

Radiation and Hereditary Breast Cancer

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As you are aware, radiation therapy is a common treatment method for breast cancer. Mammograms also emit radiation. Unfortunately, radiation damages unaffected cells too. Since unaffected cells are healthier, they are better able to repair themselves and are less likely to have long-term damage. As you know there are several hereditary cancer syndromes that increase a patient's risk to develop breast cancer. These individuals have a genetic mutation in every cell in their body. If cells that do not have cancer receive radiation, and have a genetic mutation, these cells may not be as readily able to repair themselves, therefore the benefits of radiation therapy differ by genetic syndrome. Below are brief explanations of different genetic mutations that cause hereditary breast cancer and the effect of radiation exposure:

BRCA1 and BRCA2- When mutated, these genes lead to a high risk for breast and ovarian cancer. When working properly, these genes repair specific types of DNA breaks that frequently occur from aging and environmental toxins. In individuals who are born with *BRCA1* or *BRCA2* mutations, the mutation prevents the gene from being able to repair damaged DNA, and the accumulation of errors in DNA frequently leads to cancer.

When an individual with a *BRCA1* or *BRCA2* mutation develops cancer, they might consider radiation treatment. Radiation therapy causes DNA errors that are repaired by normal-functioning *BRCA* genes. Although counterintuitive, having a *BRCA* mutation does not seem to further increase recurrence risk among patients who receive radiation therapy.¹ However, accelerated partial breast irradiation (APBI) is a newer form of radiation. APBI for *BRCA* positive patients are considered to be “unsuitable for APBI outside of a clinical trial” as studies have not yet been carried out to determine the benefits and risks of APBI within this group.⁴

Mammograms: For several years, NCCN guidelines recommend mammograms beginning at age 25 for most women who have *BRCA* mutations. However, in September of 2012, the *British Medical Journal* published a study that found that women with *BRCA* gene mutations may be more likely to develop breast cancer if they receive mammograms at younger ages.² The study involved about 2,000 European women over the age of 18 who had *BRCA* mutations. They found at least a 43% increased risk to develop breast cancer if they had mammograms before the age of 29. Further research is needed, but health care providers and patients may consider MRI and/or ultrasound as an alternative for screening for women with *BRCA* mutation under the age of 30 in the future.

Important Consideration: Evidence is conflicting on the influence of radiation on women who have *BRCA* mutations. Although some forms of radiation do not appear to increase the recurrence risk of breast cancer in women with *BRCA* mutations, it is important to keep in mind that these women are already at high risk to develop second breast cancers. Radiation therapy as described above is used in the context of breast conservation. Any individual with a *BRCA* mutation should discuss all potential options, including prophylactic mastectomy, with their health care providers.

TP53- Individuals who have this gene mutation have Li-Fraumeni syndrome and are at high risk for breast cancer and increased risk for childhood sarcomas, brain tumors, and adrenocortical carcinoma, and other tumors. *TP53* is a tumor suppressor gene that has an important role in many different stages of the cell cycle, and helps with DNA repair and facilitates in the death of cells that are defective. Cells that contain *TP53* mutations appear to be resistant to radiation.⁵ These cells grow even more rampant when normal cells become damaged and can no longer protect themselves. Patients with *TP53* mutations

who receive radiation are more likely to develop cancers in the radiation field. Radiation is contraindicated in individuals who have *TP53* mutations.

Other genes- There are other rare genes related to hereditary breast cancer (i.e. Peutz-Jeghers syndrome and Cowden syndrome, caused by *STK11* and *PTEN* mutations respectively, amongst others). Unfortunately there is still a paucity of data concerning recurrence risk and second malignancies in the context of these and other hereditary mutations.³

Radiation can be very useful for diagnosing and treating cancer. However, special considerations must be made for patients who have specific hereditary syndromes. Awareness of one's hereditary cancer syndrome status is important for patient surveillance and management. *Health care providers should use caution when considering radiation in the context of hereditary breast cancer.*

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