

THE ABCOPAL EFFECT:

The Effect of Radiation & Provenge on the Immune System

By: Mark Scholz, MD

In general, the word “radiation” has very negative connotations. Many people therefore, will be surprised to hear that some forms of radiation actually stimulate the immune system. Yes, I said stimulate. You probably thought I meant to say suppress. Of course, radiation to the whole body, such as what Japanese people were exposed to at Nagasaki, does suppress the immune system, sometimes to a fatal degree. Allow me to use a clinical story to illustrate how radiation may actually stimulate the immune system.

Clinical Case Study

A 54-year-old physician was diagnosed February 2011 with a PSA of 233. His scans were positive for bone and lymph node metastases. He immediately started Casodex and Lupron and his PSA briefly dropped down to 2 but subsequently rose to 10.8 in July of 2011. A prostatectomy in September showed 25 of 71 nodes with cancer. After his surgery the PSA continued to rise to 20 and another scan showed extensive cancer in almost every bone. At that point he underwent treatment with Provenge, the FDA approved immunotherapy for prostate cancer. At the same time he was also administered spot radiation to two small areas of cancer in his backbone. Afterwards, by January of 2012, his PSA dropped down to 0.47! Even so, six months later the PSA started rising again, up to 6. So he began Nilutamide, a feeble hormone medicine we rarely use anymore. Surprisingly his PSA again dropped to 0.8 and another scan showed that his previously enlarged lymph nodes had shrunk back to normal size.

Subsequently, when his PSA started to rise again and he began taking a combination of Xtandi and Zytiga, also with good results. However, by January of 2013 his bone pain started to return. Therefore, he elected to try a second cycle of Provenge given in combination with spot radiation. All the bone pain resolved.

To this day he continues to fight his disease with all available means including new agents such as Xofigo, an injectable form of radiation and XL-184, a medication that was recently FDA approved to treat thyroid cancer. As of the time of this article being written he continues to work fulltime with a PSA that hovers around 7.

In my experience dramatic cancer reversals like this with Provenge therapy alone are rare. Immune treatment is expected to retard the progression of the cancer, not cause a dramatic reversal. When something unexpected like this happens it leads one to consider that the results in this case are partially attributable to the addition of the spot radiation. This possibility is not as farfetched as you might think. Immuno-stimulatory effects from radiation have been reported frequently enough to garner a specific name—the Abscopal effect.

The Abscopal Effect

The Abscopal effect works as follows. When radiation incites direct damage to tumor cells, the immune cells in the blood are drawn toward the radiation-damaged cells. This close approximation of immune cells with tumor cells enables the immune cells to “detect” new tumor antigens being released from the dying cancer cells. Once the immune cells, “get the scent” of the cancer, the immune cells can then travel and attack cancer tumors outside the radiation field in other parts of the body.

Of course, radiation therapy kills cancer cells directly, inducing DNA damage to the neoplastic cells. The accumulation of DNA breakdown, and consequent insufficient DNA repair, inside the cancer cell is what triggers the irradiated cells to die. But this direct radiation effect only occurs to the cancer cells in the pathway of the radiation beam. The Abscopal effect is the observation that cancerous tumors in non-irradiated areas of the body also shrink, presumably by means of newly activated immune cells.

*Provenge® an autologous cellular immunotherapy product designed to stimulate an immune response against metastatic, hormone refractory prostate cancer. Provenge consists of autologous peripheral blood mononuclear cells, including antigen presenting cells, which have been activated by being “cultured” with a recombinant human protein composed of prostatic acid phosphatase (PAP), an antigen expressed in the majority of prostate adenocarcinomas. The PAP is chemically linked to granulocyte-macrophage colony-stimulating factor (GM-CSF) which is an immune cell activator.

The optimal method for inducing an Abscopal effect is yet unknown. But now new advances in radiation technology enable doctors to safely administer large doses of radiation to small, sensitive areas of the body without causing serious collateral damage to the normal cells that surround the tumor. So new technology, rather than needing long sequences of daily radiation extended over many weeks, can increase necrotic damage to tumors and further enrich the immune system with cancerous antigenic material with a single dose of radiation.

Researching How Often the Abscopal Effect Occurs

Considering that radiation seems to enhance the anti-tumor immune response, boosting this immune response even further with an immunotherapy like Provenge* is an attractive idea to test in a larger group of patients in a formal clinical trial. It’s logical to consider that that radiation and Provenge together will cause a greater anti-cancer immune effect than either method by itself.

Presently, very little is known about how anti-cancer therapies like radiation interact with immunotherapy in a clinical setting. However, 21st Century Oncology, based in Phoenix, is going to be opening an interesting clinical trial designed to determine if tumor cell death occasioned by radiation therapy augments the anti-tumor responses from Provenge. In this study, patients treated with spot radiation and Provenge in combination will have their tumor responses tracked with the latest scanning technology using C11-acetate PET scans. (See below for information on these clinical trials).

“As I have worked on the concept of combining radiation therapy and immunotherapy since 1999, we believe clinical trials in this area provides an opportunity to share the latest, state-of-the-art advances with the oncology community,” said Steven E. Finkelstein, M.D. Dr. Finkelstein is a board-certified radiation therapist and the National Director of the Translational Research Consortium, the research arm of 21st Century Oncology. “We are confident that the information we learn from clinical trials and research we conduct today will improve outcomes for patients with cancer moving forward.”

Dendreon, the manufacturer of Provenge, and 21st Century Oncology should be commended for designing and implementing a visionary new clinical trial that incorporates a variety of innovative ideas in the area of immunology, radiation therapy and imaging. This trial will benefit patients by giving them access to state-of-the-art technology while at the same time advancing our understanding of how immunotherapy works. □

For information on these clinical trials go to our website <http://prostate-cancer.org/> or give us a call at (310) 743-2116