

# RADIATION TREATMENT OF PROSTATE CANCER & RISK OF SECOND CANCERS

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Exposure to high doses of ionizing radiation, whether from a nuclear explosion or from radiation therapy for cancer, has long been known to increase the risk of cancer formation. A growing body of clinical data is helping to further develop our understanding of secondary radiation-induced cancers.

Much of our current understanding about radiation-induced cancer is based upon long-term observation of the Japanese survivors of the World War II atomic bombings in Hiroshima and Nagasaki. In particular, an increased incidence of leukemia, myeloma, and cancers of the thyroid, breast, lung, stomach, esophagus, ovary and bladder has been identified in atomic bomb survivors who were close to ground zero.

Following the catastrophic failure of the Chernobyl nuclear reactor in Ukraine, in 1986, an excess of leukemia and thyroid cancer among workers who were involved in the clean-up of the reactor's contaminated debris has already been documented.

More recently, several studies have reported upon the incidence of secondary cancers in adults who were treated with radiation therapy for lymphoma during childhood and adolescence. An increased incidence of cancers of the lung and the female breast has been confirmed among patients who previously underwent extended-field chest irradiation (also known as mantle radiation therapy) for Hodgkin's Lymphoma, and these secondary cancers typically occur 15 to 20 years following treatment. Rare cancers of the bone and cartilage, called sarcomas, have also been associated with prior radiation therapy treatments. Now, a new research study suggests that certain forms of prostate cancer radiation therapy may also be linked to an increased risk of subsequent radiation-induced secondary cancers.

Currently, there are several different treatment approaches available for prostate cancer therapy. Surgery can be performed to completely remove the prostate gland (prostatectomy) when the tumor is still confined to the prostate. Implants of radioactive seeds, placed within the prostate gland (brachytherapy), can also be used to destroy cancer within the prostate. External beam irradiation is another form of radiation therapy, but unlike brachytherapy, external beam irradiation is delivered by a machine that concentrates radiation onto the prostate gland from a source external to the body. Although great progress has been made in fine-tuning the delivery of radiation to the prostate gland with both brachytherapy and external beam irradiation, there is, inevitably, some "collateral damage" that occurs to the organs and tissues that surround the prostate, as it is impossible to confine 100 percent of the delivered radiation dose to the prostate gland alone.

A new study, in the *Journal of Urology*, evaluated the cancer treatment records of more than 240,000 men who had previously been treated for prostate cancer with prostatectomy, brachytherapy, external beam radiotherapy or a combination of brachytherapy and external beam radiotherapy between 1988 and 2003. The data for this study was collected from the massive Surveillance, Epidemiology and End Results (SEER) national cancer database, which is maintained by the National Cancer Institute. This study was conducted by researchers from Columbia University and the Mount Sinai Medical Center.

In this study, the authors compared the incidence of subsequent cases of cancers of the bladder and rectum occurring in these 243,082 men. The men who underwent prostatectomy alone, and who did not receive any radiation therapy, essentially served as the “control group” for this study.

An almost insignificant increase in the risk of bladder cancer was seen in the men who underwent brachytherapy alone. However, there was a more pronounced and statistically significant increase in the risk of *both* bladder cancer *and* rectal cancer observed among the men who received either external beam radiotherapy alone or combined brachytherapy and external beam radiotherapy. Compared to the men who underwent prostatectomy alone, external beam irradiation was associated with an 88 percent increase in the *relative risk* of developing bladder cancer, and a 26 percent increase in the *relative risk* of developing rectal cancer. Among those men who received *both* brachytherapy *and* external beam radiotherapy, the *relative risk* of developing bladder cancer was 85 percent higher than what was observed in the men who underwent prostatectomy alone, while the *relative risk* of developing rectal cancer was 21 percent higher. (It should be noted that “*relative risk*” is a measure of the difference in risk between two patient treatment populations, and is not the same as the “absolute risk” of developing a particular disease.)

In this retrospective study, which involves a relatively short duration of clinical follow-up, external beam irradiation for prostate cancer (either administered alone or in combination with brachytherapy) was associated with a significant increase in the risk of developing subsequent cancers of the bladder and rectum.

Since most studies of radiation-induced secondary cancers have shown an average biological lag time of 15 to 20 years between radiation therapy and the diagnosis of secondary malignancies, the findings of this study may actually underestimate the long-term risks of secondary bladder and rectal cancers in men who have previously received external beam radiotherapy as treatment for their prostate cancers. At the same time, however, recent and continuing improvements in the accuracy of radiation therapy delivery have significantly reduced the “innocent bystander” effect, whereby clinically significant doses of radiation are absorbed by the organs that surround the prostate gland (namely, the bladder and the rectum). As a final note, all retrospective studies that are based upon prospectively collected data, such as this study, are subject to potential

biases, including the “completeness” of the clinical data that is present within large databases such as the SEER database. However, based upon a large body of clinical literature on this topic, the findings of this particular study are not at all surprising, or unexpected.

All patients who are planning to undergo therapy for prostate cancer should first talk with their oncologists about the unique risks and benefits associated with each potential treatment option before choosing the best and most appropriate form of therapy.

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