Radiation Therapy in the Modern World

Deborah Citrin, M.D., Senior Investigator in CCR's Radiation Oncology Branch, came to the NIH in 2001 as a radiation oncology resident after completing her medical training at Duke University. She continued her training through the CCR Clinical Investigator Development Program, which is specifically designed to aid in the transition between a mentored position and that of an independent investigator. In 2007, Citrin became a Tenure-Track Investigator and was awarded tenure earlier this year. Throughout her years of training and service, Citrin has been committed to improving the efficacy of, and reducing the complications that arise from, one of the most effective treatments we have for cancer: radiation.

The goal of all of my work is to improve radiation treatment for patients who have cancer, either by further sensitizing tumors to radiation damage or protecting healthy tissue from it. Radiation therapy works by bombarding cells with highly energetic electromagnetic waves or particles, either from an external source or an internally placed radioactive source. The radiation can damage DNA and other molecules in all cells, but rapidly proliferating cells like cancer are most vulnerable to destruction. In one sense, radiation was one of the first targeted treatments for cancer; like surgery, it is localized to a particular treatment area. And, thanks to improvements in the underlying technology, we have had impressive advances in radiation treatment delivery over the last century, such that we are able to better target tumors and spare most normal tissue. Nonetheless, damage to healthy tissue is still a concern whenever radiation is applied.

(Photo: R. Baer)

Radiation Therapist Dramane Niambele and Deborah Citrin, M.D., prepare a patient in a TrueBeam™ unit.

Protecting the Healthy

Radiation fibrosis is a scarring, which can occur in organs like the lungs or the skin, causing tremendous complications, morbidity, and even mortality. It has often been considered an irreversible side effect. We have studied radiation fibrosis extensively in the laboratory, with the goal of developing therapeutics. Unlike acute radiation injury, this kind of scarring can happen months to years after treatment. Thus, we have to develop longer-term models in animals and cell cultures than typical cancer models. It can take four to six months to study, treat, and follow the progression of fibrosis in mouse models, making these experiments time consuming and expensive.

We've known since the 1960s that inflammation is very important in radiation injury; you can visualize it in stained tissues. Because of its involvement in inflammation and fibroblast activation, many in the field have focused on TGF-β as a key molecular driver of radiation fibrosis.

Instead of focusing on this single molecule or the late time point at which we see the manifestation of