UT Southwestern

THE TARGET

News from the Department of Radiation Oncology

VOLUME 7, SPRING 2015

Heavy ion therapy on the horizon

An international conference on heavy ion therapy and research, followed by a National Cancer Institute award to fund the planning of heavy ion research, has kick-started the effort to bring this advanced cancer therapy to patients in the U.S.

Representatives from leading heavy ion therapy facilities worldwide gathered in Dallas in November to help guide the U.S. entry into heavy ion cancer therapy.

What's Inside

Page 1 story Heavy ion therapy on the horizon

Early conceptual rendering of the proposed heavy ion therapy and research center on the UT Southwestern campus

UT Southwestern Medical Center is leading a Texas consortium of researchers to establish the country's first National Center for Heavy Ion Radiation Therapy, which would serve as a home for clinical care and research using heavy particles for innovative new cancer treatments.

The National Cancer Institute (NCI) has awarded UT Southwestern a $1 million grant to plan the research part of the center. Dr. Hak Choy, Chair and Professor of Radiation Oncology, is the principal investigator for the Texas award.

"Heavy ion radiation therapy represents the next quantum leap forward in cancer care. It is not currently available in the U.S., and our location would be the first of its kind in the country," Dr. Choy said.

In the U.S., more than 50 percent of cancer patients are currently treated using energetic photons, electrons, or protons. Heavy ions are the electrically charged nuclei of elements more massive than the single-proton hydrogen nucleus. Carbon-12 is currently the heavy ion most used for cancer therapy in centers worldwide.

"The efficacy of heavy ion radiation therapy for certain cancers has already been established by foreign institutions, which have conducted clinical trials and found profound increases in overall disease-free survival," Dr. Choy said. "However, this therapy needs a more thorough and rigorous scientific approach to uncover its full potential. Additional clinical trials, improvements in accelerator technology, and improvements in understanding the underlying biology are all still critically needed."

Heavy ion radiation delivers a beam that is more potent and more precise than either conventional beam or proton therapy. It is particularly well suited for treating radioresistant tumors, as well as for treating targets near sensitive structures such as the spine and brain.

The Texas-based consortium consists of researchers from UT Southwestern, The University of Texas MD Anderson Cancer Center, Texas A&M University, Prairie View A&M University, Baylor College of Medicine, The UT Health Science Center at San Antonio, The UT Medical Branch at Galveston, and NASA, in addition to national and international collaborators. The Texas consortium project was one of two awarded preliminary planning grants.

The U.S. pioneered heavy ion radiation therapy at the Lawrence Berkeley National Laboratory in 1954, but lack of funding shuttered the program in 1993, allowing other countries, fueled by extensive government support, to take the lead. Eight fully operational heavy ion radiation therapy centers now exist worldwide in Japan, Germany, Italy, and China.

In preparation for the launch of a U.S. heavy ion effort, UT Southwestern held an inaugural International Symposium on Ion Therapy (ISIT) in November 2014 in Dallas, bringing together representatives of leading heavy ion centers from around the globe to discuss the best practices and latest advances in particle therapy treatment and technology. Sixty-seven participants representing 23 institutions from Europe, Asia, and the U.S., as well as vendors and the White House Office of Science and Technology Policy, attended the event.

Several goals emerged from the meeting, according to UT Southwestern's Dr. Arnold Pompos, an Assistant Professor and medical physicist. "In the realm of physics, fast real-time determination of where energy is going to be deposited in tissue followed by fast real-time, irradiation plan adjustment, together with tissue motion management, would enable us to use heavy ions in novel clinical ways," Dr. Pompos said.

"In terms of biology and clinical use, one of our consortium's biggest goals is to evaluate the biological effectiveness of various ions and effectively utilize them when patient irradiation plans are constructed," he added. "Clinically, there is still a need to conduct thorough, scientifically designed clinical trials to uncover the histology, sites, tumor conditions, and types that will benefit most from irradiation with heavy ions."

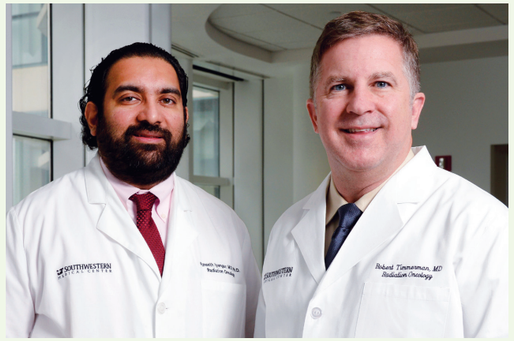
SBRT combined therapy doubles lung cancer survival

Combining stereotactic body radiation therapy (SBRT) with a standard chemotherapy regimen more than doubled survival rates for certain stage IV lung cancer patients, UT Southwestern cancer researchers report.

The combination of erlotinib with SBRT improved overall survival time to 20 months compared to historic 6- to 9-month survival times among erlotinib-only treated patients. The combination improved progression-free survival from the historical two to four months to 14.7 months for similarly selected lung cancer patients.

Results were reported recently in the *Journal of Clinical Oncology*.

"Our approach dramatically changed the pattern of relapse. We saw a shift in failure from existing, local sites to new, distant sites," said senior author Dr. Robert Timmerman, Vice Chair and Medical Director of Radiation Oncology. "This shift resulted in a surprisingly long remission from the reappearance of cancer in treated patients."



Dr. Puneeth Iyengar and Dr. Robert Timmerman

The phase II clinical trial involved 24 patients with stage IV non-small cell lung cancer whose cancer had continued to spread during their initial therapy. Such patients typically have poor survival rates, and SBRT is not typically used in these patients, said first author Dr. Puneeth Iyengar, Assistant Professor and Director of Clinical Research of Radiation Oncology.

The revolutionary SBRT technique is a type of radiation therapy in which a few very high doses of radiation are delivered from multiple angles to small, well-defined tumors. The goal is to deliver a radiation dose high enough to kill the cancer while minimizing exposure to surrounding healthy tissue and organs.

SBRT has been shown to offer better cure rates in certain instances, particularly for cancers that have metastasized, said Dr. Timmerman, who was one of the first researchers in the world to use SBRT techniques initially developed for brain tumors to treat cancer in the body.

According to the National Cancer Institute, lung cancer was diagnosed in an estimated 224,210 men and women during 2014. Five-year relative survival rates remain low at just 16.8 percent. Of these cancer cases, about 85 percent fall into the category of non-small cell lung cancer.

Other UT Southwestern researchers in the study included Dr. Hak Choy, Chair of Radiation Oncology; Dr. Chul Ahn, Professor of Clinical Sciences; Dr. David Gerber, Associate Professor of Internal Medicine; Dr. Jonathan Dowell, Associate Professor of Internal Medicine; Dr. Randall Hughes, Associate Professor of Internal Medicine; Dr. Ramzi Abdulrahman, Associate Professor of Radiation Oncology; postdoctoral researcher Dr. Zabi Wardak; and researchers from the University of Colorado School of Medicine.

CPRIT awards $2.6m to UTSW Radiation Oncology

The Cancer Prevention and Research Institute of Texas (CPRIT) will fund three different projects totaling $2.6 million led by faculty members in the Department of Radiation Oncology.

The funded projects include:

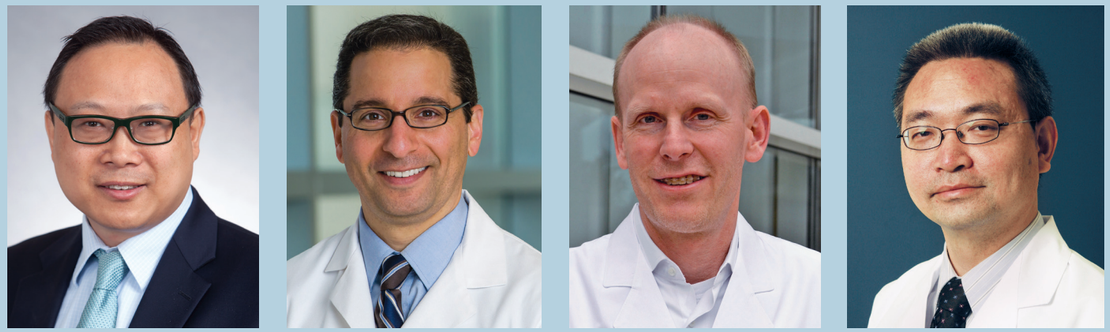
- Translating online adaptive radiotherapy from lab to clinical practice (principal investigators Steve Jiang, Ph.D., and David Schwartz, M.D.)
- Peripheral nerve tolerance to single-session stereotactic irradiation (principal investigator Paul Medin, Ph.D.)
- A phase I trial of stereotactic HYpofractionateD RadioAblative (HYDRA) treatment of advanced laryngeal cancer (principal investigators David Schwartz, M.D., and Weihua Mao, Ph.D.)

The first project is the result of an orders-of-magnitude increase in treatment planning speed, made possible by the recent implementation of graphics processing unit (GPU)-based computing. Researchers in the department are poised to offer real-time treatment planning to adapt to changes in the tumor target while the patient is on the table. Yet some preclinical studies are still needed to understand the feasibility, safety, and optimal workflow involved in making such real-time adaptive treatments available.

The second project represents an attempt to further understand the biological impact of stereotactic radiation, a newer approach to traditional therapy whose effects are still being uncovered. Dr. Paul Medin, who has previously assembled a body of work on SBRT dose tolerance in the spine, now proposes in his project to determine the maximum dose recommended for peripheral nerves (neural structures in close proximity to tumors), so that clinicians in the future can prescribe the maximum effective dose while avoiding nerve injury to patients.

Finally, Drs. Schwartz and Mao will lead a dose-escalation trial of SBRT given in five treatments for advanced laryngeal disease at UT Southwestern and at MD Anderson Cancer Center. This trial builds on UT Southwestern's most recent experience treating laryngeal cancer with CyberKnife and will mirror anatomic principles used for voice-preserving surgery. Important goals of this clinical trial will include: 1) the first demonstration of safe SBRT delivery for advanced larynx cancer; 2) reduced toxicity; 3) improved disease control with large-dose treatments to the primary tumor; and 4) abbreviation of treatment by several weeks, benefiting rural patients without convenient access to specialty care.

"These are all significant projects that have the potential to greatly improve the quality of cancer care for patients in the near future," said Department Chair Hak Choy, M.D. "I congratulate our investigators on their efforts."



Left to right: CPRIT awardees Drs. Steve Jiang, David Schwartz, Paul Medin, and Weihua Mao

NIH award to Wang

Converting static images into a dynamic video that can replicate a patient's breathing motion is a challenge. But medical physicist Dr. Jing Wang has a solution: SMEIR or "simultaneous motion estimation and image reconstruction," a continuously self-improving system that enables a standard cone-beam CT to predict tumor movement with submillimeter accuracy.

Dr. Jing Wang

Dr. Wang recently received a $1.5m, 4-year NIH grant to validate this concept in a project titled "Next generation 4D-CBCT for lung cancer radiation therapy."

Dr. Wang's model uses the motion between two images to refine the initial image, which is then projected forward to help refine the next image, creating a self-improving cycle.

This new approach could lower scan times while improving both image clarity and tracking accuracy. So far, SMEIR has been evaluated retrospectively in just a handful of lung patients. With further testing it could be used on a daily basis for patients receiving stereotactic treatments to improve safety and accuracy.

First GPU training course draws strong attendance

Last fall, the department held its first training in the specialized programming of graphics processing unit (GPU) processors for medical physics and medical imaging research. Seventeen participants took part in the hands-on course.

Led by course director Steve Jiang and co-directors Xun Jia and Yulong Yan, the workshop was taught by team members in the department's medical physics division who have gained a global reputation for the application of GPUs to radiotherapy.

The new field of medical GPU computing represents an unprecedented increase in data processing speed for solving scientific problems. Computations that took hours or even days using conventional CPUs take just a few seconds using GPUs.

Participants learned CUDA and OpenCL programming and additionally received some GPU codes developed at UTSW.

The next training dates for GPU programming, as well as other department professional education offerings, can be found on the Radiation Oncology department website at utsouthwestern.edu/radiationoncology.

Education and Research Seminar Series

Lectures sponsored by the Department of Radiation Oncology are free and open to interested professionals, including physicians, physicists, radiation therapists, biologists, and students. For more information, please contact RadOncLectures@utsouthwestern.edu.

† Radiation Oncology Residency Program Visiting Professor Lecture

‡ Molecular Radiation Biology Visiting Lecture

April

‡ Speaker: Peter McKinnon, Ph.D.
From: St. Jude Children's Research Hospital
Date: Wednesday, April 15
Time/Place: Noon–1 p.m./NC8.212
Subject: Maintaining Genome Stability in the Nervous System

† Speaker: Albert Koong, M.D., Ph.D.
From: Stanford University
Date: Friday, April 24
Time/Place: Noon–1 p.m./NF3.106
Subject: Gastrointestinal Oncology

May

† Speaker: John Breneman, M.D.
From: University of Cincinnati
Date: Friday, May 8
Time/Place: Noon–1 p.m./NF3.106
Subject: Pediatric Malignancies

Continuing Medical Education

Beginning with this issue, the Department of Radiation Oncology will offer free Continuing Medical Education credit to readers who read the designated CME article and successfully complete a follow-up test online. You can complete the steps necessary to receive your AMA PRA Category 1 Credit(s)™ by visiting **https://cme.utsouthwestern.edu/content/em1509a**.

Radiation therapy with heavy ions: physical, biological, and clinical rationale

After completing this activity, the participant should be better able to:

- Differentiate the physical and biological characteristics of ion beam therapy from those of standard electron or photon therapy
- Identify tumor types well suited to ion beam therapy
- Discuss the current state of clinical experience with ion therapy

Introduction

Tissue irradiation for cancer therapy historically has followed two main goals: 1) to increase conformity of deposited energy to the tumor target, with the aim of putting a more therapeutic dose to the target while maintaining the same healthy tissue absorption; and 2) to increase the biological effects of deposited energy in the target, with the aim of causing more biological damage with the same amount of deposited physical energy. (This increase in biological effect should happen in the target but not in the healthy tissue.) Keeping in mind these two goals, clinicians and scientists have evaluated various forms of ionizing radiation technology over the years.

At first, only superficial tumors were treated because only low-energy X-rays were available, prohibiting irradiation of deeply seated tumors. As technology advanced, it became possible to treat deeply seated tumors with high-energy X-rays (called photons). Further technological improvements in X-ray collimation and the introduction of accelerated protons[1, 2] allowed even higher dose conformity to the target, though the biological effects of the absorbed dose remained more or less unchanged. The introduction of accelerated heavy ions (ions heavier than protons) to cancer care[3, 4] has revolutionized the field of radiation oncology because their usage allows for meeting both of the goals stated above. In the following four sections we will describe the physical, biological, and clinical rationale for heavy ion cancer therapy as well as the technology needed for its clinical implementation.

Physical advantages of heavy ion cancer therapy

The energy deposited to tissue via ionizing radiation either directly hits the DNA molecule of the cell and alters its bonds or splits surrounding water molecules and creates highly reactive free radicals that, if located in the vicinity of DNA, attack its bonds and alter it. Depending on the severity of the DNA damage, the cell is either capable of DNA repair or will die. The DNA damage caused by ionizing radiation is correlated with the amount of absorbed energy per unit mass of tissue, called the absorbed dose. The higher the absorbed dose, the more severe the DNA damage is.

A dose can be deposited via so-called conventional radiation (photons), relatively light, charged particles (protons), or charged particles heavier than a proton (for example, the nuclei of carbon atoms). Figure 1 shows how the absorbed dose behaves as a function of depth in a homogeneous water phantom (mimicking a patient's body) with low-energy X-rays, high-energy photons, and carbon ions. The low-energy X-rays exhibit an exponential decrease of their absorbed dose, making them unfit to be used for deeply seated tumors. The high-energy photons, like the 18MV photon beam in Figure 1, are more suitable for such deeply located tumors, but a substantial dose is still absorbed upstream and downstream of a thin tumor target (located at, say, 12.75cm depth).

In contrast, the depth profiles of charged particles exhibit a significant increase in dose at the end of their range, the so-called Bragg peak. Its position can be tuned to tumor depth by carefully selecting the incoming heavy ion's kinetic energy. The imparted energy per tissue density and unit track length (called the linear energy transfer, or LET) is proportional to the square of the projectile electric charge and inversely proportional to the square of its speed. For example, a therapeutic carbon nucleus (12C6+) with a range of 12.75cm in water initially carries a kinetic energy of about 3000 mega electron volts and loses about 0.01 mega electron volts per micrometer when it enters tissue. At the Bragg peak this loss is 10 times larger. Despite the Bragg peak giving an illusion of being very sharp, not all heavy ion particles stop at the same depth, leading to some range uncertainty as shown in the Figure 1 small panel. The heavier the ion is, the less pronounced this effect is, making the carbon ion peak sharper than, for example, a proton peak[5,6] and making carbon ion beam range prediction much more accurate than that of the proton beam. This range uncertainty is of clinical relevance but can be mitigated by not trying to stop the ion beam right in front of a sensitive organ.

Heavy ions have a huge advantage in comparison to photons and protons in terms of how rapidly the dose falls off at beam edges (called the penumbra, the lateral distance where the dose falls from 80% to 20% of its peak value). At tumor depths beyond 7cm this penumbra is larger than 10mm for photons and even larger for protons, while the carbon ion beam fall-off is below a couple of mm even for the largest therapeutic depths.[7] This allows placing the lateral edge of the heavy ion beam rather close to critical organs to utilize the very sharp dose fall-off.

Note that along its trajectory, the heavy ion projectile (due to nuclear interactions) fragments into lighter nuclei.[8,9] These fragments are often unstable and radioactive and continue to travel slightly beyond the Bragg peak, creating the small absorbed dose tail on the curve in Figure 1. But this also gives rise to another big advantage of heavy ions in that they can be imaged with positron emission (PET-CT) scanners, enabling in vivo dose monitoring.[10,11]

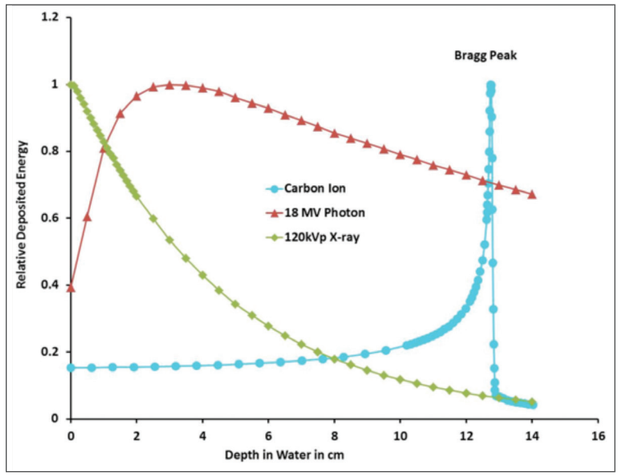


Figure 1

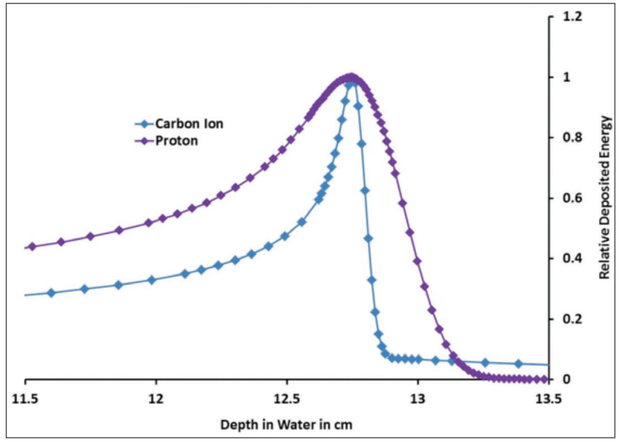


Figure 2

Figure 1 shows the relative dose deposited in a water phantom as a function of depth for: X-rays generated by electrons accelerated in a 120 thousand-volt electric field; high-energy photons generated by electrons accelerated in an electric field of 18 million volts; and fully stripped nuclei of carbon atoms accelerated by 42 million volts. The curve peaks represent the maximum deposited dose. Note that for high-energy photons to deposit the same dose to the region where the Bragg peak occurs with carbon ions, healthy tissue at 3.5cm depth must receive 40% more dose. Figure 2 compares the Bragg peak width of carbon ions and protons at a depth of 12.75cm. Carbon and proton data courtesy of Uli Weber.

Radiobiological advantages of heavy ion beams

The difference between how photons and heavy ions ionize tissue affects their biological effectiveness. The relative biological effectiveness (RBE) of a heavy ion is defined as the ratio of the dose needed to be delivered by photons to the dose delivered by heavy ions in order to achieve the same biological endpoint. The RBE depends on several parameters, such as: i) tissue type; ii) biological endpoint; iii) amount of absorbed dose; iv) heavy ion type; v) linear energy transfer (LET); and vi) oxygen content of the tissue. Consequently, RBE is different at every point of the irradiated tissue. This is taken into consideration during treatment planning.

The shape of the logarithm of cell survivor fractions (SF) resembles an inverted parabola for photon irradiation but is very linear for heavy ions. As a consequence, the RBE is the largest for small doses and decreases as the dose increases.

Conventional radiotherapy of oxygen-deficient (hypoxic) tumors is a big challenge because they tend to be radioresistant, often needing three times more dose to achieve the same tumor kill as in norm-oxic tumors. Heavy ion irradiation shows promising results,

namely that this ratio is substantially decreased and approaches the value of one. Furthermore, the RBE for hypoxic cells is greater than those of norm-oxic ones, showing the big potential role for heavy ion irradiation.[12-14]

In vitro radiobiological experiments have shown that the RBE exhibits maxima at different LET values depending on the heavy ion type (even if the depth, tissue type, biological endpoint, and tissue oxygenation are the same). For example, the RBE max occurs at around 25keV/micron for protons but at 10 times higher LET for neon ions and at around 200keV/micron for carbon ions.[14-17] This is a consequence of differences between lighter and heavier ions in their track structure (or spatial distribution of dose across a trajectory). This fact explains the huge biological advantage carbon ions exhibit with respect to photons and protons, namely that their RBE is relatively low and close to that of photons or protons in the entrance region of the body (where healthy tissue is located) but their RBE is high at the Bragg peak placed at the tumor. Even though the value of LET at which the maximum RBE occurs for a given heavy ion type is almost independent of what biological endpoint is considered (cell inactivation, DNA damage, etc.), the magnitude of this maximum RBE strongly depends on the tissue's biological properties. Cells with poor repair capacities show little or no RBE increase for heavy ions with respect to protons, but cells with strong repair capabilities (e.g., radioresistant tumors) exhibit large RBE maxima and therefore are clinically well suited for heavy ion irradiation.[18,19]

Heavy ion therapeutic beam technology

The production of therapeutic photon radiation is relatively cheap and simple and is done by accelerating light electrons in an electric field of 18 million volts and colliding them with a tungsten target. The produced radiation is laterally collimated to conform to the tumor shape, but multiple entry directions are needed in order to spread out the unwanted upstream dose (Figure 1) to a large tissue volume. Such irradiators are relatively small, about twice the size of a human body.

Protons and heavier ions need much greater acceleration (e.g., 860 million volts) to reach therapeutic depth. This is done via circular accelerators of about 20 meters in diameter.

Charged particles have a third unique advantage over photons. Their electric charge can be utilized to control their lateral direction of motion by a magnetic field, which can be used to precisely position the heavy ions within the tumor lesion. This delivery technique is called pencil beam scanning.[20]

Clinical experience with heavy ion radiotherapy

The potential physical and biological advantages of heavy ion therapy relative to conventional X-ray irradiation have long been of interest to radiation oncologists. Charged particle therapy for cancer treatment began in the mid-1950s in Berkeley, California, at a facility initially designed for basic particle physics research, subsequently known as the Lawrence Berkeley National Laboratory (LBNL).[21] Clinical studies of various types of charged particle irradiation, including proton, helium ion, neon ion, and carbon ion therapy, continued at the LBNL through 1992.[21] This pioneering research laid the framework for subsequent clinical investigations into the utility of heavy ion radiotherapy.

In 1994, investigators at the HIMAC facility located at the National Institute for Radiological Sciences (NIRS) in Chiba, Japan, began treating patients with carbon ion radiotherapy, and in 1997 the Gesellschaft fur Schwerionenforschung (GSI) facility in Darmstadt, Germany, also began a carbon ion cancer treatment program. The latter program was subsequently discontinued, and the Heidelberg Ion-Beam Therapy (HIT) Center began operations in 2009.[21] Multiple other carbon ion treatment programs have initiated patient treatments at various facilities in Japan and Europe over the past 15 years (see Table 1). Although there are numerous proton treatment centers in the United States, since the closing of the heavy ion cancer treatment program at the LBNL there have been no active treatment facilities delivering this therapy in the U.S.

Most carbon ion radiotherapy treatments to date have been delivered through a limited number of fixed-beam portals. Rotating gantries, well established in isocentric X-ray irradiation, are a recent addition to carbon ion radiotherapy treatment facilities, as is the use of pencil beam scanning (as opposed to passive scattering) beam treatments. These advances are expected to facilitate and improve on delivery of carbon ion therapy in its current form.

A systematic approach to dose-escalation studies with carbon ion radiotherapy was instituted at NIRS at the program's inception, and, to date, well more than 7,000 patients have been treated with carbon ion irradiation at this center. Phase I and II protocols at NIRS primarily evaluated hypofractionated treatment regimens. Multiple tumor types have been studied, including (given the unique physical and biological aspects of carbon ion irradiation) salivary gland and skull base tumors previously deemed appropriate for clinical study with neutron and proton radiotherapy.[22] More common malignancies such as lung, breast, and prostate cancer have also been studied.

Early-phase studies established tolerable and effective dose-fractionation regimens (with or without concurrent chemotherapy) for various tumor sites. In general, these studies have shown carbon ion radiotherapy to be a safe and efficacious treatment for a broad spectrum of tumors, including those commonly considered to be radioresistant. How these results compare to the best results seen with contemporary X-ray-based irradiation or chemo-irradiation is a subject of much debate.

So far there are no phase III randomized clinical trials comparing carbon ion radiotherapy with X-ray or proton radiotherapy. Such lack of randomized comparisons between unconventional and conventional radiation methods has been a major source of contention over the expansion of proton facilities in the United States (where the controversy stems from lack of proton versus X-ray studies).[23] However, there is growing interest in conducting such studies. Promising results from such trials may help facilitate the growth of carbon ion radiotherapy facilities in the U.S.

A review of treatment results from the NIRS for patients with locally advanced pancreatic cancer (LAPC) illustrates the potential clinical benefits of carbon ion radiotherapy. LAPC is associated with a very poor prognosis, with inadequate local control outcomes with conventional treatments (chemotherapy and/or radiotherapy with X-ray irradiation), and frequent development of metastatic cancer. Median survival for patients treated with current standard therapies is around one year, and two-year survival is only about 10-20%. Investigators at NIRS conducted a phase I/II trial for selected patients with LAPC.[24] The number of radiation fractions was set at 12, and patients were also treated with concurrent gemcitabine. The dose-per-fraction was escalated and a total dose of 55.2 GyE was safely reached, as was a concurrent gemcitabine dose of 1000 mg/m2. For patients treated in the dose range of 45.6 to 55.2 GyE, the 2-year overall survival was 54%.

These and other promising results with carbon ion radiotherapy may represent the clinical realization of the putative benefits of heavy ion treatment. Further clinical research is necessary to determine the true role of carbon ion treatments in modern clinical oncology. Results from randomized comparisons with X-ray therapy, at least in some tumor sites, are expected to help further define this role.

Arnold Pompos, Ph.D., is a medical physicist and Assistant Professor of Radiation Oncology; Jeffrey Meyer, M.D., is a radiation oncologist and Assistant Professor of Radiation Oncology.

**References viewable in the online version of the article at https://cme.utsouthwestern.edu/content/em1509a.*

Center and Location	Year Operations Began	Type of Ion Used
Heavy Ion Medical Accelerator in Chiba (HIMAC) *Chiba, Japan*	1994	Carbon
Hyogo Ion Beam Medical Center *Hyogo, Japan*	2002	Carbon, Proton
IMP-CAS *Lanzhou, China*	2006	Carbon
Heidelberg Ion Beam Therapy Center *Heidelberg, Germany*	2009	Carbon, Proton
Gunma University Heavy Ion Medical Center *Gunma, Japan*	2010	Carbon
Centro Nazionale di Adroterapia Oncologica (CNAO) *Pavia, Italy*	2011	Carbon, Proton
Saga Heavy Ion Medical Accelerator *Saga, Japan*	2013	Carbon
SPHIC *Shanghai, China*	2014	Carbon, Proton

Table 1. Current heavy ion treatment facilities

First intraoperative treatment at UTSW

Doctors performed UT Southwestern's first intraoperative radiation treatment recently on a 69-year-old male patient with a cord-compressing lesion on his upper (T-12) spine.

Dr. Michael Folkert

The procedure was performed by Assistant Professor of Radiation Oncology and brachytherapy specialist Michael Folkert, M.D., Ph.D., and Associate Professor of Neurological Surgery Kevin Morrill, M.D.

This delicate operation involved the removal of tumor-damaged vertebrae and the placement of a cage to serve as a reconstructed spine. There was a moment when the patient was connected by only his exposed spinal cord, with no protective vertebrae.

While the cord was exposed, Dr. Folkert placed a flexible phosphorus-32 applicator directly on the dura, the sheathlike membrane that covers the spinal cord, at the location of the lesion. The patient received 10 Gy of radiation over the course of 11 minutes to a depth of 1mm.

"This was a radical surgery in an attempt to get rid of every last bit of disease," Dr. Folkert said.

Physicians are normally limited in their ability to surgically remove cancer from the dura because of the dura's critical role in protecting the spinal cord. "You don't want to cut it, so microscopic disease may be left behind," says Dr. Folkert. "Brachytherapy offers a solution."

The patient was scheduled afterward to receive SBRT treatment. In a paper published in the journal *Brachytherapy*, Dr. Folkert demonstrated 90 percent control in certain spinal patients treated with p-32 and SBRT.

Very few facilities can provide intraoperative brachytherapy, which is generally available at only larger academic cancer centers in the U.S. "It requires careful multidisciplinary coordination between the surgical, radiation oncology, and medical physics services – something at which UT Southwestern excels," Dr. Folkert said.

Support group for oral, head and neck cancer comes to campus

UT Southwestern is now sponsoring a monthly support group for patients and survivors of oral and head and neck cancers, in partnership with the national nonprofit Support for People with Oral and Head and Neck Cancer (SPOHNC).

Assistant Professor of Radiation Oncology Dr. David Schwartz was instrumental in starting the SPOHNC chapter at UT Southwestern's Dallas campus, having served on the group's national medical advisory board. Other UT Southwestern supporters include Associate Professor Dr. Baran Sumer, social worker and co-facilitator Sharon Tavenner, and Simmons Cancer Center nurse navigator Tam Burks.

The group is self-run by volunteer survivors in the community.

"SPOHNC can have an enormously positive impact through meeting the psychosocial needs of patients as well as preserving, restoring, and promoting physical and emotional health," Mrs. Tavenner says.

Attendees of the first SPOHNC meeting

Support group meetings are held on the first Saturday of every month, from 10 a.m. to noon, in the Radiation Oncology facility at 2001 Inwood Rd.

For more information, please contact Sharon Tavenner at 214-645-8537.

Clinical Trials

BRAIN

042011-075 Interstitial radioactive iodine implants for the treatment of pan-invasive pituitary macroadenomas

042011-050 Phase II trial of hippocampal-avoiding whole brain irradiation with simultaneous integrated boost for treatment of brain metastases

BREAST

New– 092012-058 Randomized, double-blind, vehicle-controlled pilot study of the efficacy and safety of HylaCare in the treatment of acute skin changes in patients undergoing external beam radiotherapy for tumors of the breast

102012-020 A phase II trial of ixabepilone and stereotactic body radiation therapy (SBRT) for patients with metastatic breast cancer

072010-015 A phase I study of CyberKnife® partial breast irradiation (PBI) for early-stage breast cancer

GASTROINTESTINAL

032012-025 Phosphatidylserine-targeting antibody bavituximab in combination with capecitabine and radiation therapy for the treatment of stage II and III rectal adenocarcinoma

GENITOURINARY

New– 092013-013 Phase II study of stereotactic ablative radiotherapy (SABR) for low-risk prostate cancer with injectable rectal spacer

New– RTOG 924 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

122013-030 A phase II trial of stereotactic ablative body radiation therapy (SABR) for patients with primary renal cancer (RCC)

12013-041 A phase II trial of high-dose IL-2 and stereotactic ablative body radiation (SABR) for patients with metastatic clear-cell renal cell cancer (mRCC)

102012-026 Phase II trial of sipuleucel-T and stereotactic ablative body radiation (SABR) for patients with metastatic castrate-resistant prostate cancer (mCRPC)

RTOG 0815 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

RTOG 0534 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

GYNECOLOGIC

082013-064 A phase II study for image-guided hypofractionated radiation boost therapy for definitive treatment of locally advanced cervical cancer

RTOG 1203 A randomized phase III study of standard vs. IMRT pelvic radiation for postoperative treatment of endometrial and cervical cancer (TIME-C)

HEAD AND NECK

New– 112013-007 A phase I study of reduced-volume hypofractionated, PET-directed intensity modulated radiotherapy concurrent with weekly cisplatin chemotherapy for T1/NO-2 squamous cell carcinoma of the head and neck

New– 072014-041 Randomized phase II and phase III studies of individualized treatment for nasopharyngeal carcinoma based on biomarker Epstein Barr virus (EBV) deoxyribonucleic acid (DNA)

New– RTOG 3501 Tryhard: a phase II, randomized, double-blind, placebo-controlled study of lapatinib (Tykerb) for non-HPV locally advanced head and neck cancer with concurrent radiation

06213-052 A phase 1 CyberKnife accelerated hemilarynx stereotactic radiotherapy study for early-stage glottic larynx cancer

RTOG 1216 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

RTOG 3501 A phase II randomized, double-blind, placebo-controlled study of lapatinib (Tykerb) for non-HPV locally advanced head and neck cancer with concurrent chemoradiation

RTOG 0920 A phase III study of postoperative radiation therapy (IMRT)/- cetuximab for locally advanced resected head and neck cancer

LUNG

Small Cell Lung Cancer

CALGB 30610/RTOG 0538 A phase III comparison of thoracic radiotherapy regimes with cisplatin and etoposide in limited small cell lung cancer

RTOG 0937 Randomized phase II study comparing prophylactic cranial irradiation alone to prophylactic cranial irradiation and consolidative extracranial irradiation for extensive disease small cell lung cancer (ED-SCLC)

Non-Small Cell Lung Cancer

RTOG 839 Randomized phase II study of preoperative chemoradiotherapy +/- panitumumab followed by consolidation chemotherapy in potentially operable locally advanced (stage IIa, N2+) non-small cell lung cancer

92013-070 Maintenance chemotherapy versus consolidative stereotactic body radiation therapy (SBRT) plus maintenance chemotherapy for stage IV non-small cell lung cancer (NSCLC): a randomized phase II trial

RTOG 1306 A randomized phase II study of individualized combined modality therapy for stage III non-small cell lung cancer (NSCLC)

062012-53 A randomized phase I/II study of nab-paclitaxel, or paclitaxel, plus carboplatin with concurrent radiation therapy followed by consolidation in patients with favorable-prognosis inoperable stage IIIA/B NSCLC

052011-093 Phase III randomized study of standard versus accelerated hypofractionated image-guided radiation therapy (IGRT) in patients with stage II-III non-small cell lung cancer and poor performance status

SPINE

072010-134 A phase II study of stereotactic body radiation therapy (SBRT) and vertebroplasty for localized spine metastasis

RTOG 0631 A phase II/III study of image-guided radiosurgery/SBRT for localized spine metastasis

For more information, please contact Clinical Research Manager Jean Wu at 214-633-1753 or jean.wu@utsouthwestern.edu

UT Southwestern
Harold C. Simmons
Cancer Center

The future of cancer care, today.

NCI·CC
A Cancer Center Designated by the National Cancer Institute

PRESORTED
NON PROFIT
US POSTAGE
PAID
TWMS

Department of Radiation Oncology
5801 Forest Park Rd.
Dallas, TX 75390-9183

Department of Radiation Oncology at UT Southwestern

Physicians who would like to make a referral may call the department's main clinic number at 214-645-8525 or UT Southwestern's physician referral line at 214-645-8300 (toll-free 866-645-5455) for adult patients, or 877-445-1234 for pediatric patients.

W.A. Monty and Tex Moncrief Radiation Oncology Building

5801 Forest Park Rd.
Dallas, TX 75390-9183

Annette Simmons Stereotactic Treatment Center at UT Southwestern Zale Lipshy University Hospital

5151 Harry Hines Blvd.
Dallas, TX 75390-9183

Harold C. Simmons Comprehensive Cancer Center–Radiation Oncology

2001 Inwood Rd.
Dallas, TX 75390-9183

Visit us on the Web

Patient care: **utswmedicine.org/radonc**
Education & research: **utsouthwestern.edu**

facebook.com/UTSWRadiationOncology