Brachytherapy Method Using Individualized Applicators to Increase Efficiency in Skin Tumors Treatment

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Abstract

Brachytherapy method using individualized applicators to increase efficiency in skin tumors treatment is presented. Skin tumors are one of the most common types of cancer in the world. Nonmelanoma skin basal cell and squamous cell skin carcinomas, known as NMSCs, are the most common cancers. The main purpose of this work is to comprehend basic treatment methods of skin tumors. The other purpose is to emphasize advantages and impact of the brachytherapy method using individualized applicators. Earlier skin tumor treatment methods are surgery and external (electron beam) radiotherapy. However, the brachytherapy method not widely used in skin tumor treatment process provides more efficient results due to the usage of individualized applicators specially produced for patients. Conclusively, individualized applicators provides more benefits and the fact that these applicators are improved much facilitates treatment process.

Keywords: Cancer, skin tumour, brachytherapy, individualized applicators
1. Introduction

In recent years, the cancer rate have been increasing due to the change in living and nutritional conditions [1]. According to the GLOBOCAN 2020 report published by the International Agency for Research on Cancer (IARC) affiliated with the World Health Organisation (WHO), 50.6 million cancer patients have been reported worldwide in the last 5 years, the data is collected from 185 countries. There were 19.3 million new cases and 10 million deaths due to cancer in 2020. Based on the collected data, it has been determined that one person in every 5 people has been diagnosed with cancer at least one time throughout their life, and one person in every 8 men and one person in every 11 women die due to cancer. In the same year, approximately 234 thousand new cases and 126 thousand deaths due to cancer were reported in Turkey. It is predicted that this rate will have increased up to 47% by 2040 [1,2]. Skin cancer is one of the most common types of encountered cancer in the world [3]. According to the WHO report, approximately 3 millions pre-cancerous lesion and 132 thousand malignant new skin cancer cases emerge every year [4]. As to Turkey, melanoma type skin cancer has increased up to 237% in the last 30 years. Melanoma, which creep to other organs, involved the majority of all skin cancer deaths [5].

Various methods such as surgery, chemotherapy and radiotherapy are applied for cancer treatments in the field of oncology. These treatment modalities are singly used or in combination one another in many types of cancer. Determining the treatment method depends on tumor type, size, location, patient performance status, patient preference and possible side effect factors. One of the common preferred methods in the treatment of skin tumors is radiotherapy. The radiotherapy is a treatment method that demolish the cancerous area by sending radiation energy in determined doses from a certain distance to the skin surface. The most important influencing factor of the efficiency of radiation therapy is that the patient is irradiated under the same conditions in each session. To enable this, various immobilization products and mold masks produced specifically are utilized for each patient. The most common immobilization tools are thermoplastic masks. Thermoplastic masks are stretched and forming to fit the patient's contours. This process causes the mask to have different thicknesses and hole diameters [6]. For this reason, some areas of the skin are more exposed to radiation and cause skin reactions. It is not possible for thermoplastic masks to provide the same immobilization in every fraction unless they are properly fixed in localizations such as the nose and ear. When
this problem is not solved, traditional radiotherapy may be insufficient to provide dose homogenization in skin tumor treatments.

Brachytherapy is one of the methods used in cancer treatment. It is the most effective method in protecting healthy tissues and implementation of radiation therapy focused on diseased tissues [7]. Electron beam radiotherapy are insufficient in the treatment of deep tumors in the body and therefore interstitial brachytherapy treatment is applied. Interstitial brachytherapy is a treatment method which is applied by placing applicators containing radioactive wires inside the body, near or in touch with the area where the tumor is located. This method requires anaesthesia and a surgery room environment [7,8]. The brachytherapy can be applied as interstitial or superficial application options. Interstitial brachytherapy aims to place the radioactive source directly into the lesion. In superficial applications, mold and superficial contact applicator are used. Mold applications are based on the technique of taking personalized molds in different anatomical regions. The usage of superficial applicators is implemented by ensuring direct contact of the applicator on flatter areas.

There are only a few medium voltage therapy devices in Turkey, but high dose rate (HDR-afterloading) brachytherapy devices are widely used. In cases where complex treatments are required due to tumor localization, personalized applicators, which are created with 3D printers, can be combined with brachytherapy devices and can be successful, especially in the treatment of complex skin cancers, without increasing the environmentally risky organ doses.

2. **External Beam Radiotherapy Methods**

Various radiotherapy methods are used in skin tumor treatments. The choice of treatment is decided by taking into consideration the histology of the lesion, its location, the patient's age, cosmetic and functional status. Surgery and radiotherapy are preferred for lesions that will not cause cosmetic or functional disorders in young patients. Radiotherapy can be applied before or after surgery. Surgery can be dangerous for older patients, so radiotherapy singly is often preferred. To briefly talk about the radiotherapy method, it is the usage of ionizing radiation in the treatment of cancer. Radiotherapy is a treatment method that demolish the cancerous area by sending radiation energy in determined doses from a certain distance to the skin surface. In radiotherapy applications, the choice of method is decided in accordance with the size, depth, and
location of the tumor. Methods are named in accordance with the type of radiation sent from the device.

In the electron method, healthy tissues under the tumor area can be protected due to the rapid deep dose reduction. Depending on the energy used, deeply penetrated tumors can be irradiated. If used in the treatment of superficial lesions, the aim is to increase the skin dose up to 100% by using bolus. However, it is difficult to protect healthy tissues around the tumor area. In addition, because of the fact that the masks fixed on the bolus are shaped by hand, the difference in thickness and air gaps prevent the planned dose from being delivered equally to the tumor area.

Although high-energy photons are not routinely used in skin cancer treatment, they are rarely used in advanced-stage lesions with deep invasion. Compared to other forms of treatment, it may be necessary to use multiple fields to achieve homogeneous dose distribution. This may lead to an increase in the dose of organs at risk around the tumor. So as to reduce the risk of chondritis, the daily fraction dose should be kept below 3 Gy. If large areas are treated, lower fractions are preferred. This may cause long treatment processes and serious side effects on healthy tissues.

Medium voltage X-ray therapy is the most commonly used radiotherapy method in the treatment of skin tumors. 75-100 kV energies are used for superficial lesions and 200-250 kV energies are used for deeper lesions. Medium voltage devices are quite scarce in Turkey, they are difficult to install and disadvantageous in terms of accessibility. Figure 1 shows the radiotherapy device in which the mega voltage device is also used.
Superficial tumors are not regularly shaped and deformation is often observed in the patient’s skin tissue. For this reason, mega voltage devices used in radiotherapy should focus on damaged tissue and it is difficult to preserve intact tissue. It is not possible to give the same dose of radiation to entire tumor area with mega voltage radiotherapy [9].

3. **Brachytherapy Method**

Traditional radiotherapy applications are insufficient in the treatment of deep tumors in the body. Brachytherapy treatment is especially used in the treatment of intrabronchial, intrauterine and any intra cavitary cancer types. Sometimes anaesthesia may be required in brachytherapy treatment. In brachytherapy treatment, radioactive wires are placed inside the body of patient for delivering damaged tissue-focused treatment. In this way, healthy tissues around the treatment area are protected and radiation therapy is applied in equal dosage to damaged tissues. It is the most effective method in protecting healthy tissues and implementation of radiation therapy focused on diseased tissues [10].

![Brachytherapy Device](image)

*Figure 2: Brachytherapy Device*

As seen in Figure 2, brachytherapy devices are portable devices, that are easy to access and use. Any desired treatment for skin cancer can be applied in hospitals or treatment centres with these devices. These favourable features of brachytherapy application have led to the idea that it can also be used in the treatment of skin tumors. When the applications of the method are examined, it is seen that many works have been conducted pertaining to this issue from different perspectives.
British Columbia Cancer Agency, one of the institutions worked regarding this issue, applied the superficial mold brachytherapy method to a total of 59 patients between the ages of 45-97 with skin tumors and the surface molds were specially shaped to the contours of the patient's area to be treated. Complete response rate was 96.8%. Partial response has been received from two patients and this could not be evaluated for response. The most common toxicities observed in patients have been skin dryness, dermatitis, pain and feeling of fatigue. Serious toxicities have not been observed. This treatment has resulted in a positive alternative option for patients who do not want or cannot undergo surgery due to skin malignancies [11]. In a study conducted by Goethe University with the Frankfurt Cancer Institute and the German Cancer Research Center; individualized 3D printer-based mold high dose rate (HDR) brachytherapy (BT) treatment have been applied to elderly and frail patients with facial skin tumors close to critical organs that are difficult to treat. As a result of experiment, HDR-BT with 3D printer based molds for use in facial skin cancer is well tolerated for elderly, frail patients, functional inoperability, and who cannot undergo radical surgery due to tumor location or patients not suitable for definitive EBRT. It has been determined to be a safe treatment option [12]. In study a conducted by G. Bieleda et al. in 2022 developed an applicator with 3D printing in the brachytherapy treatment of skin cancer for the treatment of basal cell carcinoma (BCC) and squamous cell carcinoma (SCC) tumors. Surgery is very effective in these skin tumors but in areas of the face where skin lesions are common and surgery is not recommended as there may be a risk of permanent injury. The study was carried out using low-cost equipment and free software for patients with a certain type of skin cancer and 3D printer applicator is being prepared for brachytherapy treatment of these skin cancer patients. All doses in the prepared report were given lower than the planned dose and the dose given was sufficient. Brachytherapy treatments applied to the surface of the skin, it is the standard treatment method for non-melanoma skin cancers and local control was achieved in 93-95% of these cases [13]. Semi-automatic treatment planning improved and clinically tested for 3D printable applicator holders in study conducted by Guthier et al. Digitizing information takes a long time and automates treatment planning as this workflow. Compared to printing full applicators, it has been shown to reduce complexity of 3D printing, the amount of materials to be used, length of printing time and the amount of quality assurance required. This proposed methodology was also concluded improves overall treatment plan quality in complex HDR-BT and potentially impact patients’ treatment outcomes [14].
Brachytherapy applications are not yet widely used in skin tumor treatments, and works are continue in this field. Appropriate applicators are needed patients’ skin tissue areas to be treated in order to apply brachytherapy method in superficial tumor treatments. It is important for treatment efficiency that the applicators fully adapt to the tissue in each treatment session. It allows that, the applicators used in brachytherapy fix the patient’s treatment area, ability to apply the planned dose amount in treatment and protection of healthy tissues. Unlike intentional brachytherapy, this method does not require surgery or anaesthesia. Expanding the use of brachytherapy treatment method in skin cancer patients may provide better results. Unlike many other types of cancer, patients with skin cancer are expected to survive for a long time. Therefore, the patient is desired to live a quality life. The ability of patients to receive treatment by living in their own comfort zone without leaving their hometown minimizes the psychological problems caused by the disease. When the applicator is attached, the area to be treated reaches the maximum dose, while the surrounding tissues are not affected as in medium voltage treatments. Designing the appropriate applicator for the patient not only increases the effectiveness of the treatment, but also ensures fixation of the treatment areas, application of the planned dose amount and protection of healthy tissues.

4. Result

Due to carried studies with developing technology, more efficient treatment methods have been being developed in addition to the treatment methods used for cancer diseases. The brachytherapy, offered as an alternative to the medium voltage radiotherapy treatment method used in skin cancers, is more accessible and cheaper. As a result of studies and researches, the brachytherapy application provides more efficient results in skin cancer in a shorter time. The usage of the developed applicators for the treatment area is a better option for various superficial tumor treatments, head and neck tumors, for patients who cannot undergo surgery and for people who do not respond radiotherapy. The brachytherapy method to superficial tumors with individualized applicators make it possible to increase treatment efficiency, protect healthy tissues and reduce treatment costs.

5. Discussion and Conclusion
It is thought brachytherapy method may allows accurate and safe radiotherapy to be applied to skin tumors in every hospital that has brachytherapy. Mega voltage devices are more expensive, difficult to install and have a disadvantage in terms of accessibility than other devices. This option makes brachytherapy treatment more convenient for skin cancer treatments. It is possible to protect the deformed surface tissues of patients by using individualized applicators produced with accessible tissue-equivalent materials. Damaged tissue focused treatment application and protection of healthy tissues can be achieved owing to radioactive wires placed inside applicators. The usage of applicators is difficult to fully adapt to the treatment area because of skin tissue deformation in superficial tumors. Individualized applicator models can be made with CT image from taken patients and applicators can be fully adapted to the patient surface texture with precision 3D printers. It is sufficient to have CT scan data of patients for applicator modeling and design. In this way, individualized applicators are produced by taking CT scans of patients who need superficial brachytherapy treatment in different cities, countries and treatment centres and patients can be sent to relevant institutions and hospitals.

References

[1] https://gco.iarc.fr/today/fact-sheets-cancers


