BEAM'S EYE VIEW

NEWSLETTER of the DEPARTMENT OF RADIATION MEDICINE
LOMA LINDA UNIVERSITY
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INTRODUCTION TO THIS ISSUE

Jerry D. Slater, MD, Chair

Every patient treated in our department is served by several people, some of whom the patient never sees. This is certainly true of our medical physics team, led by Dr. Baldev Patyal. Radiation oncology is a technology-driven discipline that must serve patients accurately and reliably. The medical physics team plays an essential role in ensuring this outcome, and so is featured in this issue.

Herein we also report on two recent publications, a recent seminar, and some history. All deal with research, the foundation on which all patient care rests. One of its goals is to explore the potentialities—and also the limitations—of the tools we use to serve our patients.

THE MEDICAL PHYSICS TEAM

"Unseen" and "unsung," two semantically related words, often are used together in reference to people who do important work that nobody knows about. The words fit some members of the Department of Radiation Medicine, at least from the patient's perspective. During their time at Loma Linda, radiation oncology patients meet physicians, nursing and clinic staff, and, most often of all, therapists in the treatment rooms, but they almost never meet the physicists and dosimetrists who make up an integral part of their care.

Medical physics is headed by Baldev R. Patyal, PhD, DABR, FAAPM. He has led the group since 2004. Dr. Patyal received undergraduate and initial graduate training in physics in India, followed by an MS in physics from the University of California, Riverside, and a PhD in physics from Washington State University, Pullman, WA. After a five-year stint at Cornell University, Ithaca, NY, where he worked on magnetic resonance studies of molecular dynamics in complex biological systems, he decided to pursue medical physics. Accordingly, he obtained an MS in radiation oncology physics and subsequent clinical training from the University of Texas Health Science Center, San Antonio. He came to Loma Linda in 1998.

The medical physics team is large and diverse, befitting the multiple tasks its personnel perform. These tasks comprise clinical, educational, administrative, and research components. In their clinical role, physicists interact with radiation oncologists, dosimetrists, and therapists on radiation treatment delivery to patients via external-beam radiation or brachytherapy. Additionally, a medical physicist oversees technological and technical aspects such as commissioning (ensuring that a machine or software will treat a patient safely); calibration (ensuring that a machine delivers radiation as it should; i.e., that one gray (Gy) of dose is the same in Loma Linda as it is anywhere else in the world); and quality assurance (QA; ensuring that a machine or software can be trusted to deliver radiation accurately and safely to every patient, every day).

As Dr. Patyal puts it: "In a nutshell, the job of a radiation oncology physicist is about building trust in the system. Physicians feel assured that the prescriptions they write for their patients will be delivered safely and accurately; patients feel assured that they are being healed by an unseen, unfelt radiation beam and that they are in good hands."

Front row, left to right: Ning Wang, PhD, Physicist 2; Eric Ramirez, MS, Physicist 1; Anh Ly, MS, Lead Physicist, Clinical Operations; Yuwei Zhou, PhD, Medical Physics Resident; Ric Bun, Dosimetrist 2; Felice Hyppolite, Dosimetrist 2. Back row, left to right: Stan Barnes, Dosimetrist 2; David Watt, Dosimetrist 2; Baldev Patyal, PhD, FAAPM, Chief Physicist; Edward Garoian, Dosimetrist 2; Prashanth Nookala, MS, Physicist 2; David Choi, PhD, Lead Physicist, Conventional Therapy; Oscar Mercado, BS, Calibration Physicist; Abiel Ghebremedhin, PhD, Lead Physicist, Proton Therapy. Not shown: Sara Gill and Cinira Johnson, Dosimetrists 2.

In addition to an advanced degree (MS or PhD) in the relevant field, a medical physicist receives specialized training through a residency in medical physics, and is certified by the American Board of Radiology (ABR) to practice independently as a medical physicist in clinical radiation oncology physics.

In addition to physicists, medical dosimetrists are an integral part of the medical physics team. A dosimetrist works at the interface of the clinical requirements of the radiation oncologist (what the patient needs), the physical requirements of the machines (what the treatment machines can do), and the calibration requirements (what are the dosimetric constraints of measured beam data for accurate delivery of radiation). In essence, a dosimetrist occupies a uniquely specialized position in the radiation delivery chain, having the responsibility to translate clinical, physical, and calibration requirements into a treatment plan for each patient, and presenting it to the radiation oncologist. Medical dosimetrists have an advanced degree (BS or MS) in a relevant field, and training in clinical medical dosimetry (treatment planning). In addition, they are certified by the Medical Dosimetry Certification Board (MDCB) to practice as dosimetrists in clinical radiation oncology.

The education component of the medical physics team comprises several aspects. Dr. Patyal founded and directs the department's residency program in Therapeutic Medical Physics; the program is accredited by the Commission on Accreditation of Medical Physics Education Programs (CAMPEP) and thus far has graduated five residents. He also founded an accredited certificate program in medical dosimetry; this program is now administered by the School of Allied Health Professions and has graduated about 30 students. Dr. Patyal is responsible for scheduling lectures in radiation physics for radiation oncology residents and monitoring their progress in the concepts of clinical radiation physics, which plays an important role in their careers as radiation oncologists. In addition, the physics team supports the didactic and clinical aspects of the radiation therapy technology program, also run by the School of Allied Health Professions.

Administrative responsibilities are varied. Team members develop, maintain, and update protocols, procedures, and policies for all physics-related tasks. Further, the team participates in seeking accreditation of the department's clinical practices (via Radiation Oncology Practice Accreditation (ROPA) administered by the American College of Radiology) and obtains dosimetric credentialing of new treatment techniques from the

Imaging and Radiation Oncology Core (IROC, at M.D. Anderson Cancer Center, Houston). The team works closely with LLUH's Office of Radiation Safety to maintain mandatory regulatory compliance of all machines and procedures.

Clinical physics research is driven by the department's current needs and future goals. This work, considered broadly, encompasses clinical projects and development projects. In the former category, physicists support clinicians through dosimetry support, treatment planning, data collection, validation of new treatment techniques, and dosimetric credentialing of clinical protocols. One such example is a clinical outcome study using a new proton treatment technique: Coffman AR, Sufficool DC, Kang JI, Hsueh CT, Swenson S, McGee PQ, Nagaraj G, Patyal B, Reeves ME, Slater JD, Yang GY. Proton stereotactic body radiation therapy for liver metastases–results of 5-year experience for 81 hepatic lesions. *J Gastrointest Oncol*. 2021 Aug;12(4):1753-1760. Development projects may include feasibility studies of new treatment techniques; clinical evaluation and implementation of new patient positioning systems for more accurate, more versatile, and more efficient treatment delivery; more precise organ motion management; and development of special detectors for small-field dosimetry measurements. Some examples of projects completed are: Wang N, Ghebremedhin A, Patyal B. Commissioning of a proton gantry equipped with dual x-ray imagers and a robotic patient positioner, and evaluation of the accuracy of single-beam image registration for this system. *Med Phys*. 2015 Jun;42(6):2979-2991, and Yeo I, Nookala P, Gordon I, Schulte R, Barnes S, Ghebremedhin A, Wang N, Yang G, Ling T, Bush D, Slater J, Patyal B. Passive proton therapy vs. IMRT planning study with focal boost for prostate cancer. *Radiat Oncol*. 2015 Oct 24;10:213.

The medical physics team works (literally) day and night to serve patients. From treatment planning to machine calibration to quality assurance, the team's work underscores the entire treatment process.

RESEARCH REPORTED

Investigators in the Department of Radiation Medicine participate in ongoing research and publish articles in peer-reviewed journals. Much of this work involves collaboration with investigators in other departments at LLUH. This is highlighted by two recent publications and a seminar.

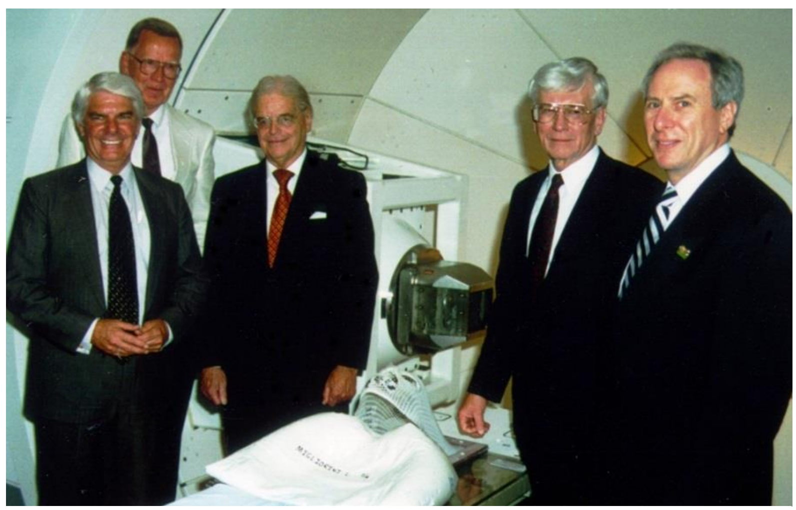
Cancer of the pancreas remains a highly lethal malignancy despite advances in treatment. It is the third leading cause of cancer death in the United States. Treatment is delivered via combined modalities, but toxicity limits most patients' ability to tolerate the full paradigm. "Treatment of locally advanced pancreatic cancer with current standard modalities is unsatisfactory," said the principal investigator, Dr. Gary Yang, in reporting a phase II proton clinical trial published in the August issue of the *Journal of Gastrointestinal Oncology*. Dr. Yang and his colleagues opined that proton beam therapy may result in lower toxicity and enhanced efficacy, and could contribute to improved clinical outcomes for patients with this disease. In the study, patients received gemcitabine plus tyrosine kinase inhibitor prior to concurrent capecitabine with proton therapy, followed by oxaliplatin and capecitabine. Resulting data suggested that using proton therapy as part of a combined-treatment approach was safe and well tolerated, thus warranting further investigation: Sanghvi SM, Coffman AR, Hsueh CT, Kang J, Park A, Solomon NL, Garberoglio CA, Reeves ME, Slater JD, Yang GY. A phase II trial of gemcitabine and erlotinib followed by ChemoProton therapy plus capecitabine and oxaliplatin for locally advanced pancreatic cancer. *J Gastrointest Oncol* 2022:13(4),1989-1996. This investigator-initiated trial was supported by the James M. Slater, MD, Proton Treatment and Research Center, and involved collaborators in the departments of Medical Oncology and Surgical Oncology. The preliminary finding was presented at the ASTRO 2020 annual meeting.

Another article, published in the September issue of *Frontiers in Oncology*, is a collaborative work with colleagues in the Department of Basic Sciences and the Center for Genomics: Katerji M, Bertucci A, Filippov V, Vazquez M, Chen X, Duerksen-Hughes PJ. Proton-induced DNA damage promotes integration of foreign plasmid DNA into human genome. *Front Oncol* 12:928545. doi: 10.3389/fonc.2022.928545. Insights gained from this study enable investigators to better understand the contribution of proton exposure and DNA damage to HPV integration and the risk of subsequent carcinogenesis, thus directing researchers toward strategies aimed at preventing malignancies in HPV-infected patients.

In a research seminar occurring on September 7, Dr. Juli Unternaehrer of the Department of Basic Sciences presented that department's Research In Progress seminar entitled: "Cancer cell aggressiveness caused by conventional vs. proton irradiation." Dr. Unternaehrer presented the latest results supported by a GCAT grant co-led by Dr. Marcelo Vazquez from the Department of Radiation Medicine. The objective of this grant is to understand molecular mechanisms by which photon and proton irradiations result in invasiveness and stemness in cancer cells, and to develop strategies to improve outcomes in radiotherapy approaches for ovarian cancer (OC) and glioblastoma (GBM) by inhibiting epithelial mesenquimal transition (EMT). The specific aims of this project are: 1) determine whether protons and photons differ in their potential to modulate cancer cell stemness, proliferation, and invasiveness; 2) determine mechanisms by which radiation increases invasiveness and stemness; and 3) develop strategies to optimize the effects of ionizing radiation on tumor cells. Assessing preliminary results using cell reporters to detect stemness, the research team concluded that proton and photon irradiation cause similar increases in stemness in OC cells and in GBM cells; differences between proton and photon irradiation are small. Using cell reporters for EMT showed that proton and photon irradiation cause similar increases in OC cells, while photon irradiation causes greater increases in mesenchymal state in GBM cells.

DID YOU KNOW? ….

It is well known that Loma Linda University pioneered the hospital-based delivery of proton radiation therapy in 1990. It may not be so well known that proton beams were first used to treat patients in 1954, in a physics research laboratory at the University of California (Berkeley), and that the first published literature on the therapeutic use of protons was offered about a decade earlier. The author, Robert R. Wilson, PhD, was a physicist. Wilson had received his PhD from Berkeley and knew of the work of John H. Lawrence, MD, on neutron beam treatments, and so was aware of employing particle beams for medical purposes. He realized that proton beams offered potential properties for treatment that neutron beams lacked, notably that they gave the physician the ability to control dose deposition. It was controllability that appealed to Dr. James M. Slater when he was considering ways to improve radiation treatment and reduce side effects for patients treated at Loma Linda. Dr. Slater often said, "The radiation oncologist's whole task is to place ionizing radiation where it is needed and avoid placing it where it isn't needed." Proton beams, as Wilson demonstrated, could help the physician to accomplish that. In 1995, the Department of Radiation Medicine acknowledged Dr. Wilson's seminal insight by naming Gantry Room 1 in his honor.



Naming of Gantry Room 1 in Dr. Wilson's honor, 1995. Left to right: Congressman Jerry Lewis, R-Redlands; Philip V. Livdahl, former deputy director of Fermi National Accelerator Laboratory; Dr. Robert R. Wilson; Dr. James M. Slater; Daniel S. Goldin, Administrator, National Aeronautics and Space Administration.