.
- Studying the effect of targeting the different immune checkpoints with radiation and chemotherapy in solid cancers.
- Developing novel approaches for single cancer cell imaging with different radiotracers.
- Investigating stem cell based approaches to minimize radiation damage to normal tissues, specifically the gastrointestinal (GI) tract and the salivary glands.
- Collaborating with SLAC National Accelerator Laboratory to study the effects of ultra-high radiation dose rate (FLASH) and very high-energy electrons (VHEE) on survival of tumor cells and normal tissues.
- Developing new methods of CT and PET scanning to map the function of the lungs and distinguish malignant lung nodules from benign ones.
- Studying the effects of radiation on tumor cell migration and metastases.
- Studying the use of perfusion CT in predicting treatment response to radiotherapy for rectal, pancreas, and liver tumors.
- Developing robotic ultrasound guided radiotherapy for liver tumors.
- Combining total skin irradiation with novel biologics to improve treatment response and duration.
- Collaborating with the School of Engineering to create decision analysis solutions for patient-centric prostate cancer treatment decision-making.

ADVANCED RADIATION ONCOLOGY RESEARCH AND TREATMENT

The department offers the most advanced radiation oncology treatments in the world with the overall goal of delivering high dose radiotherapy to the tumor while maximally sparing the surrounding normal tissue. These therapies include:

- Stereotactic body radiotherapy (SBRT), stereotactic ablative radiotherapy (SABR) or stereotactic radiosurgery (SRS), which combines computerized imaging with radiation therapy for highly precise delivery of radiation to tumors and allows for the treatment to be completed in less than one week. We offer these treatments using the most advanced radiotherapy machines including CyberKnife and TrueBeam.

- High-dose rate temporary interstitial and intracavitary brachytherapy, which places a very high-energy radiation source inside the body near the tumor for a brief period of time.
- Intensity Modulated Radiotherapy (IMRT), which delivers radiotherapy via dynamically shaped beam fields from multiple angles.
- Volumetric Modulated Arc Therapy (VMAT), the most advanced type of IMRT, which allows the sparing of normal tissues and rapid delivery of treatment.
- Image guided radiotherapy (IGRT), which combines real-time tumor imaging with radiotherapy to maximize the precision of radiation therapy treatments.
- Intraoperative radiotherapy (IORT), which focuses a high dose of radiation onto residual tumor cells during surgery.
- Other modalities include total skin electron therapy, total body irradiation (TBI) with peripheral stem cell or bone marrow reconstitution, and total lymphoid irradiation (TLI) for immunosuppression.

CURRENT STUDIES INCLUDE:

Multiple/Variety

- Development of Novel Serum Markers for Monitoring Response to Anti-Cancer Therapy (VAR0006)
- Imaging and Biomarkers of Hypoxia in Solid Tumors (VAR0032)
- A Novel Therapy for Radiation-induced Xerostomia Using Human Salivary Stem Cells (VAR0050)
- Study of Biomarkers Indicative of Radiation Exposure (VAR0060)
- Pilot Study of the Optimization of Gene Expression Biomarkers and Bioassay for Radiation Biodosimetry Using Human Blood Irradiation Experiments to Study Gene Expression Changes Following Radiation Exposure (VAR0116)

Brain

- Exploration of Activity of RAD001 in Vestibular Schwannomas and Meningiomas: An NF2 Therapeutic Development Consortium Trial (BRNCNS0006) (SOON TO OPEN)
- Randomized Phase III Trial of Memantine and Whole-Brain Radiotherapy with or without Hippocampal Avoidance in Patients with Brain Metastases (NRGCC001)

Blood and Marrow Transplant (BMT)

- Study of the CytoRADx Assay to Measure Absorbed Dose of Radiation Received by Patients Receiving Radiation Therapy during Conditioning for Bone Marrow or Peripheral Blood Stem Cell Transplantation (HEM0044)

Breast

- Molecular and Cellular Analysis of Breast Cancer (BRS0040)

Gynecologic

- Phase I Pilot Study Evaluating Vaginal Dilator Use and Toxicity Following Vaginal Brachytherapy (GYN0005)
- Tissue and Plasma Biomarkers of Lymph Node Involvement in Cervical Cancer (GYNCVX0002)
- Phase I Pilot Study to Evaluate the Prognostic Value of Perfusion CT for Primary Cervical Cancer (GYNCVX0003)

Head & Neck

- Identification and Characterization of Novel Proteins and Genes in Head and Neck Cancer (ENT0008)
- Identification of Secreted Markers for Tumor Hypoxia in Patients with Head and Neck or Lung Cancers (ENT0016)
- A Randomized Study of Topical Dilute Hypochlorite (Modified Dakin's Solution) Treatment for the Prevention of Radiation Dermatitis in Head and Neck Cancer (ENT0042)
- Randomized Phase II and Phase III Studies of Individualized Treatment for Nasopharyngeal Carcinoma Based on Biomarker Epstein Barr Virus (EBV) Deoxyribonucleic Acid (DNA) (NRGHN001)
- Phase II Randomized Trial of Transoral Surgical Resection Followed by Low-dose or Standard-dose IMRT in Resectable p16+ Locally Advanced Oropharynx Cancer (ECOG3311)
- A Randomized Phase II Trial for Patients with p16 Positive, Non-Smoking Associated, Locoregionally Advanced Oropharyngeal Cancer (NRGHN002)

Liver

- Feasibility of 3D Perfusion Ultrasound for Liver Cancer SABR Planning and Response Evaluation (HEP0048)
- International Randomized Study of Transarterial Chemoembolization (TACE) versus Stereotactic Body Radiotherapy (SBRT) / Stereotactic Ablative Radiotherapy (SABR) for Residual or Recurrent Hepatocellular Carcinoma after Initial TACE (HEP0052) (SOON TO OPEN)

Lung

- 4D-CT-based Ventilation Imaging for Adaptive Functional Guidance in Radiotherapy (LUN0034) (SOON TO OPEN)
- Phase II Trial of Individualized Lung Tumor Stereotactic Ablative Radiotherapy (SABR) (LUN0048)
- A Pilot Study of Perfusion CT for Lung Tumors Treated with Stereotactic Ablative Radiation Therapy (SABR) (LUN0072)
- Phase III Comparison of Thoracic Radiotherapy Regimens in Patients with Limited Small Cell Lung Cancer also Receiving Cisplatin and Etoposide (RTOG0538-CALGB30610)
- Randomized Phase II Trial of Individualized Adaptive Radiotherapy Using During-Treatment FDG-PET/CT and Modern Technology in Locally Advanced Non-Small Cell Lung Cancer (NSCLC) (RTOG1106)
- A Randomized Phase II Study of Individualized Combined Modality Therapy for Stage III Non-Small Cell Lung Cancer (NSCLC) (RTOG1306)

Lymphoma

- A Phase II Study of Non-myeloablative Allogeneic Transplantation Using Total Lymphoid Irradiation (TLI) and Antithymocyte Globulin (ATG) in Patients with Cutaneous T Cell Lymphoma (BMT206)
- A Single-arm Phase 2A Study of MN-IL-12 (rHu-IL12) in Patients with Cutaneous T Cell Lymphoma (CTCL) Undergoing Low-dose Total Skin Electron Beam Therapy (LD-TSEBT) (LYMNHL0133)
- A Phase 1/2, Non-randomized, Open-label, Multicenter, Dose Escalation and Expansion Study of Intratumoral Injections of SD-101 in Combination with Localized Low-dose Radiation in Patients with Untreated Low-grade B-cell Lymphoma (LYMNHL0120)

Melanoma

- A Pilot Study of Ipilimumab in Subjects with Stage IV Melanoma Receiving Palliative Radiation Therapy (MEL0005)

Pancreas

- A Randomized Phase III Study Evaluating Modified FOLFIRINOX (mFFX) with or without Stereotactic Body Radiotherapy (SBRT) in the Treatment of Locally Advanced Pancreatic Cancer (PANC0015)

Prostate

- A Phase I Study Evaluating the Efficacy and Safety of Sodium Selenite in Combination with Palliative Radiation Therapy in Patients with Metastatic Castration-resistant Prostate Cancer (PROS0047)
- Feasibility of Using Trans-Perineal Clarity Autoscan Ultrasound Imaging for Prostate Motion Management, Tissue Characterization, and Treatment Monitoring (PROS0055)
- A Phase I/II Study of High-Dose-Rate Brachytherapy as Monotherapy for Prostate Cancer (PROS0065)
- Assessment of 3D Transperineal Ultrasound Imaging with Matrix Array Transducers as a Potential Imaging Modality for Adaptive Prostate and Post-Prostatectomy Radiotherapy (PROS0070)
- A Randomized Phase III Trial of Hypofractionated Post-Prostatectomy Radiation Therapy (HypoRT) Versus Conventional Post-Prostatectomy Radiation Therapy (NRG-GU003) (SOON TO OPEN)
- Androgen Deprivation Therapy and High Dose Radiotherapy with or without Whole-Pelvic Radiotherapy in Unfavorable Intermediate or Favorable High Risk Prostate Cancer: A Phase III Randomized Trial (RTOG0924) (SOON TO OPEN)

Sarcoma

- A Phase II Study of Hypofractionated Stereotactic Radiotherapy in the Treatment of Metastatic Pediatric Sarcomas of Bony Sites (SARCOMA0014) (SOON TO OPEN)
- Pilot Study to Explore the Role of Circulating Tumor DNA in the Management of Patients with Soft Tissue Sarcoma (SARCOMA0016)

Survivorship

- Feasibility of a Computerized Neurocognitive Intervention Program in the Early Post-Transplant Setting (PEDSHEM0004)

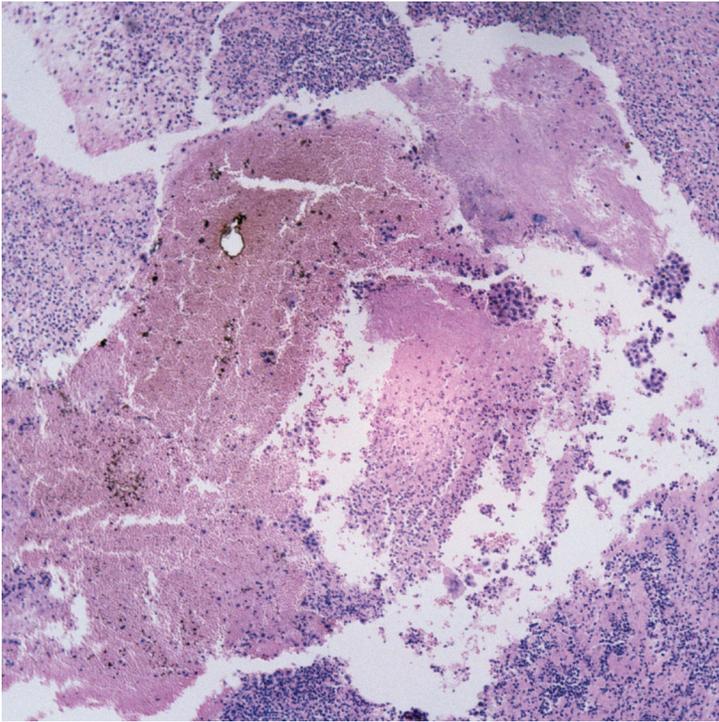
Skin

- A Pilot Study of Ipilimumab in Subjects with Stage IV Melanoma Receiving Palliative Radiation Therapy (MEL0005)

• *highlighted studies are Stanford investigator initiated*

Developmental Therapeutics

Phase 1 and 2 Clinical Research Program for Multiple Cancers



Stanford Cancer Center's Developmental Therapeutics (DT) Program, led by director Shivaani Kummar, MD, offers Phase 1 and 2 clinical trials designed to evaluate new treatment for cancer. Other faculty participating in this effort include Drs. Heather Wakelee and Joel Neal (lung cancers), A. Dimitrios Colevas (head and neck cancers), George Fisher and Pamela Kunz (GI cancers), George Sledge, Suleiman Massarweh, Mark Pegram and Melinda Telli (breast cancers), Sunil Reddy (melanoma), Ranjana Advani (lymphomas), and Branimir I. Sikic.

DT Program Director Dr. Kummar is a Professor of Medicine in the Stanford Division of Oncology and former leader of the National Cancer Institute's Developmental Therapeutics Clinic and Early Clinical Trials Development Program. Dr. Kummar's research interests focus on developing novel therapies for cancer. She specializes in conducting pharmacokinetic and pharmacodynamic driven first-in-human trials tailored to make early, informed decisions regarding the suitability of novel molecular agents for further clinical investigation. Her studies integrate genomics and laboratory correlates into early phase trials, establishing the proof of mechanism and proof-of-concept in these trials. She has published numerous articles

in medical journals and serves on a number of national and international scientific committees.

As a translational clinical studies program, Developmental Therapeutics brings together outstanding physicians with internationally regarded scientists to develop novel therapies and diagnostic modalities that utilize cutting-edge science and technologies. The program offers the opportunity for patients to enroll in clinical trials evaluating novel anticancer therapies. The overall goal of the program is to facilitate the development of promising, new treatments for cancer while ensuring the highest standards of patient safety.

Below is a sampling of currently available Phase 1 and 2 studies.

PHASE 1 AND 2 STUDIES

Multiple Solid Tumor Sites

- A Phase 1b/2, Open-label, Multicenter, Dose-escalation Trial of Intratumoral Injections of SD-101 in Combination with Pembrolizumab in Patients with Metastatic Melanoma (METS0003)
- A Phase 1 / 2 Dose Escalation and Cohort Expansion Study of the Safety and Tolerability of Urelumab Administered in Combination with Nivolumab in Advanced/Metastatic Solid Tumors and B Cell Non-Hodgkins Lymphoma (VAR0126)
- Phase 1 / 2, First-in-Human, Dose-Escalation Study of X-396 in Patients with Advanced Solid Tumors and Expansion Phase in Patients with ALK+ Non-Small Cell Lung Cancer (VAR0098)
- A First-in-Human Phase 1, Dose Escalation, Safety and Pharmacokinetic Study of PF-06647020 in Adult Patients with Advanced Solid Tumors (VAR0130)
- A Phase 2 Basket Study of the Oral TRK Inhibitor LOXO-101 in Subjects with NTRK Fusion-Positive Tumors (VAR0136)
- A Phase 1 / 1b, Open-Label, Multicenter, Repeat-Dose, Dose-Selection Study of CPI-444 as Single Agent and in Combination with Atezolizumab in Patients with Selected Incurable Cancers (VAR0141)