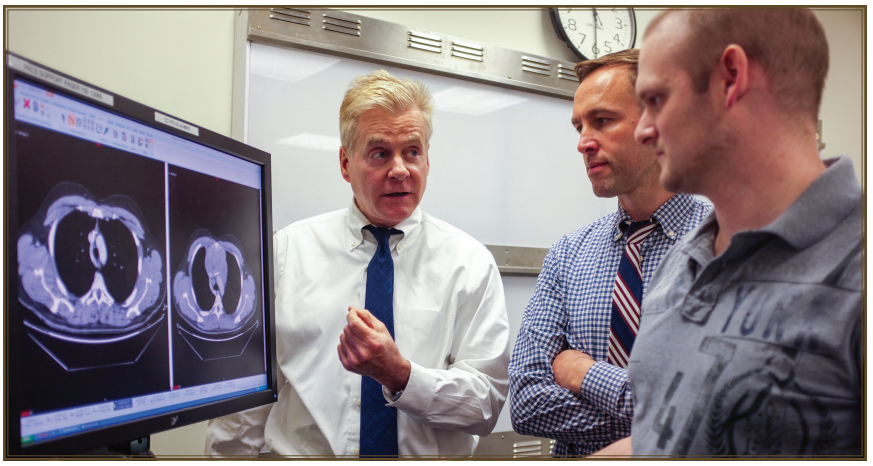
Radiating Good Health

A new study may eliminate the need for radiation in the treatment of a rare B-cell lymphoma.

Electromagnetic radiation caused Marie Curie's untimely death from cancer at the hands of her own Nobel Prize-winning research. Radiation is also, of course, a key part of the therapeutic arsenal against cancer, along with chemo-, immuno-, and targeted therapies. Curse or cure, radiation operates essentially through DNA damage. Cancerous cells are more vulnerable to treatment, but healthy cells also succumb, leading to known side effects. More recently, it has been recognized that therapeutic radiation can seed new tumors, even decades after its administration.

That is why a group of researchers led by Wyndham Wilson, M.D., Ph.D., and Kieron Dunleavy, M.D., of CCR's Lymphoid Malignancies Branch, has set out to do away with radiation in the treatment of primary mediastinal B-cell lymphoma. This rare subtype of B-cell lymphoma primarily affects people in their teens and twenties, making the potential long-term consequences of radiation exposure particularly concerning. The researchers felt that by focusing on this single subtype and taking advantage of newer, more targeted therapies, they could both improve outcomes and eliminate radiation from the treatment strategy.

Based on prior work on related cancers, Wilson and his colleagues conducted a single-arm study of a chemotherapy regimen consisting of dose-adjusted etoposide, doxorubicin, and cyclophosphamide with vincristine and prednisone, combined with the monoclonal antibody rituximab (DA-EPOCH-R) in 51 patients with primary mediastinal B-cell lymphoma over a 13-year period. The results of this work were published in the *New England Journal of Medicine* earlier this year.



(Photo: R. Folkers, NCI)

Wyndham Wilson, M.D., Ph.D., and Kieron Dunleavy, M.D., reviewing CT scan with 26-year-old male patient (far right). Scan on right side of screen shows 15 cm mass in mediastinum and scan on left shows complete remission 7 months later.

"The outcome of our study is the best that has ever been reported in primary mediastinal B-cell lymphoma," said Wilson. "And it is the only outcome that has been reported without radiation." Following patients for an average of five years, the clinicians found that 93 percent of patients experienced no recurrence of the cancer, and that the overall survival rate was 97 percent. Oncologists are often reluctant to talk about outright cures, but Wilson noted that after a couple of disease-free years, the chances that patients relapse with this type of lymphoma are virtually zero. "We follow patients for many, many years, and we simply do not see relapses after that time."

Part of their therapeutic regimen involved a strategy developed by Wilson for pharmacodynamically adjusting the dosages to match individual patients' responses. Because individuals clear drugs that enter the body at different rates, the same dose administered systemically will not result in the same concentration of drug at the tumor. Wilson's strategy ties the amount of drug administered to a cellular response to chemotherapy, namely, the number of white blood cells remaining in circulation.

Learning about early results from the study presented at a conference, clinicians at Stanford University Medical Center decided to begin treating their patients with DA-EPOCH-R. Their retrospective analysis of 16 patients treated from 2007 through 2012 provided independent confirmation of the effectiveness of this treatment strategy. Similarly, in 2010, the Non-Hodgkin's Lymphoma Berlin–Frankfurt–Münster (NHL-BFM) study adopted DA-EPOCH-R for children and adolescents with primary mediastinal large B-cell lymphoma and reported equally strong results. "If I were a patient or referring oncologist," concluded Wilson, "I'd be pretty hard pressed not to try a regimen that is producing these outcomes."

To learn more about Dr. Wilson's research, please visit his CCR Web site at http://ccr.cancer.gov/staff/staff.asp?name=wwilson.