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GEC-ESTRO ACROP recommendations in skin brachytherapy

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ABSTRACT

Purpose: The aim of this publication is to compile available literature data and expert experience regarding skin brachytherapy (BT) in order to produce general recommendations on behalf of the GEC-ESTRO Group.
Methods: We have done an exhaustive review of published articles to look for general recommendations.
Results: Randomized controlled trials, systemic reviews and meta-analysis are lacking in literature and there is wide variety of prescription techniques successfully used across the radiotherapy centers. BT can be delivered as superficial application (also called contact BT or plesiotherapy) or as interstitial for tumours thicker than 5 mm within any surface, including very irregular. In selected cases, particularly in tumours located within curved surfaces, BT can be advantageous modality from dosimetric and planning point of view when compared to external beam radiotherapy. The general rule in skin BT is that the smaller the target volume, the highest dose per fraction and the shortest overall length of treatment can be used.
Conclusion: Skin cancer incidence is rising worldwide. BT offers an effective non-invasive or minimally invasive and relative short treatment that particularly appeals to elder and frail population.

The incidence of skin cancer has been rising over the past decades. World Health Organization (WHO) estimates that currently 2–3 million non-melanoma skin cancers (NMSC) occur globally each year with one in every three cancers diagnosed being a skin cancer [1]. These data are most likely underestimated. The incidence rates in Europe varied between 40–130/100,000 person-years for basal cell carcinoma (BCC) and 8–30/100,000 person-years for squamous cell carcinoma (SCC) respectively [2]. A trend in increasing incidence in older population has been confirmed [3]. It is expected that NMSC may soon start to represent a major public health problem and pose a significant burden to any health care system. Many patients with NMSC referred for radiotherapy are older, frail, have unresectable tumours or contradictions to surgery due to advanced age or co-morbidities. This issue already introduces a bias in data analysis and comparison with other treatment methods. Various radiotherapy techniques have been developed to treat skin cancer: superficial and orthovoltage X-rays, electron and megavoltage photon treatment, and brachytherapy (BT) in all the modalities: low dose rate (LDR), high dose rate (HDR), pulsed dose rate (PDR), and electronic BT. Due to logistics of LDR application, this modality has been gradually abandoned. The treatment choice is usually based on institutional resources and specialist experience and should consider local control, cosmesis, toxicity and convenience/expected compliance of the treatment.

BT is an appropriate and effective treatment option for selected skin cancers, mainly NMSC that are not better served by surgical removal, non-radiotherapy treatment modalities, or external beam radiotherapy (EBRT) [4]. There are several advantages of HDR and PDR BT when compared with EBRT that should be considered in the decision making process. BT is usually delivered as a hypofractionated course, three or two times a week, rather than daily, which translates into fewer treatment visits for a patient, particularly useful for elderly and frail patients. The dose is delivered in a short period of time. Computer-based treatment planning allows for an optimized dose distribution. A rapid fall in dose beyond

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radioactive source makes it possible for increased tumour control while sparing the surrounding tissue and shorter overall treatment duration reduces risk of tumour cell repopulation. There are no randomized controlled trials, systemic reviews and meta-analysis in literature regarding skin BT and there is wide variety of prescription techniques successfully used across the radiotherapy centers [5]. All the recommendations in this paper have a level of evidence IV (LOE IV: based in retrospective cohort studies, no prospective studies); and grade of recommendation B (GOR B: Strong or moderate evidence for efficacy but with a limited clinical benefit, generally recommended) [6].

Modalities of BT applications in skin

Current skin applications in brachytherapy can be classified in two modalities [7,8]:

- Superficial, also called contact brachytherapy or plesiotherapy.
- Interstitial, with the insertion of plastic tubes or rigid needles.

Superficial modalities involve moulds and flaps for larger lesions, and radionuclide based shielded applicators and electronic based shielded applicators for small volume lesions. Interstitial BT is applied to deeper located and/or very irregular tumours.

An excellent review of those different modalities and details on the applicators from physics point of view have been published by the American Brachytherapy Society (ABS), with an updated review of relevant papers on skin BT [9].

Superficial brachytherapy

Surface moulds

Mould BT is a technique of delivering BT by an applicator that is usually custom made and designed to provide a more constant and reproducible frame for source positioning. Mould can be used for flat surfaces and irregular shapes. A customized mould can be constructed from specialized polymers, acrylic resin, wax (such as those used in dentistry) or a thermoplastic material or similar in which the catheters are embedded [10,11] (Fig. 1). Moulds fit to the external patient surface and the catheters must remain in the exact position as closely as possible to tumour surface to provide adequate dose coverage of tumour volume and increase the distance to other normal surrounding structures. In postoperative BT the gradient can overdose the skin, therefore the catheters must be placed at a few mm of distance from the skin, preferably 5 mm. Conformal custom moulds are often utilized for complex shapes and irregular surfaces like the earlobe or nose. An irreversible hydrocolloid can be used for making impression. Cerrobend alloy or thin lead is chosen for shielding purposes [12]. A thermoplastic mask with catheters embedded in wax or resin is useful for an accurate reproducibility for extensive lesions of the scalp. Low-cost 3D printers are a promising solution for the customization of the HDR BT applicators but regulatory materials' approval is required for clinical application [13]. Published studies involving mould technique have shown good local control and cosmesis [14–20] (see separate file for table).

The dose prescription point with moulds is usually 3–5 mm under the skin surface but in case of advanced tumours with deep ulcer or deep dermis infiltration, it should be at least 3–5 mm under the deepest point of a given tumour, defined by an appropriate imaging, therefore interstitial BT or EBRT should be considered in such cases.

The ABS in 2001 made specific recommendations for head-and-neck cancer patients [21]:

1. Superficial (<5 mm thick) tumours can be treated with fractionated HDR using moulds.
2. Suitable sites for mould therapy include scalp, face, pinna, lip, buccal mucosa, maxillary antrum, hard palate, oral cavity, external auditory canal, and the orbital cavity after exenteration.
3. A total HDR dose equivalent to about 60 Gy LDR (prescribed at 5 mm depth) is recommended. The actual HDR dose per fraction and number of fractions can be varied to suit individual situation (site and treatment volume). HDR can be used as a boost to 45–50 Gy EBRT (LDR equivalent doses of 15–30 Gy).

Surface flaps

In case of non-excessive surface irregularity, commercially available flaps may be used. These consist of regular layers of silicon-based material or linked pellets of 10 mm in thickness or diameter in which the catheters are embedded. Ten mm inter-catheter distance and a minimum of 5 mm distance to the skin are assured. Typical prescription depth with flaps is less than 5 mm under the skin. The available flaps are the Freiburg™ flap (Elekta Instrument AB, Stockholm, Sweden), the H.A.M.™ (Mick Radio-Nuclear Instruments and Eckert & Ziegler BEBIG, Berlin, Germany), and the Catheter Flap set™ (Varian Medical Systems, Palo

Fig. 1. 53 year old with 12 months non-healing ulceration on the left middle finger. Biopsy confirmed SCC. No bony invasion. Prior unsuccessful treatment with cryotherapy. On examination: 2.1 cm × 3.1 cm lesion. Skin US 1.9 mm total tumour depth, 3.6 mm from the top of the tumour to bone. Treatment: Skin HDR brachytherapy 37.5 Gy in 8 fractions, treatment twice a day over 4 days. Results at 18 month follow-up. (Example of surface moulds and flaps).

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