UT Southwestern

THE TARGET

News from the Department of Radiation Oncology

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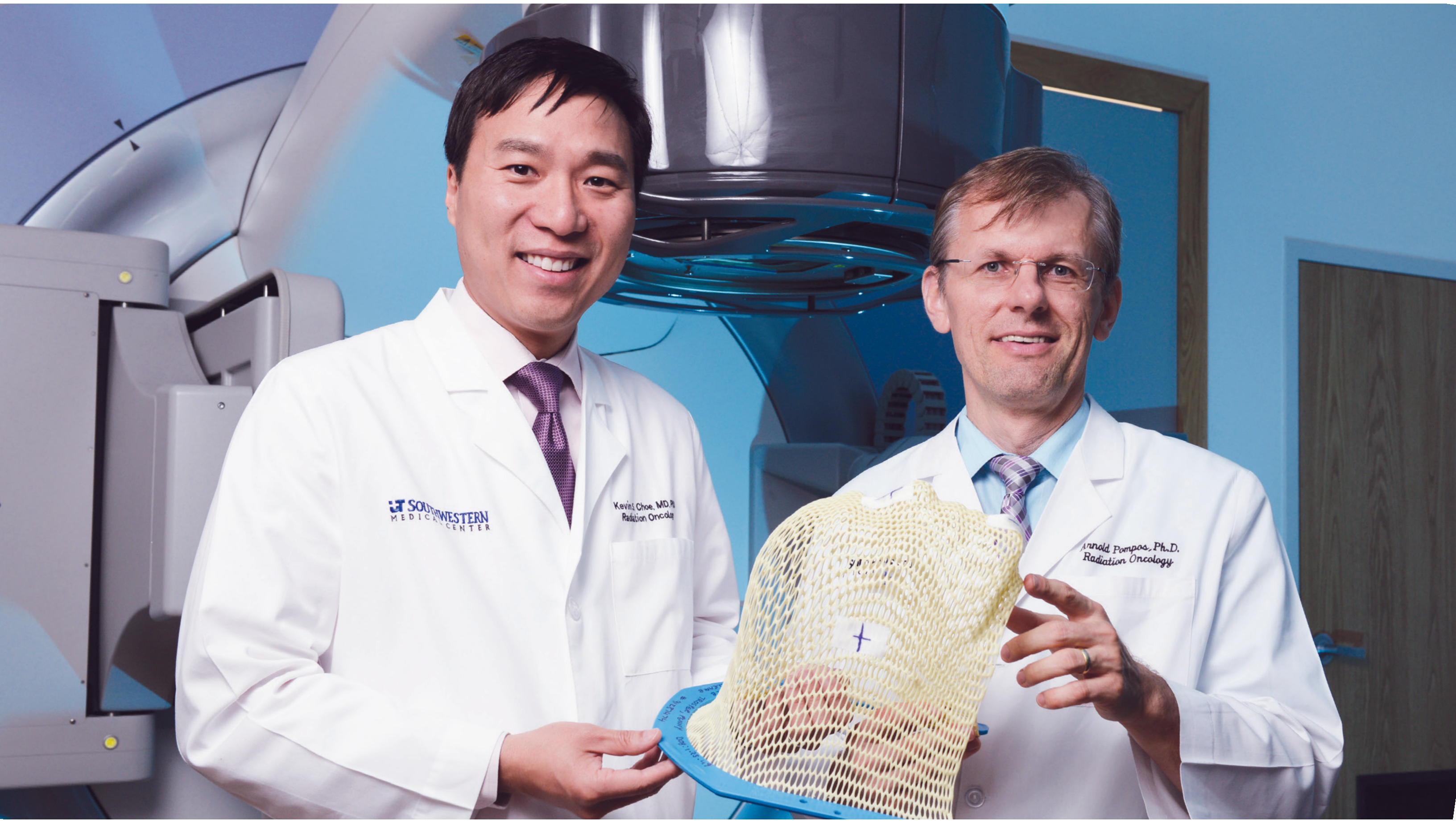
Revving up the treatment process with onsite simulation, planning, and treatment (OSPT)



Kevin Choe, M.D., (left) and Arnold Pompos, Ph.D., implemented the protocol that drastically reduces patient waiting time on the first visit.

What's Inside

Radiation therapy has historically been a multistep process, involving a consultation, a CT simulation scan, and a waiting period while dosimetrists and physicians design a plan, and finally, plan verification and treatment. Patients typically wait about a week to receive their first treatment.

But a new process developed at UT Southwestern Radiation Oncology has recently demonstrated this waiting time can be shrunk to just a few minutes, primarily by automating some processes. And the department has recently launched an ambitious program to begin treating certain patients within about 30 minutes of their first consultation here.

"We want to change the paradigm of how we treat patients," says Assistant Professor and medical physicist Arnold Pompos, Ph.D., who co-led the initiative internally. "In the future, the whole experience will be dramatically different. We will no longer send patients home from their consultation in a state of uncertainty about when their treatment is going to begin."

The new workflow process has been dubbed "onsite simulation, planning, and treatment (OSPT)," meaning that patients remain in place, lying on the treatment table, while physicians and physicists quickly perform real-time treatment planning and delivery.

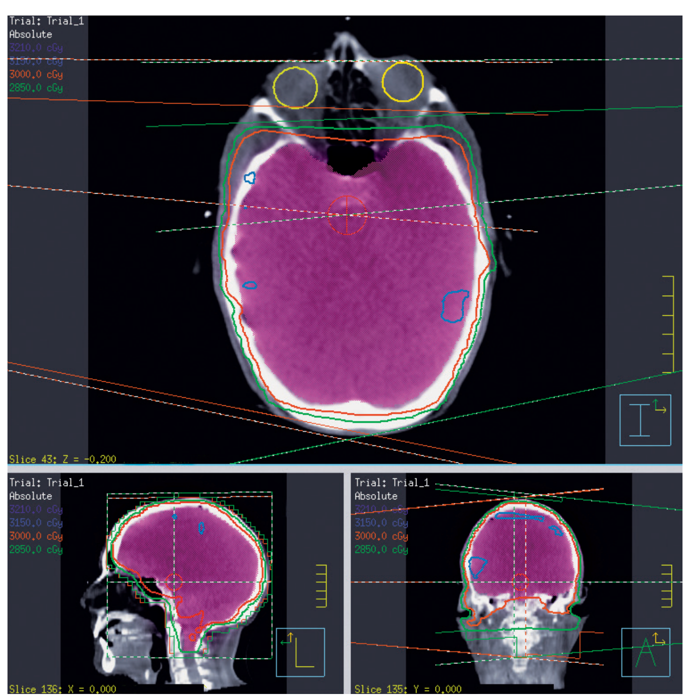
Rather than go to a separate CT room for imaging, the patient is set up on a treatment machine with onboard cone beam CT imaging capability. Images are automatically exported to a program that auto-contours the outlines of the area to be treated, which takes about one minute. Another auto-planning program then creates an optimal treatment plan for the delivery of radiation—about five minutes. Doctors and physicists improve, modify, and verify the plan rather than develop one from scratch.

OSPT was implemented for the first time this summer with a handful of patients needing whole-brain radiation for the treatment of brain metastases. Whole-brain radiation was selected as the pilot site for OSPT because of the relative simplicity of planning.

All treatments so far have taken place on the department's Elekta Agility linear accelerator. Anh Le, Ph.D., a recent addition to the department's faculty, created a software option that modified the Agility's traditional cone beam CT acquisition to acquire primary imaging for planning purposes.

"When we brought up this new paradigm, it turned out the system had the potential to fulfill this need in the hands of an expert—such as Dr. Le—who knows what to do," says Dr. Pompos. "Currently, we are trying to set up similar tools on other machines and talking to vendors about how to make this a seamless, fully automated process from cone beam acquisition to the moment of radiation delivery."

Auto-planning is accomplished using vendor-supplied software, although current tools are somewhat limited. There are future plans to incorporate the department's own GPU-based planning research into the process, based on the pioneering work of Medical Physics and Engineering Division Chief Steve Jiang, Ph.D., who has led the industry's emerging use of GPU processors for radiation planning calculations. Vendors are also striving to provide improved auto-planning software.



Whole brain plan for actual patient using OSPT protocol. Planning target volume is in pink.

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>
> *— Assistant Professor and medical physicist Arnold Pompos, Ph.D.*

The OSPT process currently takes an average of 37 minutes from the time the patient enters the treatment room until he or she exits. The unique context of OSPT requires all members of the team—attending physicians, physicists, therapists, and dosimetrists—to work closely and at the same time to quickly modify, approve, and implement the plan.

"It's a collective approach that requires everyone to work together like gears in a well-oiled machine," Dr. Pompos says. "The better we understand the details of each step and how the individual pieces fit together in the workflow, the more we're able to reduce the time of each step."

In the future, the department plans to expand OSPT to more disease sites with more complicated plans, such as those for lung cancer and prostate cancer. For now, most whole-brain patients here will continue receiving the expedited treatment.

The OSPT process was initiated by Department Chairman Hak Choy, M.D., and spurred by the planning of a new radiation treatment facility at UT Southwestern. With that facility in mind, faculty members have been challenged to reassess and, in some cases, reinvent old processes based on newer technology.

"We are always striving to give the best treatment to the patient in the most convenient way," says Kevin Choe, M.D., Ph.D., Assistant Professor of Radiation Oncology and a specialist in treating brain cancer. "If we can minimize traveling back and forth for multiple appointments and also minimize wait time using this expedited method, we think it will result in an improved patient experience."

Dr. Pompos agrees. "People who need cancer treatment don't want to leave empty-handed after their first appointment, thinking 'why are they sending me home?'" he says. "For the patient, this is going to alleviate potential anxiety about that gap in treatment time. For radiation oncology professionals, more uniform processes mean less possibility for error."

Education and Research Seminar Series

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

† Radiation Oncology Residency Program Visiting Professor Lecture

* T2R2 Translational Research Series

‡ Cancer Center Grand Rounds

November

‡ Speaker: Ralph Weichselbaum, M.D.
From: University of Chicago
Date: Friday, November 7
Time/Place: 11:30 a.m.–12:30 p.m./NB2.EEF auditorium
Subject: Academic Medicine

† Speaker: Simon Powell, M.D.
From: Memorial Sloan Kettering
Date: Friday, November 14
Time/Place: Noon–1 p.m./NF3.106
Subject: Specialty–Breast

December

* Speaker: Richard Kolesnick, M.D.
From: Memorial Sloan Kettering
Date: Wednesday, December 10
Time/Place: Noon–1 p.m./NC8.212

† Speaker: Charles Thomas, M.D.
From: Oregon Health & Science University
Date: Friday, December 12
Time/Place: Noon–1 p.m./NF3.106
Subject: GI/Thorax

* Speaker: Ge Wang, Ph.D.
From: The Biomedical Imaging Center at Rensselaer Polytechnic Institute
Date: Thursday, December 18
Time/Place: Noon–1 p.m./NC8.212

KRAS gene mutation inhibitor found

Radiation oncologist Kenneth Westover, M.D., Ph.D. recently was awarded a $900,000/3-year grant from the Cancer Prevention and Research Institute of Texas (CPRIT) to study structure-guided kinase inhibitor design for cancer therapy. The award follows closely on the publication of Westover lab findings of a selective inhibitor of the KRAS gene mutation.

The molecule, SML-8-73-1 (SML), interferes with the KRAS gene, or Kirsten rat sarcoma viral oncogene homolog. The gene produces proteins called K-Ras that influence when cells divide. Mutations in K-Ras can result in normal cells dividing uncontrollably and turning cancerous.

Researchers have tried unsuccessfully to develop a drug to inhibit K-Ras for some 30 years. The new finding was recently published online in the journal *Proceedings of the National Academy of Sciences*.

The CPRIT grant is one of 12 Individual Investigator Research Awards made in August by CPRIT to UTSW faculty for innovative research projects. Dr. Westover is also the recent recipient of a V Foundation grant ($200,000/2 years) for rational development of GTPase active site inhibitors.

Blocking DNA repair for glioblastoma

Department researchers led by Sandeep Burma, Ph.D., have demonstrated both in cancer cell lines and in mice that blocking critical DNA repair mechanisms could improve the effectiveness of radiation therapy for glioblastomas.

Radiation therapy causes double-strand breaks in DNA that must be repaired for tumors to keep growing. Scientists have long theorized that if they could find a way to block repairs from being made, they could prevent tumors from growing or at least slow down the growth, thereby extending patients' survival. Blocking DNA repair is a particularly attractive strategy for treating glioblastomas because these tumors are highly resistant to radiation therapy. In a study, UT Southwestern researchers demonstrated that the theory actually works in the context of glioblastomas.

"This work is informative because the findings show that blocking the repair of DNA double-strand breaks could be a viable option for improving radiation therapy of glioblastomas," says Dr. Burma, Associate Professor of Radiation Oncology in the Division of Molecular Radiation Biology at UT Southwestern.

Researchers in the Burma lab found that enzymes called cyclin-dependent kinases (CDKs) involved in cell division activate homologous recombination (HR) by phosphorylating a key protein, EXO1. In this manner, the use of HR is coupled to the cell division cycle, which has important implications for cancer therapeutics. These findings were published April 7 in *Nature Communications*.

Department welcomes new trainees

Radiation Oncology was pleased this summer to welcome our newest residents in radiation oncology and medical physics, all highly qualified trainees who joined our program after an extremely competitive selection process.

Joining our 12-person radiation oncology trainee group are:

- **Dan Ishihara, M.D., Ph.D.**—graduate of Albert Einstein College of Medicine
- **Steven Lau, M.D., Ph.D.**—graduate of University of Cambridge and University of California, San Diego
- **Vasu Tumati, M.D.**—graduate of New York Medical College

Our newest medical physics trainees are:

- **Matthew Webster, Ph.D.**—graduate of University of California, San Diego
- **Luo Ouyang, Ph.D.**—graduate of UT Southwestern Graduate School of Biomedical Sciences

We look forward to working with these outstanding scholars and medical professionals as they advance their training in the field.

Brachytherapy expert joins Radiation Oncology, helps launch intraoperative program

Assistant Professor Michael Folkert, M.D., Ph.D., has been recruited to UT Southwestern Radiation Oncology to spearhead the launch of a comprehensive intraoperative brachytherapy practice within the department.

"Intraoperative radiation therapy will allow us to directly treat tumor beds that are exposed during surgery," says Dr. Folkert. "We can completely circumvent the need to go through healthy tissue to reach the target."

Dr. Folkert originally studied nuclear engineering at the Massachusetts Institute of Technology (MIT) and earned his Ph.D. in radiological sciences through the Harvard-MIT Division of Health and Technology. He began his career in medical physics at the Massachusetts General Hospital, but his close work with radiation oncologists there soon turned his interest to medicine.

He later earned a medical degree at Harvard Medical School and then completed his residency in radiation oncology at Memorial Sloan Kettering Cancer Center, where he pursued a specific interest in brachytherapy research, publishing numerous papers and helping develop devices, protocols, and techniques to deliver brachytherapy treatment to spine, esophageal, and rectal lesions.

At UT Southwestern, Dr. Folkert is initially working with the Department of Ophthalmology to offer brachytherapy eye plaque treatment for patients with intraocular tumors.

With this treatment, rice-sized "seeds" of radioactive iodine-125 are placed into a thin gold shield, which is attached to the back of the patient's eye through a surgical procedure. After about three days, when the full dose (70-85 Gy) is delivered, the eye plaque is removed.

Dr. Yuguang He, M.D., Associate Professor of Ophthalmology, will initially examine patients and refer them to Dr. Folkert to discuss options for radiation treatment. After the radiation team creates a plan for radiation delivery and assembles the plaque, the two physicians will together verify the location of the tumor in the operating room, and Dr. He will perform the surgery to attach the eye plaque device.

Brachytherapy is preferred for the eye over standard external beam treatment in many cases because it can minimize toxicity while preserving the patient's vision.

Intraoperative brachytherapy for many other sites, including head and neck, abdominal, and pelvic tumors will soon become possible when shielding is completed in one of the operating rooms of the new William P. Clements Jr. University Hospital, which opened in November.

"Intraoperative brachytherapy may improve local control, particularly for gastrointestinal tumors and recurrent head and neck tumors," says Dr. Folkert. "With this technique we can hope to curatively treat even patients with locally advanced cancers requiring extensive surgery, and patients who have had their disease return after prior external beam radiation therapy."

Treating ocular melanomas with an eye plaque that holds radioactive seeds—the first step in the department's new program.

Lazy Susan-style table developed for total body irradiation

The rotating IRIS provides uniform dose distribution during total body irradiation.

UT Southwestern radiation oncologists and physicists recently created a rotating, lazy Susan-type device that can turn patients a full 360 degrees while undergoing total body irradiation in either the supine or prone positions.

"Traditional extended source-to-surface total body irradiation (TBI) techniques can be problematic in terms of patient comfort and/or dose uniformity," says Assistant Professor Xuejun Gu, Ph.D., one of the developers of the indexed rotatable immobilization system (IRIS).

"Patients who stand during the procedure can become tired very easily and shift, which necessitates replanning," says Dr. Gu. "When patients stand, it's also not possible to give a dosimetrically accurate dose. It's a very old-school approach to radiation therapy.

> "This work aims to develop a comfortable TBI technique that achieves a uniform dose distribution to the total body while reducing the dose to organs at risk for complications."
>
> —*Assistant Professor Xuejun Gu, Ph.D.*

"This work aims to develop a comfortable TBI technique that achieves a uniform dose distribution to the total body while reducing the dose to organs at risk for complications."

The IRIS includes a base layer, a rotating disc, and a full body frame as the top layer. The universally adaptable base layer anchors to CT and LINAC couch tops of all major vendors using standard indexing bars common to radiotherapy immobilization devices.

The top layer (full body frame) is fully indexed in the coronal plane to enable accurate image-guided patient setup as well as matching of multiple isocenters. The top layer also serves to immobilize the patient to reduce movement out of radiation ports. A rotating disc situated between the base and top layers allows the top layer to rotate around a pivot point.

The entire body CT scan is split into two sections due to the limited scan length of CT scanners. The patient is scanned headfirst from head to upper thigh, and then feetfirst, following 180-degree rotation of the frame. These two CT scans are imported into the Pinnacle system and concatenated using Pinnacle's concatenation tool.

Treatment planning matches multiple isocenter volumetric modulated arc (VMAT) fields of the upper body and multiple isocenter parallel-opposed fields of the lower body.

Radiation Oncology is currently using the new device to treat patients requiring TBI.

Clinical Trials

BRAIN

072012-094 A prospective, multicenter trial of NovoTTF-100A together with temozolomide compared to temozolomide alone in patients with newly diagnosed GBM

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

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

E3F05 A phase III study of radiation therapy with or without temozolomide for symptomatic or progressive low-grade gliomas

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 stage III rectal adenocarcinoma

GENITOURINARY

New–122013-030 A phase I 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 A 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

RTOG 1115 A phase III trial of dose-escalated radiation therapy and standard androgen deprivation therapy (ADT) with a GnRH agonist vs. dose escalated radiation therapy and enhanced ADT with a GnRH agonist and TAK-700 for men with high-risk prostate cancer

GYNECOLOGIC

New–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

06213-052 A phase I 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 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

RTOG 1008 A randomized phase II study of adjuvant concurrent radiation and chemotherapy versus radiation alone in resected high-risk malignant salivary gland tumors

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 A 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

New–RTOG 839 A 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

New–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 A 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 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.

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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.

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