

Side effects of radiation therapy: Why me?

Most lung cancers are treated with radiation therapy, often in high doses. Although these treatments are absolutely required to prolong life (by killing the tumor or slowing its growth), radiation treatment can have negative side effects that are known collectively as RILT (radiation-induced lung toxicity). These side effects can include cough, shortness of breath, chest pain, and low-grade fever as well as severe scarring of the lung itself, resulting in loss of lung function. Why some people develop these side effects and others do not is not clearly understood. This article reviews a number of factors that may predict or determine why some patients experience RILT and others do not. These include:

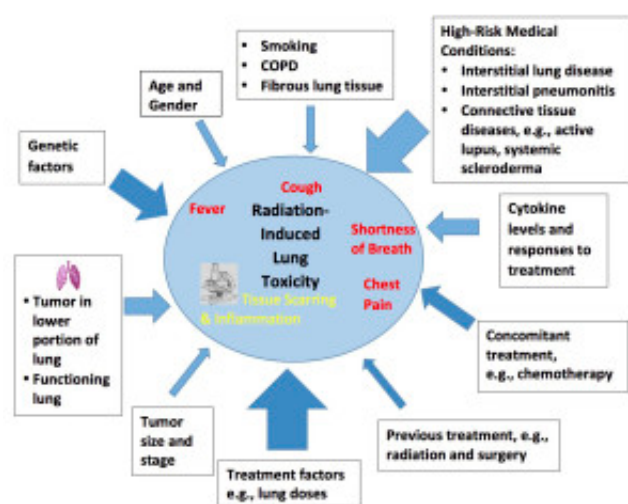


Fig. 1. Factors affecting radiation-induced lung toxicity. Toxicity symptoms are indicated in red text within the blue oval; presentation is indicated in yellow. The importance of the factor to the toxicity is indicated by the thickness of the arrows. Thicker arrow indicates a greater effect.

Age: Older patients are generally more susceptible to radiation side effects, but there is no clear cut-off age at which the side effects start.

Smoking: Interestingly, people who smoke at the time of their lung cancer diagnosis appear to suffer less lung toxicity from their radiation treatments, perhaps because their lungs are already damaged from the effects of smoking. Healthy lungs are more susceptible to radiation side effects.

Other lung diseases: Patients whose lungs are already fibrous or thickened from other causes (for example, interstitial lung disease) are much more susceptible to side effects of radiation therapy, and often must be treated with lower doses of radiation. Lung cancer patients who already have COPD (chronic obstructive pulmonary disease) or emphysema may suffer fewer radiation-induced side effects, depending on how well their lungs are

working.

Tumor location and size: Radiation that is directed at tumors located in the lower portion of the lung appears to cause more side effects. It is unclear if size and stage of the tumor can predict whether a patient has side effects from radiation therapy.

Previous treatments (radiation therapy, chemotherapy): There is limited data available to determine whether previous treatment with radiation or chemotherapy for lung cancer affects a patient's susceptibility to radiation-induced toxicity.

Genetic factors: Genetics plays a role in determining how sensitive a patient is to radiation therapy and may be the most important factor involved. Many research studies are currently underway to determine a patient's "genetic signature." Slight differences, called single nucleotide polymorphisms or SNPs (pronounced "snips"), in genes that control how cells respond to damage in their DNA have been correlated with an increased chance of suffering from radiation toxicity. The more of these "unfavorable" genetic differences that a patient has, the greater the risk (and perhaps degree) of toxicity the patient experiences.

Biological markers: Current research is also focused around the role of certain proteins, called cytokines, that are produced by cells in response to inflammation and other injury. One of these proteins is TGF- β , and high levels of TGF- β in the blood seem to be correlated with toxic side effects of radiation therapy. However, many factors can cause high levels of TGF- β , not just the body's reaction to the radiation therapy. It is hoped that analysis of cytokine levels before, during, and immediately after radiation therapy may predict how the patient will ultimately respond to radiation dose. This will allow the treating physician to treat not just the tumor, but the patient as a whole, and help to avoid or treat the toxicities that can be associated with radiation therapy.

Patients and physicians look forward to the day when "personalized medicine" is advanced enough such that the physician can predict who is at risk for radiation-induced toxicities and adjust the patient's treatment plan accordingly. That day will be here sooner than we think.

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