The Surgical Role of Radiation in the Treatment of Melanoma

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Honors Biology
1/8/13

ABSTRACT

Radiation, specifically x-rays, is the treatment method that this paper will be focusing on.

The objective of this review paper is to delve into what makes radiotherapy different from the other treatment methods of melanoma, and why and how it is used. Radiotherapy is an effective method of treating melanoma, and this paper will show how extraordinary it can be when it is used safely and correctly.

INTRODUCTION

Cancer is when abnormal cells that have been mutated divide uncontrollably. There are several different types of cancer, but the one that will be focused on in this paper is melanoma. Melanoma is a skin cancer that begins in a certain type of skin cell called melanocytes, which provide pigment for the skin, eyes, and hair (American Cancer Society 2013). It is the deadliest skin cancer and results from unrepaired DNA damage to skin cells (Skin Cancer Foundation 2013). This occurs often from excess exposure to Ultraviolet Radiation. The damaged DNA in the skin cells then triggers genetic mutations, which cause the cells to multiply rapidly and form malignant tumors (SCF 2013). Melanoma is most commonly found on the back, chest, legs, or face areas (ACS 2013). It is mainly found in the form of oddly colored (too dark or too light) or oddly shaped (too large or too small) moles (ACS 2013).



(Right) A mole that is both too awkwardly shaped and too dark to be a normal mole (Skin Cancer 2000).

Melanoma is usually curable when recognized and treated in Stage 1, but is extremely dangerous when neglected and can spread quickly to other parts of the body, where it can then be tough to treat or even fatal. There are four main treatment choices for melanoma:

Surgery, Chemotherapy, Biological Therapy, or Radiation Therapy. Surgery is the most commonly used melanoma therapy, and consists of cutting out the melanoma and the surrounding tissue to ensure no cancer cells remain. Surgery is used in nearly every occasion but when it cannot completely kill the cancer cells, the other choices must be used. If the melanoma is in Stage 3 or 4, chemotherapy can be used because although melanoma does not normally respond well to chemo, the cancer has already transferred to other parts of the body and cannot be taken out by surgery. Chemotherapy is the use of drugs to kill cancer cells, and can either be taken through the mouth or injected into the bloodstream. Another alternative is biological therapy, or immunotherapy, which is a form of treatment that uses the body's immune system to prevent the melanoma from coming back after surgery. The final treatment method is radiation. Radiation or radiotherapy, uses high energy waves, such as x-rays or gamma rays to kill cancer cells. Radiotherapy is used to control melanoma that has spread to the brain, bones or other parts of the body. Radiation kills the cancer cells so that they cannot divide or reproduce, preventing DNA Replication.

(Cancer Compass 2013).

TYPES OF RADIATION

External Radiation

External beam radiation therapy (EBRT) is a type of radiation therapy that directs a beam of radiation from outside the body at cancerous tissues inside the body.

EBRT delivers high-energy rays to tumors, using a special X-ray machine called a

linear accelerator. This machine allows radiation to be delivered from any angle and shapes radiation beams to the contour of the tumor. Radiation oncologists use EBRT to target a tumor with higher, more precise doses of radiation, while minimizing damage to healthy tissue and nearby organs. As a result, EBRT can reduce the risk of side effects typically associated with radiation treatment. EBRT is an outpatient procedure. This technique does not carry the standard risks or complications associated with major surgery for melanoma, which can include surgical bleeding, post-operative pain or the risk of stroke, heart attack or blood clot. The procedure itself is painless. EBRT poses no risk of radioactivity to the patient or others with whom the patient have contact. (Cancer Treatment Centers of America 2001).

Internal Radiation

Internal radiation therapy (also known as brachytherapy) delivers radioactive material to a location very close to the tumor from a source placed inside the body. Methods of delivery include injection, ingestion, or implantation. Radioactive materials are delivered to melanoma cells via monoclonal antibodies (cloned antibodies from a single parent cell), and laboratory-produced, infection-fighting proteins that can attach to targeted cancer cells. Cancer cells, including melanoma cells, have special marker substances on their surface, known as antigens. Monoclonal antibodies circulate through the bloodstream until they find melanoma cells with the target antigen. The antibodies then bind to the melanoma cells and signal other immune cells to help destroy or contain the tumor. When radioactive material is attached to the antibody, radiation is released directly

into the tumor to kill melanoma cells. The effectiveness of monoclonal antibodies as a stand-alone treatment or when coupled with radiation or chemotherapy is currently being investigated in clinical trials.

(Melanoma Center 2010).

USES OF RADIATION

Radiotherapy as a Primary Method of Treatment

Radiotherapy is rarely used as a primary treatment instead of surgery, which is the curative treatment of choice for all types of primary melanoma incisions. Poor performance status of the patient with severely low pain tolerance or refusal of proposed surgery are potential but less plausible motives in clinic for replacing surgery with radiotherapy. More frequent indication for upfront radiotherapy is lentigo maligna melanoma (LMM). Particularly when LMM is extensive and located on the face of elderly patient, radiotherapy is a good alternative to surgery. An experiment was conducted with a total of 107 patients. Of those 107, 3 local recurrences were observed 13-44 months after radiotherapy. Time to complete regression of the lesion (incision) after irradiation took up to 24 months. Regional node (organizer tissue) metastases (spread of cancer to different organs) developed in 3 patients 6, 8 and 18 months after therapy, respectively, whereas in one patient, pulmonary (lung) metastases occurred 44 months after treatment. All theses patients had their primaries (original tumor area) controlled. Thus, whenever surgery attempting to achieve clear margins would result in excessive mutilation, either cosmetic or functional, or in elderly patients, it should be

replaced with radiotherapy, which is effective and has curative potential in LMM. Because the incidence of regional metastases is extremely low, no elective irradiation of regional lymphatics is required. Primary curative radiotherapy should be attempted also in localized inoperable mucosal melanoma (MM) where it is considered the most effective treatment modality. 70% of the melanoma can be controlled by radiotherapy alone in MM, which could be then further improved by utilizing high-linear energy transfer (LET) radiation.

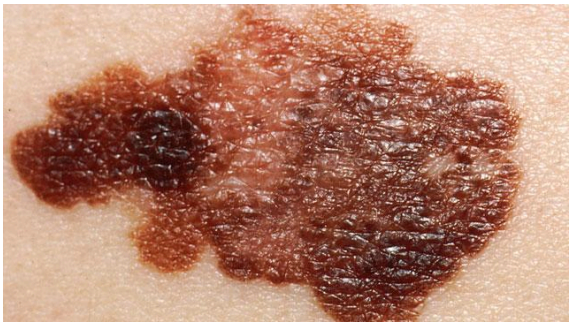
(Strojan 2010).

Adjuvant Radiotherapy

Adjuvant radiotherapy is radiation that is used after surgery to significantly reduce the risk of recurrence. Postoperative radiotherapy depends on the risk estimate for recurrence, treatment related side-effects and the possibility for successful salvage when recurrence occurs. The risk for serious complications after post-op radiotherapy is low. Factors that influence control are close or positive margins, early and/or multiple recurrences, extensive satellitosis (build up of neuroglial cells, which protect neurons) desmoplasia (growth of fibrous tissue) or neurotropism (attacking of tissue), and MM primaries (aggressive neoplasm, or build up of tissue). Recurrence may be related to the presence of neurotropism and inadequate surgical margins. Radiotherapy adds significant control after surgery. A study showed that after lymphadenectomy (cutting out of the lymph nodes) for recurrence of melanoma, less than 25% of patients considered to be at high risk of recurrence. The factors contributing to an increased recurrence are the

presence of residual disease after surgery, tumor extension outside of a joint, nodes measuring ≥3 cm in the largest diameter, multiple nodal involvement or recurrence after previous lymph node (tissue that helps recognize and fight germs) dissection (See Below). Comparison of studies using surgery alone or surgery plus radiotherapy provides a strong argument for the effectiveness of adjuvant irradiation. Tumor control is roughly 90% in adjuvantly irradiated patients.

(Strojan 2010).



(Right) Residual disease triggers recurrence in melanoma (The Scientist 2011).

Palliative Radiation

Palliative radiotherapy is radiation used to reduce signs and symptoms related to melanoma and improve quality of patients' life, prolonging her/his lifespan. Palliative RT is to be introduced whenever surgery is not possible (i.e. tumors that cannot be cut out or poor general condition of the patient) or is deemed ineffective (i.e. multiple metastases). In general, all types of metastases or metastatic sites can be irradiated, including skin, lymphatic, brain, bone, and visceral incisions. The effectiveness of radiotherapy in palliative setting is primarily dependent on tumor burden and site. Cells from metastatic lesions (incisions) are more radioresistant than those from primary tumors (tumors remaining in their original site). Thus, the symptoms are ridden easier and more effectively when radiotherapy is done on metastatic tumors. Combined treatment, or the

use of radiotherapy and another form of cancer treatment, offers good chance for pain relief and restoration of affected neurological functions as well as delay in tumor regrowth and prolongation of symptoms-free period.

(Strojan 2010).

SIDE EFFECTS OF RADIATION

Recovery from radiotherapy depends on the tumor site, the stage and grade of the cancer, and the amount of healthy tissue that is affected during treatment. Damage to normal cells during radiation therapy may cause side effects.

Skin Changes

Skin changes are common with radiation therapy. The skin in the area of your body that is getting radiation may turn red and tender, itch, peel, or blister. Toward the end of treatment, the skin may become moist and "weepy." These effects are temporary, and the area will gradually heal when treatment is completed. The patient may notice a slight change in the color of the skin. (Web MD 2001).

(Right) An example of skin damages after radiotherapy (Fashion-Era 2007).



Fatigue

> Fatigue is another common side effect of radiation therapy. It is a sense of tiredness that doesn't seem to go away, even with rest or sleep. Some people may only have mild fatigue. For others, fatigue may be a bigger problem. It may last from 6 weeks to a year after your last radiation treatment.
>
> (Web MD 2001).

Others

> In a study done with patients after receiving radiotherapy, 46% experienced headaches, making that the most frequent side effect of radiation. However, in only one patient was the headache debilitating enough to result in a treatment delay of one week. Other less frequent side effects were nausea and vomiting. Dermatitis (inflammation of the skin) developed in two patients, and chills were noted in one patient. In no instance was therapy discontinued as a consequence of side effects.
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> (Vlock et. al. 1982).

CONCLUSION

Radiation, while not normally used as a primary method of treatment, is an integral part of melanoma treatment. Through technological advances, however, it could soon become even more important in the treatment process of Melanoma. In the near future, it may be possible for x-ray machines to locate only abnormal cells and leave the normal cells alone, eliminating possible side effects. As technology continues to progress, the different treatment methods of cancer are continuously interweaving, and this is making treatment less painful and more

effective. One can only imagine how soon cancer will be curable with the aid of technology.

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