

## Review Article

# A Review of Post-Radiotherapy Complications Necessitating an Urgency for Further Advances and Innovations in Radiotherapy

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## Abstract

The initial discovery of X-rays by Roentgen in 1895 and the use of brachytherapy after Marie and Pierre Curie discovered radium in 1898 stimulated a revolution of conceptual and technological innovations throughout the 20th century, forming the basis of the safe and effective therapies used even today. Today radiotherapy has become a standard treatment option for a wide range of cancers. But the rapid increase and enthusiasm for radium ultimately lead to its overuse. This paper offers an overview of post-radiotherapy complications to implicate the urgency for further advances and innovations in radiotherapy.

**Keywords:** Cancer; Management; Radiotherapy; Complications; Side effects; Advances; Innovations

## Introduction

Head and neck cancers and their limited treatment options have a direct impact on quantity and quality of life and the standard of normal living. Surgery, chemotherapy and radiotherapy have been used singly, concurrently or in combination for the treatment of cancers. Each of these treatment options cast various undesirable side effects. Unfortunately, both the chemo-molecules and radiation particles cannot distinguish normal cells from cancerous ones, and undesirable damage to normal tissues might occur if appropriate care is not taken to precisely localize the therapy onto the intended target. This is of particular importance for radiotherapy of cancers of the head and neck, which often mingle with or about the important normal structures that are similarly sensitive to radiation. The direct and indirect toxic effects of cancer chemotherapy and ionizing radiation affect the head and neck region especially the oral cavity [1]. This review emphasizes the urgency and need for advances, incorporation of newer scientific technologies and innovations in cancer radiotherapy.

### Challenges faced in radiotherapy

At present, radiotherapy forms a part of the management of 40% of patients cured of their disease and hence plays an important role in the care of patients with cancer [2]. Advances have been made in the past two decades, as improvements in engineering and computing have enabled technologies such as Intensity Modulated Radiotherapy (IMRT), Image Guided Radiotherapy (IGRT) and Stereotactic Radiotherapy (SRT) to be used in routine clinical practice [3]. Surgical methods, treatment techniques and fractionation schedules for the treatment of head and neck cancers should be selected keeping in mind the anatomical preservation of organs which may not necessarily translate into functional preservation [4]. There are few occasions, where, head and neck cancer patients are not

prepared optimally for radiation therapy, due to which they succumb to complications after radiation therapy [5]. The complications can range from mild to severe, depending on the dose of radiotherapy and the length of the treatment. More severe complications are reported when radiotherapy is combined with chemotherapy such as brain problems, infertility, joint problems, lymph edema, mouth problems, secondary cancers and other local changes depending on area of treatment [6]. The first and foremost challenge faced by radiotherapy is restricting the radiotherapy to the cancer affected tissues only. Most of the problems associated with post-radiotherapy are due to the presence of normal tissue in the path of radiation exposure. It is often challenging to deliver tumoricidal doses while respecting these normal tissue constraints. This is the field where the advancement in radiotherapy has to be focused to deliver the optimum dose of radiation to the appropriate site affected by cancer. At present several altered fractionation schemes have been developed in order to overcome this problem [7].

### Complications of radiotherapy implicating the urgency for further advances and innovations in radiotherapy

The risks of normal tissue complications after fractionated radiotherapy have been examined often, and have shown to depend on several factors including fraction size, tissue type, total radiation dose and the portion of an organ that is irradiated [8]. Several studies have been found in literature with regard to morbidity and mortality secondary to radiotherapy of the head and neck area [4, 9-14]. Adverse reactions to radiotherapy will depend on the volume and the area being irradiated, the total dose, fractioning, age, patient's clinical condition and associated treatments. A small increase in tumor dosage is enough for a significant increase in the complications incidence. Acute reactions happen during the treatment and most of the time, they are reversible. Late complications are normally irreversible, leading to permanent incapability and to a worsening of

quality of life, which vary in intensity, normally classified into mild, moderate and severe [15].

### **Complications of radiotherapy in the head and neck region**

At about two weeks after radiotherapy treatment, the skin over the face and neck will gradually redden or darken and may feel sore and itchy (like sunburn). This lasts for about four weeks. Due to damages to the oral mucosa, patients complain of mucositis associated pain, which usually lead to the need of analgesics during treatment. The pain intensifies whenever the patient tries to eat or drink [15]. Mucositis is even more worse when chemotherapy is used in association with radiotherapy during cancer treatment [16].

The incidences of post-radiotherapy complications see a significant rise even with small increase in tumor dosage. 80% of patients irradiated in the head and neck area, complain of "Xerostomia" or "dry mouth" [17]. The development of xerostomia results in alteration of the oral environment causing qualitative alterations in saliva like decrease of amylase activity, buffer capacity and pH, with consequent acidification [18]. Levels of electrolytes in saliva such as calcium, potassium, sodium and phosphate are also altered [19]. Patients with xerostomia complain of oral discomfort, loss of taste (dysguesia), thick sticky saliva, speech and swallowing difficulties (dysphagia). They are also susceptible to periodontal disease, rampant tooth decay (radiation caries) and oral infections by fungus and bacteria [20]. Halitosis is also a side effect of oral complications of radiotherapy. Another potential consequence of radiotherapy to the oral cavity is fibrosis around the muscles of mastication, leading to trismus [21]. Painful oral ulcerations infected by Herpes Simplex Virus is usually seen in patients who have undergone head and neck and/or total-body irradiation [22]. Oral candidosis develops consequently resulting in pain and / or burning sensation [23]. These complications finally lead to loss of appetite and weight loss due to reduced dietary intake [14,15,17]. The resultant compromised nutritional status of the patient is followed by dehydration and malnutrition necessitating hospitalization to provide intravenous fluids or parenteral hyperalimentation, thereby increasing the cost of treatment and the risk of nosocomial infections [24].

### **General Complications of Radiotherapy**

The general complications of radiotherapy may manifest as side effects of head and neck irradiation, irradiation to other body parts or full body irradiation. Other than fatigue, these present themselves as late complications about after 2-3 weeks. There is hair loss in treatment area, swelling, urinary and bladder changes, diarrhea, nausea and vomiting, changes to thyroid gland and changes in hearing. With the exception of fatigue, toxicity is associated with the anatomical location of the radiotherapy fields. The resultant defects are seen as arterial injury in the form of carotid artery and delayed cerebrovascular consequences [9], radiation fibrosis [10], late esophageal toxicity like stricture and dysphagia [11,12], pituitary-hypothalamic dysfunction [13], ocular toxicity [4], ototoxicity [4], nervous system side effects causes complications within the brain such as temporal lobe necrosis [14]; radiation induced brainstem damage seen as bulbar palsy, ataxia, trigeminal and facial cranial neuropathy, hearing loss, hemianopsia, and hemihyphesthesia [25]; cranial nerve palsy and peripheral nerve plexopathies [4]. Adding to

this agony, depending on the treated volume and dose, there is a risk of second cancers after radiotherapy which increases over the decades after treatment [26].

### **Osteoradionecrosis**

Osteoradionecrosis is usually diagnosed within months of radiotherapy or years after radiotherapy in some patients [27]. It may manifest as a small, asymptomatic bone exposure that remains for months to years and heals with conservative management, or may gradually progress, leading to fistulas and secondary infections with severe necrosis requiring surgical intervention and reconstruction [28-30].

Cancer survivors even after treatment are forced to live with restricted function of effected parts. The day to day physical pain and psychological trauma faced by these patients other than complications caused by cancer itself are very heartbreaking. These life threatening complications implicate the urgency for further advances and innovations in radiotherapy in order to reduce the suffering of cancer patients as well as cancer survivors so as to minimize overall mortality and morbidity.

### **Requirement of advances and innovations in radiotherapy**

Organ preservation is the major concept to be focused in the field of advancement and innovations of radiotherapy. The possibility of slightly higher risk for tumor recurrence that it may expose the patients to outweighs the larger quality-of-life benefits. The field of radiotherapy has undergone an amazing series of developments largely as a result of dedicated and inventive pioneers, whose conceptual and technological advances, the most important of which have been the paradigm of fractionated dose delivery, technologic advances in X-ray production and delivery, improvement in imaging and computer-based treatment planning and evolving models that predict how cancers behave and how they should be approached therapeutically [31]. Above all the emergence of new technologies and treatment protocols for cancer should be made accessible and affordable to the general public. The problem faced here is that of the rapid rise in new cancer cases and cancer survivors in the underdeveloped and developing countries, where the cancer treatment is unaffordable in private hospitals [32].

### **Conclusion**

As there is a steady increase of cancer survivors, there is a need for better medical care of cancer patients. Long term follow-up and optimal care is required for better quality of life in terms of oral health and general well-being. These complications and side-effects cause a major impact on quality of life, including psychosocial aspects of living. With the advent of newer technological inventions, cancer therapy should be made free from complications and side effects, because the health of cancer survivor is already compromised. The advancement in radiotherapy should therefore focus on restricting damage to body, both physical and psychological. This will ensure a respectable living to the individual restricting the patient to deal with the complications of cancer and not of radiotherapy. Along with this a multidisciplinary health care team is required for overall health of cancer patients, as well as cancer survivors.

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