Review Article

Current tools of radiation therapy in treatment of skin cancer

 WK Yeung 楊永基, NM Luk 陸乃明, KH Yu 余國雄

The mainstay treatment of non-melanoma skin cancer is surgery. However, radiotherapy is an effective treatment alternative in some clinical situations. The current tools of radiation therapy in treating skin cancer include low-energy X-ray, electron beam therapy and brachytherapy. This review article provides an overview of these treatment techniques.

Keywords: Non-melanoma skin cancer, radiation therapy

Introduction

The majority of non-melanoma skin cancer is well-differentiated epithelial carcinoma, either basal cell carcinoma or squamous cell carcinoma. Nowadays, most of these skin cancers can be cured by a wide variety of treatment modalities. Other than surgery, radiation therapy plays an important role in the treatment of skin cancers.

The choice of radiotherapy is dependent on several factors, such as size, location, histopathological type of the tumour, the condition and preference of patients, and the local availability of certain treatment modalities. The main advantage of radiotherapy is the possibility to treat the tumour and the area of subclinical spread with a safety margin without substantial damage to normal tissue. Hence anatomical mutilation can be minimized. The better cosmetic outcome of radiotherapy make it a good therapeutic choice for skin tumours involving nasal ala, inner or outer
The canthus of eyes, pinna of ears, oral commissure and philtrum of lip. However the disadvantages include the inability to check the treatment margins and requirement of multiple treatment sessions in order to achieve a good cosmetic outcome.

The current available tools of radiotherapy for skin cancer include low-energy X-ray beam, electron beam, and brachytherapy. The choice of these techniques depends on the tumour characteristics, the availability of machines and expertise.

**Low-energy X-ray therapy**

There is a spectrum of low-energy X-ray which is useful for treating superficial skin cancer. This includes the range from 5-20 kV (Grenz X-R) to 200-400 kV (orthovoltage). The commonest X-ray used in our clinical practice is the superficial X-ray, with the range of energy between 60-100 kV.

Low-energy X-ray is usually generated from a X-ray tube, in which an electric current runs across a electric potential (defined by its voltage) in a vacuum tube, and hits a metallic target (the anode), normally tungsten, thereby gives rise to a concentrated beam of photon (electromagnetic wave). The energy of photon beam is related to the electric potential and the characteristic of the metallic target. Different combinations of electric potential and metallic target may give rise to photon beam with different penetrative power. It is the energy of the photon produced that determines how deep X-ray can penetrate the skin tissue. The penetrative power of X-ray is represented by the half-value layer (HVL). This is defined by the thickness of material, either aluminum (Al) or copper (Cu) which can reduce the intensity of beam by half (Table 1). For example, 100 kV superficial X-ray with HVL of 2 mm Al can treat skin tumour of up to 3-4 mm in thickness.

The beam penetrative profile of low energy X-ray has the characteristic of high energy deposit at the surface and a rapid drop of intensity after entering the skin tissue for a few millimeters. The penumbra of the beam which is defined by the distance between the 90% and the 50% isodose line (IL) at the surface level is also narrow. That means the physical margin to be considered for a skin tumour is narrow, usually just 2-3 mm. Moreover, the shielding for blocking of unnecessary irradiation to normal tissue is less demanding. Usually a lead shield of 1 mm is enough to shield off the irradiation. Thus, low-energy X-ray has good physical advantage in treating skin tumour near the eyes (Figures 1-7). The shaping of irradiation field is also convenient and requires only a thin lead shield. The radiation protection requirement of the treatment room is also easily achieved.

The dosage of radiation therapy is defined by the energy deposit per unit mass of tissue across the beam. One Gray (Gy) is defined as one joule per kilogram. One Gray has 100 centi-Grays (cGy or Rad). The dosage has to be prescribed at a certain isodose level. Usually the prescription level is at the 80-100% IL. However, there is another school of thought, using 50% IL (i.e. half-value

<table>
<thead>
<tr>
<th>Radiation therapy unit</th>
<th>Operating potential (kV)</th>
<th>Typical measured HVL</th>
<th>Approximate average energy (keV)</th>
<th>HVL water or soft tissue (cm)</th>
<th>HVL in cortical bone (cm)</th>
<th>HVL in lead (cm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grenz ray</td>
<td>5-20</td>
<td>0.03 mm Al</td>
<td>7</td>
<td>0.04</td>
<td>0.004</td>
<td>–</td>
</tr>
<tr>
<td>Superficial X-ray</td>
<td>60-100</td>
<td>2 mm Al</td>
<td>30</td>
<td>1.8</td>
<td>0.3</td>
<td>0.002</td>
</tr>
<tr>
<td>Orthovoltage X-ray</td>
<td>200-400</td>
<td>3 mm Cu</td>
<td>150</td>
<td>5.0</td>
<td>2.5</td>
<td>0.03</td>
</tr>
</tbody>
</table>
Figure 1 & 2. A patient with basal cell carcinoma at the inner canthus of right eye was in preparation for superficial X-ray therapy. Right internal eye shield was inserted.

Figure 3 & 4. Superficial X-ray therapy: patient wearing the cobex cast, with lead cut-out, and wax-jig mounted on it.

Figure 5. Superficial X-ray therapy: patient in the treatment room of superficial X-ray.

Figure 6. Superficial X-ray therapy: the treatment head mounted on the patient.
level) for dose prescription. This may give rise to higher dose to the surface but lower dose to the underlying normal tissue, sacrificing the dose homogeneity in the tumour tissue. The choice of energy of X-ray is determined so that the prescription level (e.g. the 80-90% IL) can cover the tumour depth with biological margin.

To allow for normal tissue repair, and hence less normal tissue late toxicity, multiple fractionation of the treatment course is necessary. The balance between advantage of multiple fractionations and disadvantage of multiple visits has to be considered in our clinical practice, especially for old and fragile patients. The conventional dose fractionation in treating tumour is usually 66 Gy in 2 Gy per fraction, 5 fractions per week. This fractionation may not be suitable for old patients. So various schemes of dose fractionation are being used among different countries and centres. There is intention to treat large sized tumour with more total dose. However, there is no consensus how high the dose has to be given.

**Electron beam therapy**

The electron beam in clinical use nowadays can be generated in a linear accelerator which mostly has its second treatment mode of high energy (Mega-volt) photon beam. High energy photon beam is used to treat deep tumour, but electron beam can be used to treat superficial tumour, like skin tumour. The electron beam generated in the linear accelerator is produced by an electric current passing through a high energy potential in a vacuum tube. The electrons are accelerated by the microwave field. The energetic electrons are then directed by magnets in the treatment head to generate a concentrated beam.

Because of the rapid fall-off of energy deposit when an electron enters tissue, the clinically useful electron beam has to be higher in energy (4-20 Mega-volts) compared with low energy X-ray (kilo-volt). The useful energy range of electron beam in treating skin tumour is between 4-6 Mega-volts.

The dose profile of an electron beam in the tissue is very different from those of low-energy X-ray. The maximum energy deposit of an electron is not at the surface, but at few mm beneath the surface. However, it has a good distance of dose plateau, giving rise to a better dose homogeneity in the treatment depth. Its sharp dose fall-off is also advantageous in giving lower doses to the underlying tissue. When electron beam is employed to treat superficial disease like skin tumour, a bolus of tissue has to be added on the treatment surface so as to achieve the maximum dose deposit at the surface level. Usually this tissue bolus is made of wax. The thickness of this bolus is critical for the clinical outcome.

The penumbra of an electron beam is large compared with those of X-ray beam, usually 8-10 mm width at the surface level. Moreover constriction of the high isodose level occurs at the deeper tissue level (Figure 8). This implies a larger physical margin has to be considered for the treatment of tumour, compared to low energy X-ray. This limits its use in treating tumour near critical organ like the eyes.

The higher penetrative power of electron beam generated in the linear accelerator implies thicker...
Radiation therapy in treatment of skin cancer

shielding for adjacent normal tissue and for field shaping. The shielding is made of lead of more than 5 mm in thickness, usually custom-made to conform to the shape of tumour. This results in difficulty in making an internal shield like internal eye shield or intranasal shield. For superficial X-ray, an internal eye shield can be inserted under local anesthetic eye-drops, just like wearing a contact lens (Figure 9). This can shield off any unnecessary radiation from the eye. For electron therapy, this shielding device is insufficient to shield off the unwanted radiation from the eyes. This is the technical difficulty encountered in treating skin cancers near the periorbital region with electron therapy (Figures 10-14).

Radiobiological effectiveness of an electron is less than that of X-ray. The factor of radiobiological effectiveness compared with X-ray is estimated at about 0.9. This may imply the total dose prescribed should be higher in using electron beam. However, the clinical significance of this is not certain in the literature.

The dose is usually prescribed at 90% or at the maximum dose level (100% IL). The choice of

**Figure 8.** The depth isodose distribution of a 6 MeV electron. This shows the dose profile after the electron beam enter the surface of a phantom. The field size is defined by the 50% isodose line. The distance between the 50% isodose and 90% isodose is increasing along the depth. This means the effective treatment width will constrict when the beam penetrates deeper.

**Figure 9.** Internal eye shields of various size for superficial X-ray therapy.

**Figure 10.** A patient with basal cell carcinoma over left nasal ala, before radiotherapy.

**Figure 11.** A patient with basal cell carcinoma over the nose for electron beam therapy with treatment cast, bilateral eye trimmers, wax-bolus and jig.
energy and the thickness of bolus are determined so that 90% IL will cover the tumour depth with biological margin. The dose fractionation and total prescribed dose of electron beam in treating skin cancer is similar to those of low-energy X-ray.

Because of the high radiation protection requirement, the availability of an electron beam equipped with linear accelerator is mainly confined to hospital based radiation oncology centres. Together with the consideration of cost-effectiveness of a linear accelerator which can also be used in treating other visceral tumours, electron beam therapy is still a major tool used in the hospital based cancer centres.

**Brachytherapy**

The use of brachytherapy in treating skin tumour is becoming less popular after the development of modern X-ray tube. However its importance in clinical practice cannot be underestimated.

Brachytherapy is also a short distance radiation technique. It employs radioactive materials to generate radiation particles, either photon or electron. The commonly used radioactive substance has been changed from radium in the old days to cesium$^{137}$, and finally to iridium$^{192}$ nowadays. These radioactive sources are applied close to or deep into the tumour, so as to give a high local dose to the tumour, whilst sparing the adjacent normal tissue. The radioactive source can be put into a surface mould in order to be applied closely to the tumour surface (surface mould brachytherapy). Alternatively, the radioactive source can be inserted deep into the tumour (interstitial brachytherapy). Brachytherapy has been evolving from low-dose rate in the past to high-dose rate now. The technique of loading the radioactive source has also changed from pre-loading (the applicator and the radioactive source are inserted together) to afterloading (the applicator is inserted before the source). With computerization, dose optimization can be
performed by a planning system so as to give better dose conformity to the tumour shape. The afterloading technique has also improved so that the radioactive source can be inserted by remote-control using computerized electronic system rather than by manual loading. This means that the radiation exposure to the medical personnel is minimized.

The clinical useful energy of the photon emitted from the radioactive source in brachytherapy is in the range of kilovoltage (e.g. 370 kV from Ir-192). This therapeutic photon is similar to the photon from low-energy X-ray tube. It also has the similar physical advantage like rapid fall-off of dose. This makes brachytherapy very suitable for treating skin cancer.

Previously, the planning technique of brachytherapy was developed according to major guidelines, the Manchester’s system and the Paris system. With the computerization of planning technique, the planning can be easily achievable with dose optimization. In treating skin tumour over an uneven surface contour, the mould can be customized to the surface of tumour. The modern planning technique can create a good dosimetry so as to conform to the tumour shape. A good example is the treatment of large sized perineal extramammary Paget’s disease by mould brachytherapy technique (Figure 15).1

The current trend of brachytherapy is moving towards remote-control afterloading high dose rate technique with a computerized planning system. The radioactive source is stored in a radiation protected safe. During treatment, the radioactive source can be delivered automatically to the applicator through the connecting channels by an electronic device with remote-control (Figures 16-17). For mould brachytherapy, the applicator (surface mould) is placed onto the patient’s tumour with accurate localization quality control. The applicator is usually composed of multiple catheters, which are arranged in parallel and are equally separated from each other, embedded in some tissue equivalent material like wax or silicone. The radioactive source will run through these catheters inside the mould during treatment. The radioactive source is a point source propelled by an electronic controlled metallic wire. It will move in steps into each dwelling position along the catheters for a pre-planned period of time (dwelling time). The dwelling time of the radioactive source at each position will affect the dose contribution at the site. The summation of the dose contribution from all dwelling positions will give the overall dosimetry to the tumour. The complicated calculation can be performed by the computer.

When the high dose rate brachytherapy system was introduced, there was criticism on its radiobiological disadvantage. The late toxicity from high dose rate radiation was expected to be larger. However, with more knowledge on radiobiology, this late toxicity can be reduced by multiple fractionations. Subsequent clinical experience has proven that it is a good treatment technique with late toxicity comparable to that of low dose rate technique.

The disadvantage of brachytherapy in treating skin cancer is its cost-effectiveness. It is quite time-
Figure 16. A high dose rate afterloading brachytherapy machine: the afterloader.

Figure 17. The head of the afterloader with multiple channels through which the radioactive source will be delivered to the patient.

Consuming in preparing a mould brachytherapy which not only involves medical physician, but also mould laboratory technician, radiation therapists and oncologists. With equivalent clinical results, other alternative treatment like low-energy X-ray and electron therapy are usually preferred by clinicians. However, brachytherapy is more effective in treating large sized superficial skin tumour with uneven contour in which other alternatives cannot achieve a good clinical and cosmetic result.

**Conclusion**

In management of skin tumours, despite controversy exists, electron beam therapy seems to be inferior to superficial X-rays in some studies.²,³ In contrast, Tapley and Zablow, using electron beam therapy, achieved similar results as superficial X-rays.⁴,⁵ For skin tumours located at some areas, e.g. around the eyes, superficial X-ray is definitely superior to electron beam in terms of applicability. The importance of brachytherapy in treating skin tumour cannot be neglected. With the evolution of radiation therapy technique, radiation is still playing a role as an alternative in treating skin tumours.

**References**