Welcome to the Summer 2014 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, about current clinical trials available at the NCI-designated Stanford Cancer Institute. Many of these trials provide access to novel therapies including new “targeted” agents, often not available in the community.

This edition of the newsletter focuses on the Department of Radiology and the Department of Radiation Oncology. Each department is renowned for its leadership in its field, cutting edge treatments, research studies, and landmark scientific breakthroughs.

• The Stanford Radiology Department is a national leader in translational research that advances early disease detection and personalized medicine using anatomical, functional, and molecular imaging. Stanford Radiology has one of the highest National Institutes of Health (NIH) funding rankings in the country, the highest funding per faculty ranking, and is the only Radiology department in the US with five major NCI funded Centers of Excellence.
  — Stanford Interventional Radiology conducts clinical trials and basic laboratory research to discover new ways of treating cancer. Described as the ‘surgery’ of the new millennium, interventional techniques are developed and used to treat cancer with minimally invasive methods, eliminating the need for open surgery, decreasing risk, reducing pain, and promoting a speedier recovery time.
  — The Stanford Division of Nuclear Medicine is a world leader in molecular imaging. Through development of novel tracers for positron emission tomography (PET) imaging, cancer patient management is being fundamentally changed. Improved staging, prediction and monitoring of treatment, and monitoring for recurrence are available. Newer technologies for the earlier detection of cancer are also under active investigation.

• 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. Stanford Radiation Oncologists offer some of the most advanced treatments and research studies available, many of which aim to enhance tumor control while reducing the amount of radiation received by healthy tissues.

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. We, in turn, will make every effort to deliver great care to your patient, keep you informed of the patient’s treatment and response, and if clinical trial treatment is not appropriate for your patient, return them to your care.
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 the only Radiology department 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 that span bone, breast, brain, head & neck, liver, kidney, lung, non-Hodgkin’s lymphoma, prostate, and other disease sites.

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

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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 115 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.

- **In Vivo Cellular and Molecular Imaging Program at Stanford (ICMIC, SS Gambhir PI)**
  The ICMIC, one of 8 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 8 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 and Engineering.

• **Center for Cancer Systems Biology (CCSB, S Plevritis PI)** The CCSB, one of 12 new NCI funded Centers 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-nanoparticles 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 preclinical 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

- 18F FPPRGD2 PET/CT Imaging of αvβ3 Integrins Expression as a Biomarker of Angiogenesis
- 4D-CT Based Ventilation Imaging for Adaptive Functional Guidance in Radiotherapy
- 68Ga DOTA-TATE PET/CT in the Evaluation of Patients with Somatostatin Receptor Positive Tumors: Comparison to 111In-Octreotide (Octreoscan) and Contrast-Enhanced CT
- A Multi-centre, Stratified, Open, Randomized, Comparator-controlled, Parallel-group Phase III Study Comparing Treatment with 177Lu-DOTA0-Tyr3-Octreotate to Octreotide LAR in Patients with Inoperable, Progressive, Somatostatin Receptor Positive, Midgut Carcinoid Tumours
- Blood Biomarker Amplification Using Ultrasound
- Combined F18 and FDG for Evaluation of Malignancy
- Development of Radiation Free Whole Body MR Imaging Technique for Staging of Children with Cancer

Bone and Pain

- 18F Sodium Fluoride PET/CT Scanning for the Evaluation of Musculoskeletal Pain and Skeletal Abnormalities
- A Feasibility Study to Evaluate the Safety and Initial Effectiveness of ExAblate MR Guided Focused Ultrasound Surgery in the Treatment of Pain Resulting from Metastatic Bone Tumors with the ExAblate 2100
- Comparison of PET/CT and MRI for Detection of Soft tissue and Skeletal Metastases
- Utility of FDG PET for the Evaluation of Myofascial Pain Syndrome

Liver, Kidney, Lung

- Chemoembolization with or without Sorafenib Tosylate in Treating Patients with Liver Cancer That Cannot Be Removed Surgically (ECOG)
- Phase 3 Prospective, Randomized, Blinded and Controlled Investigation of Hepasphere/QuadraspHERE Microspheres for Delivery of Doxorubicin for the Treatment of Hepatocellular Cancer
- Perfusion CT as a Predictor of Treatment Response in Patients with Hepatic Malignancies
- Detection of Serum Biomarkers for Patients with a Lung Nodule Undergoing FDG-PET/CT imaging
- Feasibility Study on 3D Contrast-enhanced Ultrasound Imaging to Predict Treatment Response in Patients with Liver Metastases

Lymphoma

- A 3-Arm Randomized Phase II Trial of Bendamustine-Rituximab (BR) Followed by Rituximab vs Bortezomib-BR (BVR) Followed by Rituximab vs BR Followed by Lenalidomide/Rituximab in High Risk Follicular Lymphoma
- FLT-PET/CT vs FDG-PET/CT for Therapy Monitoring of Diffuse Large B-cell Lymphoma
- PET Imaging of Lymphoma Using Radiolabeled Rituximab
- Comparison of 18F FDG PET/CT vs 18F FDG PET/MRI

Prostate

- Transrectal Photoacoustic Imaging of the Prostate - A Clinical Feasibility Study
- Transrectal Photoacoustic Imaging of the Prostate Tissue

Uterine Fibroids

- A Phase IV Clinical Study to Evaluate Safety of the ExAblate Model 2100 Type 1.1 System (ExAblate 2100/2000 UF V2 System) - Treatment of Uterine Fibroids
- A Phase IV Clinical Study to Evaluate Safety of the ExAblate Model 2100 Type 1.1 System (ExAblate 2100/2000 UF V2 System) in the Treatment of Symptomatic Uterine Fibroids

*highlighted studies are Stanford investigator initiated*
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.
  - Basic research on gene therapy delivery. Projects focus on nonviral methods of delivery, including VIPER, a method invented and patented in the IR basic science laboratory that utilizes novel combinations of FDA-approved agents.

**CURRENT STUDIES INCLUDE**

- A Feasibility Study to Evaluate the Safety and Initial Effectiveness of ExAblate MR Guided Focused Ultrasound Surgery in the Treatment of Pain Resulting from Metastatic Bone Tumors with the ExAblate 2100
- A Phase IV Clinical Study to Evaluate Safety of the ExAblate Model 2100 Type 1.1 System (ExAblate 2100/2000 UF V2 System) in the Treatment of Symptomatic Uterine Fibroids
- Patient Long-term Follow-up to Collect Data Following MR-guided Focused Ultrasound Treatment of Uterine Fibroids with ExAblate Model 2100 Type 1.1 System
- Phase 3 Prospective, Randomized, Blinded and Controlled Investigation Of Hepasphere/Quadrisphere Microspheres for Delivery of Doxorubicin for the Treatment of Hepatocellular Cancer
- Acute Venous Thrombosis: Thrombus Removal with Adjunctive Catheter-Directed Thrombolysis (ATTRACT) for Patients with DVT
- ExAblate Conformal Bone System Treatment of Metastatic Bone Tumors for the Palliation of Pain
- Chemoembolization with or without Sorafenib Tosylate in Treating Patients with Liver Cancer That Cannot Be Removed By Surgery (ECOG)

*highlighted studies are Stanford investigator initiated*
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.
• Established the efficacy of external beam irradiation in the treatment of prostate cancer.
• Collaborated with the Stanford Department of Neurosurgery to develop stereotactic radiosurgery for the treatment of brain and spine tumors.
• 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 a specific 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 a clinical trial to target the 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 isolating circulating DNA from blood and detecting cancer-associated mutations. The method, called CAPP-Seq (Cancer Personalized Profiling by deep Sequencing), is able to accurately quantify the amount of tumor in patients with lung cancer.
- Studying the effect of targeting Galectin-1, a hypoxia induced protein and an immune modulator, in the management of lung cancer.
- 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 and very high-energy electrons 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.
- Developing and receiving FDA approval of a blood test to detect tumor-associated DNA in patients with nasopharyngeal carcinoma.
- Investigating mechanisms to activate salivary gland stem cells to improve saliva function in patients whose glands have been damaged by radiation therapy.

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 1 week.
- **Low-dose rate brachytherapy**, which permanently deposits a radiation source inside the body within the tumor.
- **High-dose rate 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 structures and rapid delivery of treatment.
- **Image guided radiotherapy**, which combines tumor imaging integrated with special linear accelerators to deliver radiation that corresponds to the exact tumor location in real-time.
- **Dynamic arc therapy**, which allows for the continuous treatment of tumors in a manner that maximally spares adjacent normal tissue.
- **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)

Brain

- A Phase I/II Study of Fractionated Stereotactic Radiosurgery to Treat Large Brain Metastases (BRN0010)
- A Phase I/II Trial of Temozolomide and Hypofractionated Radiotherapy in Treatment of Supratentorial Glioblastoma Multiforme (BRN0012)
- Exploration of Activity of RAD001 in Vestibular Schwannomas and Meningiomas: An NF2 Therapeutic Development Consortium Trial (BRNCNS0006) (SOON TO OPEN)
- Natural History of Postoperative Cognitive Function, Quality of Life, and Seizure Control in Patients with Supratentorial Low-Risk Grade II Glioma (RTOG0925)
- A Phase II Randomized Trial Comparing the Efficacy of Heat Shock Protein-Peptide Complex-96 (HSPPC-96) Vaccine Given with Bevacizumab Versus Bevacizumab Alone in the Treatment of Surgically Resectable Recurrent Glioblastoma Multiforme (GBM) (ACNA071101)

Breast

- Phase II Study to Investigate Concurrent Lapatinib and Radiotherapy in Locally Advanced or Locally Recurrent Breast Cancer and the Impact on Breast Cancer Stem Cells (BRS0027)
- Pilot Study to Investigate the Impact of Hypochlorite in the Prevention of Radiation Dermatitis (BRS0039) (SOON TO OPEN)
- Molecular and Cellular Analysis of Breast Cancer (BRS0040) (SOON TO OPEN)
- Phase II Randomized Study of Whole Brain Radiotherapy in Combination with Concurrent Lapatinib in Patients with Brain Metastasis from HER2-Positive Breast Cancer A Collaborative Study of RTOG and KROG (RTOG1119)
- A Randomized Phase III Clinical Trial Evaluating Post-Mastectomy Chest Wall and Regional Nodal XRT and Post-Lumpectomy Regional Nodal XRT in Patients with Positive Axillary Nodes Before Neoadjuvant Chemotherapy Who Convert to Pathologically Negative Axillary Nodes After Neoadjuvant Chemotherapy (RTOG1304-NSABPB51)

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)
- Phase I Trial of Metabolic Reprogramming Therapy for Treatment of Recurrent Head and Neck Cancers (ENT0031)
- 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)
- Randomized Phase II Trial of Transoral Endoscopic Head and Neck Surgery Followed by Risk-Based IMRT and Weekly Cisplatin versus IMRT and Weekly Cisplatin for HPV Negative Oropharynx Cancer (RTOG1016)

- A Randomized Phase II Study of Adjuvant Concurrent Radiation and Chemotherapy versus Radiation Alone in Resected High-Risk Malignant Salivary Gland Tumors (RTOG1221)
- A Randomized Phase II Study of Radiotherapy plus Cetuximab versus Chemotherapy in HPV-associated Oropharynx Cancer (RTOG1016)
- Randomized Phase II/III Trial of Surgery and Postoperative Radiation Delivered with Concurrent Cisplatin Versus Docetaxel Versus Docetaxel and Cetuximab for High-Risk Squamous Cell Cancer of the Head and Neck (RTOG1216)

**Esophagus**
- A Phase III Trial Evaluating the Addition of Trastuzumab to Trimodality Treatment of Her2-Overexpressing Esophageal Adenocarcinoma (RTOG1010)

**Lung**
- 4D-CT-based Ventilation Imaging for Adaptive Functional Guidance in Radiotherapy (LUN0034)
- Phase II Trial of Individualized Lung Tumor Stereotactic Ablative Radiotherapy (SABR) (LUN0048)
- Pilot Study of FLT-PET/CT for Evaluation of Suspected Local Recurrence after Thoracic Stereotactic Ablative Radiotherapy (LUN0055)
- Phase III Comparison of Thoracic Radiotherapy Regimens in Patients with Limited Small Cell Lung Cancer also Receiving Cisplatin and Etoposide (RTOG0839)
- Randomized Phase II Study of Pre-Operative Chemoradiotherapy +/- Panitumumab (IND #110152) Followed by Consolidation Chemotherapy in Potentially Operable Locally Advanced (Stage IIIA, N2+) Non-Small Cell Lung Cancer (RTOG0839)
- Randomized Phase II Study Comparing Prophylactic Cranial Irradiation Alone to Prophylactic Cranial Irradiation and Consolidative Extra-Cranial Irradiation for Extensive Disease Small Cell Lung Cancer (ED-SCLC) (RTOG0937)
- 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) (SOON TO OPEN)

**Pancreas**
- Pancreatic Cancer Radiotherapy Study Group (PanCRS) Trial: A Randomized Phase III Study Evaluating Modified FOLFIRINOX (mFFX) with or without SBRT in the Treatment of Locally Advanced Pancreatic Cancer (PANC0015)

**Prostate**
- A Phase III Trial of Short Term Androgen Deprivation with Pelvic Lymph Node or Prostate Bed Only Radiotherapy (SPPORT) in Prostate Cancer Patients with a Rising PSA After Radical Prostatectomy (RTOG0534)
- A Phase III Prospective Randomized Trial of Dose-Escalated Radiotherapy with or without Short-Term Androgen Deprivation Therapy for Patients with Intermediate-Risk Prostate Cancer: A Phase III Randomized Trial (RTOG0815)
- 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 (RTOG1115)

**Sarcoma**
- A Phase II Study of Hypofractionated Stereotactic Radiotherapy in the Treatment of Metastatic Pediatric Sarcomas of Bony Sites (SARCOMA0014) (SOON TO OPEN)

**Skin**
- A Pilot Study of Ipilimumab in Subjects with Stage IV Melanoma Receiving Palliative Radiation Therapy (MEL0005)
- A Phase II Randomized Study to Evaluate the Efficacy of Combining Ipilimumab (3mg/kg) with Different Doses/Schedules of External Beam Radiotherapy (MEL0009) (SOON TO OPEN)

*highlighted studies are Stanford investigator initiated*
Developmental Therapeutics
Phase 1 and 2 Studies for Multiple Cancers

Stanford Cancer Center’s Developmental Therapeutics Program, led by Branimir I. Sikic, MD, offers Phase 1 and 2 clinical trials using novel therapeutics. Dr. Sikic’s clinical interests are mainly in ovarian cancers and cancers of unknown primary. Other faculty participating in this effort include Drs. Heather Wakelee and Joel Neal (lung cancers), Dimitri Colevas (head and neck cancers), George Fisher and Pamela Kunz (GI cancers), Mark Pegram and Melinda Telli (breast cancers), Sunil Reddy (melanoma), and Ranjana Advani and Holbrook Kohrt (lymphomas).

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. This research focuses on early clinical studies, investigator-initiated trials, the development of analytic approaches to enhancing the discovery of drugs and targets, and the analysis of clinical trials.

To the right is a sampling of currently available Phase 1 and 2 studies.

**PHASE 1 STUDIES**

**Multiple Solid Tumor Sites**

- A Phase 1, Open-label, Dose-escalation, Safety and Pharmacokinetic Study of CDX-1127 in Patients with Selected Refractory or Relapsed Hematologic Malignancies or Solid Tumors (VAR0081)
- A Phase I Study of the Safety, Tolerability, Pharmacokinetics and Immunoregulatory Activity of BMS-663513 (Anti-CD137) in Subjects with Advanced and/or Metastatic Solid Tumors (VAR0071)
- A Phase 1 Study of Recombinant Human IL15 (rhIL15) in Adults with Advanced Solid Tumors: Melanoma, Renal Cell, Non-Small Cell Lung and Head and Neck Cancer (VAR0093)
- Phase 1, First-in-Human, Dose-Escalation Study to Evaluate the Safety, Tolerability, and Pharmacokinetics of X-396 in Patients with Advanced Solid Tumors (VAR0098)

**Lymphomas**

- A Phase I Study of PF-05082566 as a Single Agent in Patients with Advanced Cancer, and in Combination with Rituximab in Patients with Non-Hodgkin’s Lymphoma (NHL) (LYMNHL0092)