Journal of Chemical Health Risks

www.jchr.org

JCHR (2024) 14(1), 1396-1408 | ISSN:2251-6727

Unveiling the Interplay of Human Microflora in the Realm of Ionizing Radiation

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(Received: 27 October 2023 Revised: 22 November Accepted: 26 December)

KEYWORDS

Bacteria, Radiation, Prognosis, Treatment

ABSTRACT

Radiation therapy continues to play a pivotal role in cancer treatment, with heightened effectiveness achieved through precise delivery and the synergistic integration of immunotherapy. The intricate interplay among gut microbiota, bacteria, fungi, and their impact on the response to radiation therapy highlights the complex relationship between cancer biology and the immune system. Recent experiments indicate that an abundance of fungi, rather than a decrease in bacteria, hinders the efficacy of radiation therapy. Profiling a patient's microbiome, encompassing both bacterial and fungal elements, holds promise in predicting their prognosis and response to various cancer treatments, including radiation therapy, chemotherapy, or immunotherapy.

INTRODUCTION

Ionizing Radiation (IR) can ionize atoms or molecules within the human body, creating free ions when exposed to radiation. This process, as observed in studies by (1), can lead to adverse effects on the body. Previous research suggests a potential link between IR and conditions such as metabolic diseases, acute hematopoietic syndrome, and gastrointestinal syndrome (2).

The human body houses a diverse microbiome, with gut flora in the gastrointestinal tract playing a crucial role in digestion and nutrient absorption. Disruptions in the composition of these microorganisms can occur due to factors such as infections and physical conditions (3) Ionizing radiation, with its energy capable of breaking atomic bonds and emitting electrons, induces ionization. This interaction, resulting from the decay of unstable atoms (radionuclides), leads to direct and indirect effects, including the generation of free radicals and mutations in DNA molecules (1).

The impact of ionizing radiation (IR) on the human body is contingent upon the dose and exposure time, with a more pronounced effect on actively dividing cells. Certain microorganisms demonstrate resistance to higher levels of ionizing radiation, and comprehending these mechanisms is crucial for preventing dysbiosis (4). Maintaining the balance of intestinal bacteria is pivotal for regulating processes such as food digestion, nutrient absorption, and immune functions within the gastrointestinal tract (5)

As focus shifts to understanding the effects of IR on gut flora, unraveling the link between ionizing radiation and the intestinal microbiota becomes imperative for the development of radiation-related treatment approaches. Establishing correlations between the effects of IR on the gut microbiota in mammals and humans is crucial for advancing this understanding .(6)

Ionizing radiation, whether natural (from environmental radiation and cosmic rays) or artificial (emanating from sources like nuclear power plants and medical equipment), can exert both positive and negative effects on the human body. While medical procedures involving IR can be beneficial, they also carry potential risks.

Atopic Dermatitis (AD), a chronic condition that initiates in childhood, marks the beginning of the Atopic march, progressing to allergic rhinitis and allergic asthma. While a genetic predisposition is central to AD development, environmental factors such as pollution, allergens, and climate also play significant roles. Staphylococcus aureus (S. aureus) is implicated as an environmental factor in AD etiology, with its potent exotoxins sustaining the disease.(7)

Ultraviolet Radiation (UVB), an electromagnetic radiation with high energy, is utilized in AD treatment. The study explores the quantitative analysis of Staphylococcus aureus (S. aureus) and Staphylococcus

Journal of Chemical Health Risks

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JCHR (2024) 14(1), 1396-1408 | ISSN:2251-6727

epidermis (S. epidermis) and evaluates the effects of radiation on S. aureus, including its potential for clinical improvement (8).

Human Microbiome and Diagnostic Radiation

The term 'normal Flora' is commonly used, it is really a misnomer. Microbial Flora has spatial and temporal complexity that differs by individual, body niche, age, geographic location, health status, diet and type of host. Even within the same individual, the composition of the microbial Flora can vary according to changes in diet, stress, sexual behaviour, medication, hormonal changes and other host-related factors. (9)

The process of the development of normal Flora starts at birth. It is thought that colonization begins during parturition when the neonate's intestine is seeded with mostly Gram-positive facultative anaerobes from the vaginal microflora during delivery. (Farland et al., 2000)(9)

Normal flora are the microorganisms that live on the surface or inside another living organism (human or animal) or inanimate object without causing disease. Sometimes it is called commensal because of their permanent presence on body surfaces even if covered by epithelial cells and are even exposed to the external environment (e.g., respiratory and gastrointestinal tract, genital, hair, etc.). Normal flora plays an important role in immunity and inflammation. (10)

Bond Amid Gutflora and Ionizing Radiation -

Ionizing radiation (IR) induces the direct production of a significant quantity of reactive oxygen species (ROS) through the radiolysis of water. This oxidative damage mechanism disrupts the balance of the gut microbiota. The resulting oxidative stress expedites the proliferation of Proteobacteria and may adversely affect the oxygen-sensitive Firmicutes phyla, leading to dysbiosis in the gut microbiome (6)

The interplay between the gut microbiome and cancer therapies, including radiation, operates bidirectionally. Anticancer treatments have the potential to disturb the microbiome, promoting dysbiosis, and these disruptions can, in turn, influence the efficacy of the anticancer treatments .(11)

Radiation therapy (RT) targeting the pelvic region has been shown to disrupt the diversity and abundance of commensal gut microorganisms. Dysbiosis in the gut microbiome has been associated with radiation enteritis, impacting intestinal barrier function, innate immunity, and mechanisms of intestinal repair. However, it's essential to note that factors such as diet, which could act as confounders, were not thoroughly addressed in these associations (12)

Pelvic RT, a fundamental modality for treating pelvic cancers (13), has been observed to induce marked changes in the gut microbiome, including the promotion of dysbiosis (14;15) Pre-clinical studies utilizing animal models have demonstrated that RT induces significant alterations in the diversity and abundance of the gut microbiome, notably leading to a substantial decrease in Enterobacteriaceae and Lactobacillus groups (11;16)).

Another notable difference between the results presented here and previous studies is that the delivery of hypo fractionated localized RT largely avoids any direct effects on the gut, whereas chemotherapy, being systemic in nature, may also impact the gut microbiome, which can be a confounding factor in such comparisons. As demonstrated by previous work in chemotherapy and systemic-based RT, therapies such as total body irradiation (TBI) have a direct effect on gut microbiota and damage to the gut epithelial barrier, with possible transient intraperitoneal extraversion and inflammation, which can in turn influence tumour response.(17,18,19)

Gut microbes can also shape normal and pathologic immune responses to cancer therapy. One group proposed that gut bacteria modulated the effects of chemotherapy via a host of mechanisms they called 'TIMER'—that is, Translocation, Immunomodulation, Metabolism, Enzymatic degradation, and Reduced diversity. (20)

Radiotherapy is the cornerstone of modern management methods of malignant tumors, but it can also cause damage to normal tissues and produce a variety of side effects, affecting the treatment results and the quality of life of patients. (21)

radiation can cause tissue damage, which then leads to the up-regulation and amplification of inflammation. The gut microbiota has been found to participate in this process through two mechanisms: translocation and dysbiosis. Radiation destroys the intestinal barrier and mucus layer, leading to bacterial translocation and activating inflammatory reactions. (14)

CONNECTIONFLANKED BY CANCER AND FLORA -

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JCHR (2024) 14(1), 1396-1408 | ISSN:2251-6727

Recent advancements in sequencing technology have brought to light the intricate role of the gut microbiota in cancer development and the body's response to treatment, turning it into a new and compelling research focus. Often referred to as the "hidden organ," the gut microbiota plays a pivotal role in various physiological and pathological processes, influencing metabolism, vitamin synthesis, the integrity of the intestinal mucosal barrier, immune regulation, and protection against pathogens .(22)

Observations of differences in gut microbiota between individuals with oesophageal cancer and unaffected counterparts have revealed significant changes in the intestinal bacterial composition of oesophageal cancer patients. This initial evidence contributes to the understanding of the relationship between gut microbiota and oesophageal cancer. Surprisingly, gut microbiota has also shown associations with extra-gastrointestinal tumors such as breast cancer, leukemia, and lung cancer, although further research is needed to solidify these connections (23,24;25)

Multiple studies in the literature highlight that the gut microbiota not only locally influences tumor development in gastrointestinal tissues but also exerts distant effects on the development of extra-gastrointestinal tissues. For instance, metabolites in the gut microbiota, pathogen-related molecular patterns, and antigens derived from the gut microbiota can reach the liver through the hepatic portal vein, potentially impacting liver cancer. The gut microbiota itself can migrate to other closely related tissues, influencing tumor progression (26)

The composition of the gut microbiota is implicated in the efficacy and adverse effects of immunotherapy, and it is also linked to the occurrence of certain types of cancer. While only a small percentage of microbes directly cause cancer, many contribute to cancer growth through the modulation of the immune system (27)

Colorectal cancer (CRC), ranking third in global incidence and second in mortality, poses a significant health challenge. Current treatment methods for CRC, including systemic therapy, preoperative radiotherapy, and surgical local excision, have limited survival rates for patients with metastatic disease. Therefore, the development of new strategies for treating CRC is crucial (28)

In recent years, the "human intestinal flora" has gained widespread attention as a risk factor for breast cancer. The gut microbiome can influence breast cancer through various mechanisms, such as altering the body's energy balance, synthesizing genotoxins and small signaling molecules, initiating and regulating the immune response, and metabolizing drugs and indigestible food components (29)

The intestinal flora, by regulating the body's metabolism and maintaining the stability of the internal environment through its structure and metabolites, has been associated with various diseases. These include inflammatory bowel disease (IBD), irritable bowel syndrome (IBS), obesity, rheumatoid arthritis, diabetes, cardiovascular diseases, psychiatric disorders, and colorectal cancer (30,31,32,33,34,35,36,37,)

Gut Flora and Fallout Radiation

A primary metabolic function of the colonic microflora involves the fermentation of non-digestible dietary residue and endogenous mucus produced by the epithelia (38). The gene diversity within the microbial community contributes various enzymes and biochemical pathways distinct from the host's constitutive resources. The overall outcomes of this intricate metabolic activity include the recovery of metabolic energy and absorbable substrates for the host, as well as the supply of energy and nutritive products for bacterial growth and proliferation. Carbohydrate fermentation, particularly of non-digestible carbohydrates like resistant starches, cellulose, hemicellulose, pectins, gums, and some escaping oligosaccharides and unabsorbed sugars and alcohols, is a major source of energy in the colon. This process culminates in the generation of short-chain fatty acids .(39)

Colonic microorganisms also contribute to vitamin synthesis and the absorption of essential minerals such as calcium, magnesium, and iron. Carbohydrate fermentation and the production of short-chain fatty acids, especially acetate, propionate, and butyrate, enhance ion absorption in the caecum. These fatty acids play crucial roles in host physiology, with butyrate serving as a major energy source for colonocytes and being almost entirely consumed by the colonic epithelium(40). Acetate and propionate, found in portal blood, undergo metabolism by the liver (propionate) or peripheral tissues, particularly muscle (acetate). Additionally, acetate and propionate may act as modulators of glucose metabolism, potentially leading

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JCHR (2024) 14(1), 1396-1408 | ISSN:2251-6727

to lower glycaemic responses to oral glucose or standard meals, indicating improved insulin sensitivity. However, a study showed no significant effect of colonic fermentation of carbohydrates on insulin resistance (9)

Skin Microbial Communities

The human skin microbiome exhibits a profound relationship with the innate and adaptive host immune system, particularly in skin disorders like atopic dermatitis and psoriasis. Skin microbial communities contribute to the maintenance of the skin microenvironment by modulating the gene expression of host-produced immune factors and pro-inflammatory cytokines. Cancer treatments, including chemotherapy, radiation therapy (RT), and immunotherapy, can lead to prominent adverse skin toxicities such as dermatitis, rash, and alopecia, among other irritating skin reactions (41) While limited studies have characterized the skin microbial profiles associated with these toxicities, insights from pro-inflammatory skin disorders like atopic dermatitis and psoriasis can be extrapolated. Robust clinical studies are essential to investigate the role of the skin microbiome in cancer treatment-related skin toxicities (42)

A healthy skin microbiome serves as protection against pathogenic organisms, and disruptions in the microenvironment can lead to skin irritations, including acute dermatitis and psoriasis, as well as skin toxicities induced by cancer treatments (43) Future studies are likely to leverage whole-genome sequencing to explore the direct mechanisms between microbes and the host, evaluating the therapeutic targeting potential of the skin microbiome in irritated skin. By identifying key patterns in microbial dysbiosis, earlier diagnosis and improved treatment strategies can address specific quality of life (QOL) concerns.

Staphylococcus lugdunensis has been suspected to be part of the normal skin flora, particularly in the pelvic region. While some authors suggest that S. lugdunensis can be found over the entire human skin surface, others propose that its preferred site of carriage is the perineum, based on a nationwide survey of skin and post-surgical wound infections (44)

The skin microbiota plays an intricate role in various immune functions and contributes to defending the host against invading bacterial pathogens. Advancements in sequencing technology allow for the exploitation of identified healthy human skin microbiota in clinical diagnostics or therapeutic strategies. Resident microbiota may become pathogenic, especially in response to an impaired skin barrier (45)

In the context of staphylococcal and streptococcal pathogens, skin flora and intramammary infections (IMIs) serve as the main reservoir. Infections are typically spread and established during milking or nursing. Although supporting evidence for their use is minimal, udder hygiene practices common to cattle dairies are encouraged in sheep and goat dairy operations (46)

Effects of Radiation on Skin Flora

Radiation therapy skin reactions are among the most prevalent side effects, causing distress for patients. Severe radiation-induced skin reactions can sometimes restrict the delivered dose and potentially compromise treatment outcomes. While there are established best practices, approaches and patient advice have seen minimal evolution over the years and are often rooted in tradition rather than evidence. Canadian radiation therapy departments employ various skin care products and approaches, with limited exploration of national practice patterns (47)

A knowledge gap persists regarding the biological mechanisms of skin microbiome dysbiosis leading to chemotherapy-induced skin toxicities like alopecia and hand-foot syndrome. Understanding the skin microbiome and its associations with chemotherapy-related skin toxicities can facilitate the development of strategic planning and therapeutic interventions to enhance patients' well-being.

Our skin is host to millions of bacteria, fungi, and viruses constituting the skin microbiota. Similar to the gut microbiota, skin microorganisms play essential roles in protecting against invading pathogens, educating the immune system, and breaking down natural products (48,49). As the largest organ in the human body, the skin is colonized by beneficial microorganisms and acts as a physical barrier to prevent pathogen invasion. Skin disease or systemic disease can result when the barrier is compromised or when the balance between commensals and pathogens is disturbed. Human skin sites can be categorized based on their physiological characteristics—whether they are sebaceous (oily), moist, or dry (50)

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The anatomical and physiological structures of human skin constitute the protective shield of the body. Influenced by the surroundings, human skin is the site where billions of microbial communities form a unique ecosystem, continuously modulating host immunity and metabolism. Normal skin functions require integral collaborations between epidermal barriers, skin immunity, and microbial inhabitants. The composition and structure of microbial ecosystems associated with human skin are influenced by factors such as age, gender, weather, lifestyle, and the use of medicated preparations (51,52,53)

The skin microbiome is known to depend on the local "micro-environment" of the skin site. In adults, differences in bacterial population composition, diversity, and evenness exist between sites that are relatively more sebaceous, moist, or dry (54,55)

As a primary defense against infection, the skin serves as both a physical and immunologic barrier. Alongside the gut, the skin is heavily immune-surveyed and must distinguish between self and other, as well as between beneficial and pathogenic microbes (56). The skin barrier is critical for survival, preventing the escape of moisture and invasion by infectious or toxic substances. The skin is also a complex habitat for a diverse population of microbiota, colonized during the birthing process and subsequent exposure to the post-natal environment (57)

Composition of the skin microbiota - In sequencing surveys of healthy adults the composition of microbial communities was found to be primarily dependent on the physiology of the skin site, with changes in the relative abundance of bacterial taxa associated with moist, dry and sebaceous microenvironments. Sebaceous sites were dominated by lipophilic *Propionibacterium* species, whereas bacteria that thrive in humid environments, such as *Staphylococcus* and *Corynebacterium* species, were preferentially abundant in moist areas, including the bends of the elbows and the feet. (50)Several recent studies have set out to investigate the composition of microbial communities on the skin at various anatomical locations. One of the key take-home points arising from these studies is that just as the microbiome of the skin differs greatly from that of the gastrointestinal tract or oral cavity, so too do the populations from different areas of the skin. (58)

The skin microbiota primarily comprises bacteria falling into four phyla: Firmicutes, Bacteroidetes, Proteobacteria, and Actinobacteria. While these bacterial groups are recognized, strain-level identification remains unclear. Acknowledging that two different strains of the same bacterial species can exhibit profound functional differences underscores the critical need to advance research in this more functional direction. Although less understood, other resident microorganisms such as viruses, fungi, and parasites are likely to interact with the broader ecosystem and influence cutaneous immunity(57)

The human microbiome encompasses microorganisms and their collective genome residing in a specific anatomical niche. Advances in sequencing analysis, such as bacterial 16S ribosomal RNA gene sequencing, have provided substantial insights into previously obscure ecosystems operating on and within the human body. Recognizing the functionally essential metabolic roles played by microbes and their symbiotic relationship with other forms of life, the holobiont perspective characterizes humans as a multi-species entity (59).

Radiation-induced dermatitis (RID) poses a challenge for clinicians, especially since it is almost acquired by all cancer patients undergoing radiotherapy and contributes to additional healthcare expenditure. To date, detailed characterization of microbial contributions to the bioburden of skin disorders has been primarily focused on studying conditions such as atopic dermatitis, psoriasis, diabetic foot, and burns. Furthermore, the predominant concern lies with culture-based approaches, which are limited to a scanty number of microorganisms and consequently overlook the integral role of the entire microbial community (51,60,61).Cancer treatments, encompassing chemotherapy, radiation therapy [RT], and immunotherapy, have significantly enhanced cancer survival rates, yet they often give rise to skin toxicities (62). The severity of these skin toxicities varies across different treatments (63). Distressing for patients, these toxicities can alter appearance and serve as constant reminders of their illness. Treatment-related skin toxicities impacting quality of life (QOL) can curtail daily functionality, necessitate modifications in therapy schedules, and may even result in treatment termination .(63)

In the context of radiation therapy [RT], radiation dermatitis is a prevalent issue affecting up to 90% of patients undergoing RT (64,65). The severity of

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JCHR (2024) 14(1), 1396-1408 | ISSN:2251-6727

radiation dermatitis ranges from mild erythema to moist desquamation, leading to dramatic acute skin reactions (65,66), and/or chronic skin alterations that can significantly impact patients' QOL (65,67,68,69).

Approximately 95% of breast cancer (BC) patients undergoing radiotherapy (RT) experience varying degrees of radiation dermatitis (RD), significantly affecting their quality of life and aesthetics. Severe acute RD may necessitate the interruption or delay of RT. Currently, there is no consensus on the prevention and management of RD. The skin microbiota (SM), primarily consisting of bacteria and fungi, play a crucial role in skin homeostasis, and microbial dysbiosis is correlated with the onset and progression of various common skin diseases. However, research on the role of the SM in RD is currently limited. This prospective, longitudinal study aims to analyze the association of SM with RD (70)

Pulmonary Flora and Radiation

Bronchitis was identified as a reservoir for oropharyngeal bacteria, and potential pathogens were isolated from the bronchi in three patients. Individuals with central and peripheral carcinomas accompanied by chronic bronchitis exhibited the presence of both "oropharyngeal commensals" and "potential pathogens" in their bronchi, with pneumococci, staphylococci, and H. Influenza being the most prevalent pathogens in carcinoma patients (71)

Detection rates of S. pneumoniae, H. influenzae, and M. catarrhalis in nasopharyngeal secretions are highest in the 6 years and younger age group, with rates decreasing as age increases (72). H. influenzae shows a similar age-dependent distribution, with infants and older individuals carrying it less frequently and less heavily than 5 to 6-year-old children. Its nearly ubiquitous presence in individuals of all ages poses challenges in understanding its clinical significance (73)

A stable microbial system in the respiratory tract plays a crucial role in defense against pathogenic microorganisms. Disruptions in this system may allow the establishment of pathogens. The human oropharynx is typically colonized by aerobic and microaerophilic bacteria, along with anaerobes. The mucosa of the nasopharynx, trachea, and major bronchi is also colonized by both aerobic and anaerobic bacteria, coexisting without overgrowth. Furthermore, the physiological functions of the mucosa, such as a protective barrier, mucociliary clearance, and air humidification, remain unimpeded (74).

In recent years, the human microbiome, particularly the gut microbiome, has been implicated in playing vital roles in lung diseases such as chronic obstructive pulmonary diseases (COPD), cystic fibrosis, and asthma. The stable characteristics of individual microbiota over the long term suggest its potential application as a biomarker for the diagnosis and prognosis of various diseases (75)

Respiratory Microbiota And Radiation–

Radiation-induced pulmonary injury stands as a significant dose-limiting toxicity linked to thoracic radiotherapy. The widely adopted 16S ribosomal RNA sequencing technology facilitates the classification and identification of bacteria in airway microbiome analysis (76). With the widespread use of radiotherapy for thoracic tumors, including lymphoma, breast cancer, and lung cancer, radiation-induced pulmonary injury (RIPI) has become a prevalent and often unavoidable complication, contributing to a poor prognosis.

Radiation recall pneumonitis (RRP) manifests as an acute inflammatory response in a previously irradiated lung following the administration of systemic antineoplastic agents (77). It may occur at any point during treatment, with the severity unrelated to the interval between radiotherapy and antineoplastic treatment (78). Taxanes and anthracyclines are commonly associated with RRP.

Radiation-induced lung injury (RILI), involving damage to the lungs from ionizing radiation, exhibits early and late toxicity manifestations, ranging from asymptomatic to severe. Advanced treatment delivery technologies like intensity-modulated RT (IMRT), volumetric arc radiotherapy (VMAT), and stereotactic body radiation therapy (SBRT) aim to minimize lung injury by providing highly individualized radiation treatment for primary tumors. Despite being generally well-tolerated, significant lung toxicity is reported in up to 20% of cases (79,80).

Certain chemotherapeutic agents, such as doxorubicin, taxanes, bleomycin, cyclophosphamide, vincristine, mitomycin, gemcitabine, and bevacizumab, are recognized as radiotherapy sensitizers due to their synergistic effects. Taxane-induced pneumonitis appears to be higher when combined with other cytotoxic drugs, particularly gemcitabine (81)

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Radiation-induced pneumonitis results in the loss of alveolar barrier function by damaging epithelial and endothelial cells, triggering an inflammatory response characterized by increased inflammation, vascular permeability, and cytokine release. Macrophage accumulation and activation contribute to hypoxia, leading to the production of reactive oxygen and nitrogen species (ROS/RNS) and proinflammatory, profibrogenic, and proangiogenic cytokines. These factors perpetuate non-healing tissue responses, culminating in chronic radiation injury (81,82).

Radiation-induced fibrosis (RIPF) is a late effect of radiation on the lungs, developing in the third phase of radiation-induced lung tissue damage. The first phase is asymptomatic, while the second phase, radiation-induced pneumonitis, occurs within weeks to months after radiation, resulting in non-infectious lung inflammation (83)

Radiation And Brain

Radiation initiates a reparative sequence in normal tissues, commencing with the DNA damage response involving apoptosis, mitotic cell death, and cellular senescence(84). Subsequently, an ongoing cytokine cascade follows, inducing inflammation and excessive extracellular matrix (ECM) and collagen deposition. These processes are predominantly regulated by an imbalance in reactive oxygen and nitrogen species (ROS/RNS) and tissue hypoxia (85).

The side effects of radiotherapy on normal tissue can be categorized as either early (acute) or late responses, depending on tissue turnover time and their modulation by processes resembling wound healing (85). Early side effects manifest during, immediately after, or shortly (within weeks) following radiotherapy treatment (85,(86). These effects are often reversible with limited doses and high tissue turnover, such as in the oral mucosa (87) and gut, or partly reversible, as observed in the lungs (pneumonitis) (88), skin (89), and brain (memory loss and fatigue(90,91)

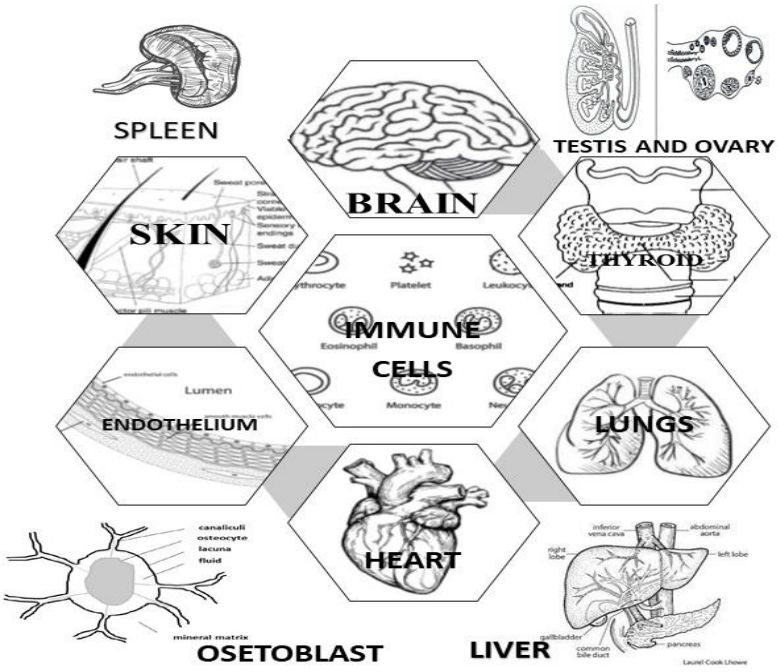

Figure.1 Radiation can mark tissues and organs

DISCUSSION

Radiation-induced salivary gland injury is prevalent in head and neck cancer (HNC) patients undergoing radiotherapy alone or in combination with chemotherapy and/or surgery. This often leads to unavoidable irradiation of peripherally located salivary glands, resulting in moderate or severe xerostomia (‘dry mouth syndrome’) in 40% of HNC patients receiving intensity-modulated radiation therapy (IMRT). This condition, characterized by hyposalivation, adversely

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JCHR (2024) 14(1), 1396-1408 | ISSN:2251-6727

affects speech, taste, mastication, deglutition, and increases the risk of oral infections and dental caries, significantly impacting the quality of life for affected patients. (92,93)

Radiation-induced brain injury (RIBI) is a common complication of radiotherapy for brain tumors, manifesting in acute, subacute, and chronic stages. Acutely, patients may experience transient and reversible symptoms such as nausea, vomiting, and headaches. Subacute symptoms include drowsiness, attention deficits, and worsening of initial symptoms, while the chronic stage, extending beyond six months, is characterized by progressive and often irreversible cognitive dysfunction and brain necrosis. RIBI's pathogenesis involves vascular and blood-brain barrier damage, immune inflammatory response, and oxidative stress. Radiotherapy-induced neurocognitive dysfunction is a significant side effect affecting adult and paediatric cancer survivors, impacting school performance, employment, and independent living. (94)

The brain, composed mainly of postmitotic neurons and glial cells, faces challenges in dissecting the contribution of each cell type to the neurocognitive dysfunction occurring as a late response (> 4 months) after radiotherapy(91).RIBI is a frequent complication of brain tumor radiotherapy or accidental radiation exposure, with the underlying pathological mechanism still unclear, and no established treatment available(95). Acute RIBI presents during and/or within days to weeks after irradiation (96). Assessing individuals exposed to various radiation doses relies largely on signs and symptoms or bio dosimetry (97) Early, accurate diagnosis of RIBI is crucial, but validated imaging methods for assessing radiation-induced injury are currently lacking. Hence, there is an urgent need to develop non-invasive imaging markers to evaluate the extent of acute RIBI(98)..

FUTURE PROSPECT

Thoroughly designed, high-caliber, and extensive investigations are essential to meticulously explore the role of ionizing radiation in dysbiosis. To deepen our understanding of this process, it is imperative to conduct studies on a larger scale, employing improved designs and extended follow-up periods. The existing evidence strongly suggests a direct correlation between ionizing radiation and dysbiosis, impacting both gastrointestinal toxicity and the efficacy of radiotherapy. A comprehensive understanding of the systemic effects of ionizing radiation and their connection to the human microbiota is crucial. The baseline microbial characteristics hold promise as predictive tools to identify patients likely to derive greater benefits from cancer treatments. Future prospective longitudinal studies, involving larger sample sizes, will facilitate the development of more intricate models. These models should incorporate essential factors such as demographics, chronic medications, exercise, diet, and biological elements that may influence the composition of the human microbiota.

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