



## Radiotherapy Treatment for Melanoma Skin Cancer Disease

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### ABSTRACT

**Background:** Melanoma is a skin disorder caused by malignant degeneration of the pigment cells melanocytes. The disease is characterized by widespread discoloration with irregular and protruding edges. In treating cancer itself, radiotherapy technology, has been found. It is a method of treating cancer using high-energy radiation rays focused on cancerous tissue to kill or stop cancer cell division. This study aims to determine the effectiveness of radiotherapy technology as a treatment solution for melanoma skin cancer. The focuses of the study in this paper are the integumentary system and skin structure, melanoma skin cancer, the body's mechanisms for melanoma skin cancer, and radiotherapy as a treatment method. **Methods:** The research method used is a literature study narrative review from various sources, to help understand the problem more deeply and completely. **Conclusions:** Melanoma, which attacks one of the body's integumentary systems, namely the skin, has a close relationship with homeostatic dysregulation and endocrine damage. However, radiotherapy can be used to cure melanoma skin cancer by shooting X-rays, damaging the cancer cells, and reducing their spread to other parts of the organs. This method is effective because melanoma skin cancer is localized or has not spread to other organs. However, the use of radiotherapy can also have a negative impact on the body and can give unwanted side effects, so consideration is needed before using this method.

### Radioterapi untuk Penanganan Penyakit Kanker Kulit Melanoma

### ABSTRAK

**Background:** Melanoma adalah kelainan kulit yang disebabkan oleh degenerasi sel pigmen melanosit ke arah keganasan. Penyakit ini ditandai dengan perubahan warna yang meluas dengan tepi yang tidak beraturan dan menonjol. Dalam penanganan kanker sendiri, sudah ditemukan teknologi radioterapi, yaitu metode pengobatan kanker dengan menggunakan sinar radiasi berenergi tinggi yang difokuskan pada jaringan kanker untuk membunuh atau menghentikan pembelahan sel kanker. Penelitian ini bertujuan untuk mengetahui efektivitas teknologi radioterapi sebagai solusi pengobatan penyakit kanker kulit melanoma. Fokus kajian dalam artikel ini adalah sistem integumen dan struktur kulit, kanker kulit melanoma, mekanisme tubuh pada kondisi kanker kulit, dan radioterapi sebagai alat penyembuhan. **Metode:** Metode penelitian yang digunakan adalah kajian literatur *narrative review* dari berbagai sumber, untuk membantu memahami materi lebih dalam dan lengkap. **Kesimpulan:** Kesimpulan yang diperoleh adalah kanker kulit melanoma memiliki hubungan yang erat dengan disregulasi homeostasis, kerusakan endokrin, dan penyebaran saraf. Namun, radioterapi dapat digunakan untuk menyembuhkan kanker kulit melanoma dengan menembakkan sinar X yang merusak sel-sel kanker dan mengurangi penyebarannya ke bagian organ lainnya. Metode ini efektif karena kanker kulit melanoma bersifat terlokalisasi atau belum menyebar ke organ lain. Namun, penggunaan radioterapi juga dapat berdampak negatif pada tubuh dan memberikan efek samping yang tidak diinginkan.



## Introduction

Cancer is the disease with the number two most patient deaths in Indonesia. One of the most common types of skin cancer is melanoma. In Indonesia, melanoma skin cancer ranks third after uterine cancer and breast cancer. Melanoma is a skin disorder that stems from the degeneration of melanocyte pigment cells toward malignancy. This disease is characterized by a discolouration that widens with irregular and prominent edges (Muhartono & Handriko, 2017). Melanoma is more common in white people because their melanin defenses are not as good as people whose skin is darker and can also occur in residents in places exposed to a lot of sunlight, one of which is Indonesia (Istighfaricha, n. d.). This is what makes the treatment of melanoma skin cancer need to be removed in the article.

The rapid development of technology greatly affects various areas of human life, one of which is in the field of health. In the treatment of cancer itself, radiotherapy technology has been found to be quite capable of handling various types of cancer, including melanoma skin cancer. Radiotherapy is a cancer treatment using high-energy radiation beams focused on cancerous tissue to kill or stop cancer cell division and is also called radiation therapy (Nurhayanti & Lusiyanti, 2006). According to Fitriatuzzakiyyah, Sinuraya, and Puspitasari (2017), out of the 10.9 million people diagnosed with cancer worldwide each year, at least 50% require radiotherapy and 60% of whom are curatively treated. For melanoma itself, it is said that radiotherapy is very effective for treating this type of cancer with only a 5% chance of reappearance and a 1.4% chance of developing melanoma.

This study aims to find out the effectiveness of radiotherapy technology as a solution to the treatment of cancer, especially melanoma skin cancer.

## Method

The research method used is a narrative review literature review, which is a study that aims to identify and conclude what has been published previously, avoid duplication, and look for areas of study that have not been observed (Ferrari, 2015). This article will discuss four focus studies: 1) the integument system and skin structure, 2) melanoma skin cancer, 3) body mechanisms in skin cancer conditions, and 4) radiotherapy technology.

### *Integument system and skin structure*

An integument system is an organ system that distinguishes, separates, protects, and informs animals of their environment. The integumental system in humans consists of skin, nails, hair, sweat glands, oil glands and mammary glands (Andriyani et al., 2015). The integument system protects the internal and external structures of the body from damage (Risnawati, 2019). The skin is one part

of the integumental system in humans and is one of the largest organs of the entire body with many functions. The skin is a sensory organ that has receptors against heat, cold, touch pain and pressure (Bolon et al., 2020).

The layer of skin and its complementary parts are divided into 3 layers, namely the dermis, hypodermis, and epidermis. The epidermis is the outermost layer of the skin, in a layered epithelium, with several layers visible. There are eccrine and apocrine sweat glands, hair, sebaceous glands, and nails in the epidermis. The outermost part of the epidermis is formed from horns in the corneum layer formed by old skin cells, while the lower part of the epidermis is called the basal layer, where there are cells that will continue to divide to form new skin cells and will continue to rise to the surface, and melanin is also found in this part (Wibowo, 2015). The big picture of the dermis is the fibres that bind together. Most are made up of collagen and the rest consists of elastin fibres with the main cellular elements in the form of fibroblasts, mast cells, and macrophages also contain many blood vessels, lymph, nerves, and sensory receptors (Brown & Burns, 2005).

The structure of the skin will support the implementation of the function of the skin. The skin has many functions including (1) covering and protecting the organs underneath, (2) protecting the body from the entry of microorganisms, (3) temperature regulation, (4) excretion, (5) synthesis, and (6) fat hoarders (Andriyani et al., 2015).

An example of one of the skin functions, namely excretion, is the expenditure of sweat. Sweat released on some parts of the body has a special odor and each is produced by the apocrine gland or odiferus (Andriyani et al., 2015). The skin also protects the human body from the UV rays emitted by the sun with melanin. In human skin, there are melanocytes which are large dendrite cells derived from kista neuralis that play a role in producing melanin pigment. The main stimulus for melanin formation is ultraviolet (UV) radiation. Melanin protects the cell nucleus in the epidermis against radiation (UV) (Brown & burns, 2005).

### *Melanoma Skin Cancer*

Cancer in general can be defined as a disease caused by abnormal cells of body tissues. Cancer cells divide and develop uncontrollably (Cancerhelps, 2014). In line with this, Prastiwi (2012) quoted in the encyclopedia (1990: 121) that cancer is the cells of body tissues that become malignant because cells divide rapidly and uncontrollably and form similar cells, but in primitive form or form become imperfect. Urip (2002) explained that from various research results, the onset of cancer is mostly due to unhealthy lifestyles such as unbalanced eating habits, smoking, drinking alcoholic beverages, excessive contact with the sun, and frequent sex partners.

Cancer is a disease that consists of various types, one of which is skin cancer. According to [Septian et al. \(2016\)](#), skin cancer is an abnormal skin cell growth that cannot be controlled. Similarly, [Wilvestra et al. \(2018\)](#) explained that skin cancer is a lump or excessive growth of skin tissue that hits part or all of the skin layer, which has an irregular structure with cell differentiation in various levels in chromatin, nucleus and cytoplasm, is expansive, infiltrative to damage the surrounding tissues, and metastasize through blood vessels and or lymph vessels.

Skin cancer has 3 main types, namely carcinomal basal cells, squamous cell carcinoma and malignant melanoma ([Hendaria et al., 2006](#)). While according to [Ardhiansia \(2019\)](#), skin cancer is divided into 2, namely:

1. Malignant melanoma (MM). Malignant melanoma is separated from other skin cancers because it has different behaviors.
2. Non melanoma, which can be divided into 3, namely:
  - a) Basall cell carcinoma (BCC), has the greatest incidence of the non-melanoma skin cancer group by 75%.
  - b) Squamous cell carcinoma (SCC)/epidermoid carcinoma.
  - c) Skin adnexal tumor (SAT).

Tan and [Dewi \(2015\)](#) explained that malignant melanoma (MM) is a skin malignancy that comes from melanocyte cells. These cells are able to form melanin so that in general MM is brown or black. There are 95 cases found on the skin, but there are several cases of malinoma found in the organs of the eyes, ears, mouth, gastrointestinal tract of the genital mucosa and leptomenigen ([Hanum & Supriana, 2019](#)).

### **Mechanisms of the Body in the Condition of Melanoma Skin Cancer**

Melanoma is a skin cancer characterized by discoloration or pigmentation of the skin accompanied by bleeding, hardening, and hives ([Hanum & Supriana, 2015](#)). The characteristics of melanoma are also characterized by the criteria of asymmetric lesions, iregular edges, then colors such as patterned, brownish, black, gray and white, with a diameter of more than 6 mm, changes in size, shape, and surface, which are getting bigger and hardened.

According to [Ramda \(2014\)](#), melanin in the body actually gives color to the skin or for pigmentation, but the occurrence of skin cancer or melanoma is caused by too much exposure to UV rays from the sun so that it can damage melanocyte cells. Damage to these cells can have an impact spread to other parts of the body. This cancer is also a type of superficial spreading that can attack the outer layer of skin (epidermis) and can enter the deeper layer again in some time (months or years).

Skin cancers, particularly melanoma, occur related to dysfunction of homeostasis and endocrine systems in the body. Homeostasis is a process that occurs continuously to maintain stability within the limits of tolerance of cell physiology, not in static conditions ([Irawati, 2020](#)). Physiologically, homeostasis determines a cell's attitude toward a condition, such as time for silence, dividing, differentiation, or apoptosis or cell death. This dysregulation will cause a breakdown of the balance of the melanin unit that triggers continuous cell division of melanocytes that will lead to the development of melanoma.

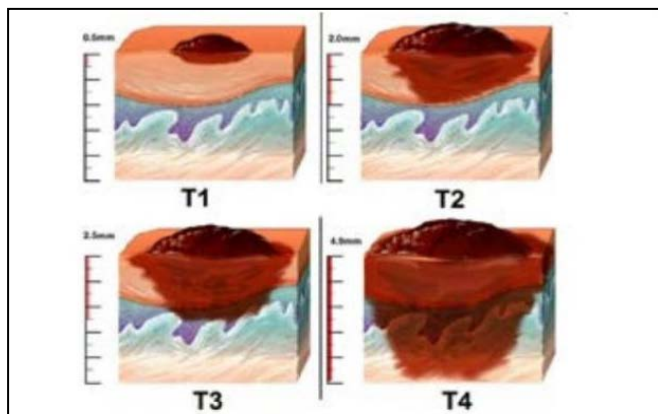
Melanoma skin cancer occurs vulnerable at an advanced age or old age. When a person has entered old age, there begins to be a hormonal imbalance so that in a long time will make carcinogens work to cause cancer ([Sudiono, 2016](#)). According to [Campbell et al. \(2002\)](#), carcinogens are chemicals that can cause cancer. MSH or melanocyte stimulating hormone is a hormone that plays a role in forming pigmentation or color on the skin ([Mardiati & Maulina, 2019](#)). This hormone can increase rapidly along with the increase in the hormones progesterone and estrogen during pregnancy in a mother ([Pratama et al., 2010](#)). This means that an increase in the hormone MSH in the body can also have a major effect on excessive melasma growth, so it can cause skin cancer cells to appear. This is what includes being an internal trigger of the body in the growth of melanoma skin cancer.

Melanoma skin cancer is certainly a thing that interferes with the function and work of cells, tissues, organs and organ systems in the human body. [Liokova et al. \(2019\)](#) explained that skin cancer cells also have the ability to metastasize, especially those that can spread to other tissues, such as fat, muscle, or bone tissue. [Tan and Dewi \(2015\)](#) explained that at level 5, the severity of the disease and its growing size certainly cause invasion or infection into the subcutaneous tissue.

Cancer usually has a stage or severity level. The "T" category is given from a scale of 1 to 4 based on how deeply melanoma tumors have grown inside the skin. Level 1, i.e. in situ melanoma involves the epidermis and there is no invasion; level 2, i.e. infiltration of the upper range of papillary dermis; level 3, i.e. melanoma cells fill and expand to the border of the papillary dermis; level 4, i.e. infiltration of the reticular epidermis, not into subcutaneous tissue; Level 5 is subcutaneous infiltration. The higher the level, the worse the patient's condition, an example of its thickness with a range of 0.6 - 1.1 mm ([Massi & LeBoit, 2004](#)). The development of melanoma in the skin can be seen in Figure 1.

At the time of the in situ level, melanoma cells are confined almost exclusively or divide the papillary dermis in the form of a single cell or small nest of melanocytes that are similar in size and number no more than 5-10 melanose

cells, then the melanocyte deposits exist along the dermal epidermis, replacing the basilar region and the spread of pagetoids (spreading upwards) that occurs at level 3 (Nickoloff et al., 2001).



**Figure 1.** Development of melanoma in the skin (Shead et al., 2018). Description: T1: 0.5-1 mm, T2:2 mm, T3:2.5-4 mm, and T4: more than 4 mm.

Shead et al. (2018) also explained the same thing, namely melanoma skin cancer is divided into 5 stages. At stage 0, melanocytes exist in their natural place, i.e. in the epidermis (outer layer of skin) and have not invaded the dermis (the second layer of skin under the epidermis). In stage 1, the tumor is thinner by about 0.8 - 1.0 mm, the cell divides slowly, no ulceration is visible under the microscope, then at this stage there is no cancer inside the lymph vessels, lymph nodes, or distant organs. In stage 2, the tumour's thickness is greater than 1.0 - 2.0 mm with ulceration or non-ulceration status, but there is no cancer in lymph vessels, lymph nodes, or distant organs. In stage 3, the thickness reaches 2.0 - 4.0 mm, melanocytes have spread to nearby vessels and lymph nodes, or nearby skin. In stage 4, the tumor gets thicker above 4.0 mm, spreads to further places, spreads to the vessels and lymph nodes as well as nearby organs such as the lungs, liver, or brain. Ulceration status means telling whether the upper skin layer of the tumor is present and intact (not ulcerated) or the lining is damaged or lost (ulceration).

**Radiotherapy Technology**

Treatment of skin cancer can be done through surgery, radiotherapy, chemotherapy, and immunotherapy (Mulyani & Nuryani, 2013). Radiotherapy is the use of high-energy waves, such as X-rays for cancer cell-killing therapy (Rosidah et al., 2017). Radiotherapy is a curative therapy that treats local cancer, so it is difficult to use for cancers that have metastasized to other organs (Soekin et al., 2017). Radiotherapy can be given before and after other treatment methods, or it can also be done in conjunction with chemotherapy (Fitriatuzzakiyyah et al., 2017).

Radiotherapy aims to kill the tumor as close and as much as possible while still protecting and minimizing exposure to normal tissue (Baskar et al., 2012). Radiotherapy uses ionizing radiation that forms ions and stores energy to the tissue cells that pass through it. This energy store will kill cancer cells and alter the genetics that will result in cancer cell death (Fitriatuzzakiyyah et al., 2017).

According to Fitriatuzzakiyyah et al. (2017), there are 5 ways radiotherapy induces cell death, namely by apoptosis, autophagy, necrosis, senescence, and mitosis death. Apoptosis is a form of programmed cell death that occurs when there is cell shrinkage and chromatin fragmentation. Autophagy is when a cell digests its part of the cytoplasm. Necrosis is the uncontrolled death of cells due to environmental conditions, such as extreme pH changes, infection, or loss of energy. Senescence is a state that a cell can't permanently divide anymore. Mitosis death occurs when cells undergo an abnormal process of mitosis because DNA damage occurs after the radiation process. The death of mitosis is often experienced by cancer cells after irradiation. The rate of tumour response depends on the level of proliferation or ability to divide it, the conditions of the surrounding microenvironment, and interaction with extracellular matter so it can be said that cancer cells do not have uniform sensitivity (Setyawan & Djakaria, 2013).

According to Baskar et al. (2012), the biological target of radiotherapy is DNA from cells. Radiotherapy can work directly or indirectly. Radiation can interact directly with a cell's DNA resulting in cell damage. Radiation can also indirectly affect DNA damage by producing free radicals from ionization or obstruction of water components in the cell. The effect is DNA damage in both chain or in one of the pills. DNA that only damages one of its pills is enough to kill a cell and disrupt its genome, but the DNA of the two damaged will be more effective and kill the cell more because it is more difficult to repair (Baskar et al., 2012).

Although radiotherapy can be a safe therapy to cure cancer, like all treatments in general, radiotherapy also has side effects on the body, especially in normal cells or tissues exposed to radiation when directed to cancer cells. According to Setyawan and Djakaria (2013), radiation beams from radiotherapy can affect the performance of several organ systems.

The first organ system affected is the circulatory system, especially in the blood that flows throughout the body. Blood cells exposed to radiation rays decrease in number due to damage to hematopoietic stem cells and progenitor cells that are very sensitive to radiation. Radiation rays from radiotherapy can also have an impact on the skin. The skin can experience hyperpigmentation or darkened skin colour after radiotherapy due to the stimulation or destruction of melanocytes. Damage to the skin is

sometimes accompanied by dysfunction of blood vessels and fibroblasts in the dermis layer.

Suppose radiation rays from radiotherapy hit the gastrointestinal or digestive organ system. There can be damage to the villi in the intestinal organs because the villi are very sensitive to radiation causing digestive malfunctions. When it hits the central nervous system, such as the brain and spinal cord, radiation rays can result in endothelial cell apoptosis that alters permeability and causes edema. Radiation rays that hit the respiratory system, especially in the lungs, can cause the release of cells from the basal membrane, the capillaries in the alveolus are severed because they are very sensitive to radiation. In addition to the description above, there are many other risks that radiation rays can pose to the performance of organ systems in the human body.

The general impact for all organ systems is that it is difficult to form mature cells that are functional or can perform their functions well in any organ system (Garau et al., 2011). All the effects of radiation on normal cells and tissues are unwanted side effects, but cannot be avoided, so it becomes a consideration before taking radiotherapy action.

## Conclusion

The skin is one part of the human integument system and can not be separated from the possibility of getting diseases, such as melanoma skin cancer. Melanoma skin cancer is characterized by the presence of dark colored lumps with irregular edges. Melanoma skin cancer can occur due to exposure to UV rays that damage melanocyte cells and affect homeostasis and endocrine function. One of the efforts to reduce the propagation of cancer cells is the radiotherapy technique. Radiotherapy is an effective technology to treat melanoma skin cancer, by firing X-rays so that it can damage cancer cells and reduce its spread to other parts of the organ. However, it cannot be denied that the use of radiotherapy also has a negative impact on the body and provides unwanted side effects. Therefore, before patients decide to use this technology, they must consider the effects that will be caused in the future.

## Declaration statement

The authors reported no potential conflict of interest.

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