PRIMEVIEW

RADIOTHERAPY TOXICITY

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As a common treatment for many cancers, radiotherapy can be used with curative intent or to palliate symptoms. However, irradiation to nearby adjacent tissues can be associated with short-term toxicity and long-term consequences.

DIAGNOSIS

Depending on the tissues affected, a range of symptoms can emerge, from dermatitis to neurological impairment. Symptoms that occur during and after radiotherapy are not necessarily caused by radiation; the mechanisms behind one symptom can be diverse and require different treatments. Radiation can also exacerbate an underlying illness — highlighting the importance of differential diagnosis. For example, post-radiotherapy cognitive decline affecting memory, verbal fluency and attention, especially in elderly patients with cancer, could be attributed to Alzheimer disease, vascular dementia or frontotemporal dementia.

In another example, a diagnosis of radiation pneumonitis can be made only when other disorders (such as infection, chronic obstructive pulmonary disease and heart failure) that cause cough and dyspnoea have been excluded. Accordingly, thorough investigation is needed to delineate the causes of symptoms experienced.

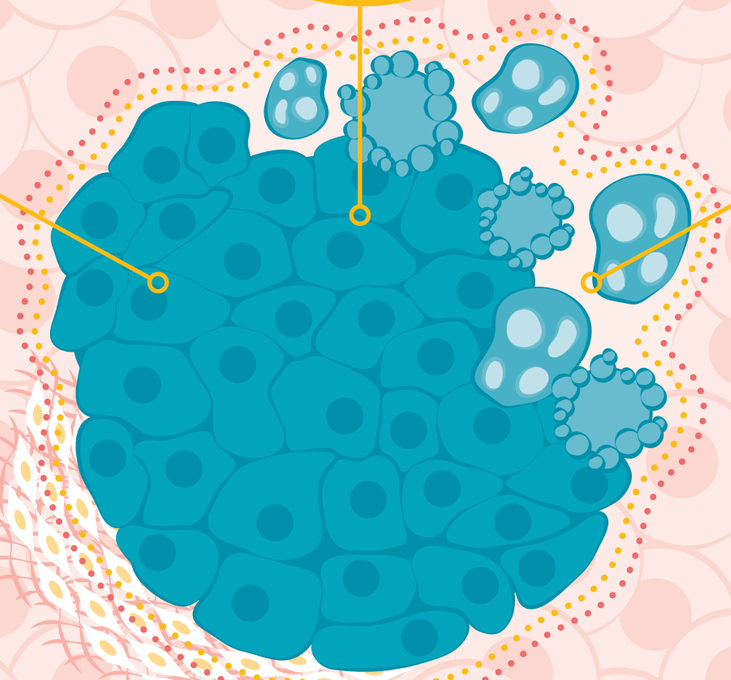
MECHANISMS

Modern radiotherapy techniques, such as stereotactic radiosurgery, can deliver many high-energy beams from different angles to precisely target small regions in all parts of the body

DNA damage triggered by radiotherapy induces a halt of the cell cycle and an attempt to repair the damage. When DNA repair capacity is insufficient, permanent cell cycle arrest (senescence) or cell death are induced

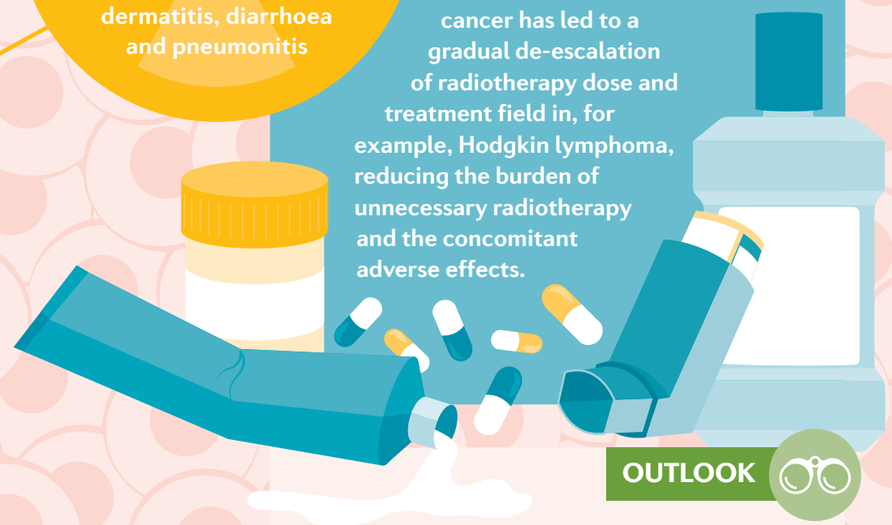
Cell death as well as radiation induce an inflammatory response that can affect normal tissues, including the skin, gut and lungs, leading to, for example, acute and subacute dermatitis, diarrhoea and pneumonitis

Persistent and exaggerated wound healing can lead to tissue fibrosis, vascular damage and consequent organ dysfunction



MANAGEMENT

The management of acute and late radiotherapy toxicity is symptomatic. For example, as inflammation has a role in many adverse effects, anti-inflammatory drugs are frequently prescribed. The organ dysfunction due to radiotherapy can be mitigated in some cases; for example, angiotensin-converting-enzyme inhibitors may be used in heart failure. Importantly, our increasing ability to stratify treatments for patients based on the molecular characteristics of their cancer has led to a gradual de-escalation of radiotherapy dose and treatment field in, for example, Hodgkin lymphoma, reducing the burden of unnecessary radiotherapy and the concomitant adverse effects.



QUALITY OF LIFE

Tissue stem cells with residual DNA damage may undergo malignant transformation, leading to second cancers years later

Late radiation effects to quality of life are greatest in patients who received high doses of radiotherapy to or near essential organs, such as the brain and the heart, and in paediatric patients. Indeed, survivors of childhood cancer who received radiotherapy are at high risk of disability, second tumours later in life, cognitive dysfunction and endocrine dysfunction. Comprehensive care involving inter-professional teams to provide physical rehabilitation, psychological support and long-term follow-up is important for addressing the complex needs of patients and survivors of cancer.

OUTLOOK

New technologies to refine the radiotherapy field, strength and delivery continue to offer promise for reducing the rate and extent of radiotherapy toxicity. Additionally, efforts using genetic analyses and imaging to identify individuals who are at high risk for radiation toxicity are underway. Exciting avenues in this regard aim to perform omics-based tests of large patient cohorts to assess the responses to radiation of tumour tissues, normal tissues and serum biomarkers to develop tools to prognosticate and predict outcomes for patients receiving radiotherapy.

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