Letter to the Editor

Comments on: "Clinical implementation of a new electronic brachytherapy system for skin brachytherapy"

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To the Editor:

We have read with an interest the article of Olga Pons-Llanas *et al*. [1] published in the Journal about the use of electronic brachytherapy (EBT) in non-melanoma skin cancer (NMSC). However, we noticed the exclusion criteria for the following tumors: lesions with a diameter greater than 20 mm, invasion of more than 4 mm, irregular anatomic areas. Besides, there are limits linked to the use of circular collimators and the daily set-up position. NMSC often have irregular shapes and diameter longer than 2 cm; besides, in most cases, NMSC are recurrent and located in periorbital area (i.e. inner canthus). In these instances, both EBT and brachytherapy are difficult and/or inadequate to treat safely most of patients. Among the new technologies, stereotactic ablative radiation therapy could be a valid therapeutic option treating "difficult NMSC".

In a recent paper [2], we reported our experience with Stereotactic Body Radiation Therapy (SBRT) in a patient with recurrent and complicated NMSC using Cyberknife System (CKS). In fact, the CKS is a possible alternative to surgery and brachytherapy in patients with recurrent NMSC located in irregular anatomical areas close to critical organs (i.e. eyes). The SBRT with image guided exceeds the limits of the set-up for relocation; the inverse planning allows to cover irregular volumes greater than 20 mm. The use of the photons X-6 MV permits to treat the lesions with invasion more than 4 mm.

Do Olga Pons-Llanas *et al*. have experience and/or data on the use of brachytherapy in "difficult areas"? In fact, in daily clinical practice many patients have "irregular and difficult" NMSC and it is important that Radiation Oncologists have more therapeutic options in these instances. We think that it is important for the authors to comment on these issues and perhaps reply within the context of this journal.

References

1. Pons-Llanas O, Ballester-Sánchez R, Celada-Álvarez FJ et al. Clinical implementation of a new electronic brachytherapy system for skin brachytherapy. *J Contemp Brachytherapy* 2015; 6: 417-423.
2. Pontoriero A, Iatì G, Conti A et al. Treatment of periocular basal cell carcinoma using an advanced stereotactic device. *Anticancer Res* 2014; 34: 873-875.

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In reply to the Letter to the Editor titled:

"Comments on: Clinical implementation of a new electronic brachytherapy system for skin brachytherapy"

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To the Editor:

We have read with an interest the letter to the Editor titled "New technologies for non-melanoma skin cancer". In this letter, the authors comment on our article [1] about the clinical implementation of a new system for skin brachytherapy (Esteya® electronic brachytherapy by Elekta, Stockholm, Sweden) and they asked for a reply to their letter. We would like to thank the authors for their interest in our publication and would like to respond to their letter.

First of all we need to clarify that in our study we chose to exclude irregularly shaped lesions, lesions with a diameter > 2 cm, and lesions with a depth larger than 4 mm because of the design of the radiation therapy system that was used. Lesions included in our work using

the specific features of the Esteya® device, in fact represent the vast majority of non-melanoma skin cancer primary presentations.

The Esteya® electronic brachytherapy system (E-eBT) is delivered with a set of applicators up to 3 cm in diameter. When treating non-melanoma skin cancer, typically a margin of 0.5 cm is added to the GTV. Consequently, the maximum diameter of lesions to be treated is 2 cm. The system has a dose-gradient of about 8% per mm, therefore with lesions deeper than 0.4 cm, the overdose at the first skin layers will exceed 130% and this might impact cosmetic outcome. This is the reason we limited inclusion to lesions with a depth of 4 mm or less. Finally, E-eBT applicators are designed with a flat surface to allow full contact with the skin. Avoiding air gaps between applicator and skin is a prerequisite because of the significant impact of air gaps on the dose to the lesion. Nowadays, we have the possibility to use a new set of more precise applicators for treatment of lesions in difficult areas.

When we say that irregular areas are not suitable for EBT, we only mean those locations that, despite applying some pressure, are not entirely in contact with the applicator. These cases should be treated with other types of brachytherapy/radiotherapy. In our experience there are only a few locations where one cannot get a flat surface by applying mild pressure. Only larger lesions in areas with angled surfaces result in bone or cartilage, for example impeding/preventing a flat surface being obtained; this can be on the inner canthus of the eye, or for example on the pinna, and on the peri-alar nose groove. We have, however, successfully treated several "difficult cases" of BCC located on for example the nasal tip, retroauricular region, and scalp with E-eBT. It is our experience that the vast majority of NMSC lesions can be treated with the Esteya® electronic brachytherapy system.

We disagree with the authors of the letter stating that "NMSC often have irregular shapes and a diameter longer than 2 cm", and "most cases of NMSC are recurrent and located in the periorbital area (i.e. inner canthus)". In fact, most NMSC are small, usually less than 20 mm, and the majority of lesions are located on the face, especially on the nose. Both surgery and radiation therapy are very effective and recurrence is usually found in less than 10% of cases. There is, however, a bias of patients submitted to radiotherapy since only difficult cases and lesions that have failed other treatments are referred. Better communication and cooperation between dermatology and RT services will improve referral and benefit both patients and care givers. For the less frequent appearing lesions with dimensions and shapes that are outside of the range included in our study, other radiotherapy treatment solutions besides Esteya® electronic brachytherapy are available such as brachytherapy moulds, isotope based brachytherapy with interstitial-or flap applicators, and treatment with electrons.

We have read with great interest the article of Pontoriero *et al*. [2] that the authors of the letter to the Editor referred to. In this article, Pontoriero *et al*. reported their experience treating a deeply invasive lesion on the inner canthus of the eye with the Cyberknife system. Although in their case report the patient seems to have a good clinical outcome, we do have some concerns with promoting this technology in general for skin cancer treatment around the eye based on this single case. We consider the risk of intrafraction-movement as high because of very long treatment time associated with the large number of beams. In addition, there are challenges associated with the dose build up in the first layers of the skin beam, the inverse planning calculation algorithm on the first fractions of millimeter of the skin, and the use of a bolus. Also, protecting the eye from radiation damage is not easy. In our opinion, more robust research is needed to prove this technique as safe and beneficial when other therapies, such as interstitial brachytherapy with more substantial evidences are available.

That new sophisticated techniques such as "Cyber Knife®" – as Dr. Pontoriero described in his letter – or particulate radiation, as a proton beam therapy, etc., could be used in selected cases, complying properly the goals for treatment of theses tumors. But on the other hand, even when it is desirable, a good knowledge on the part of radiation oncologist specialist of the full potential of these new techniques is required. The cost and complexity of these techniques, together with the necessary investment in human resources to fit the goal of these treatments, as well as short follow up of every single case referred, become, at least in our opinion, the accurate approach as a non-elective treatment for non-melanoma skin cancer.

In our practice, this type of lesions on the inner canthus use to be treated with an HDR interstitial implant, with catheters just subcutaneous, and the eyes protected with a lead sheet. Although it is small invasive procedure, in our hospitals we prefer it to IMRT because of the robustness, simplicity, eye protection, dose gradient through normal tissue, and guarantee of full coverage of the lesion. In our group, we have accumulated over years a great experience treating successfully this kind of difficult tumors with this approach.

We want to express our gratitude to both the letter authors and the Journal Editor, to have the opportunity to include this discussion.

References

1. Pons-Llanas O, Ballester-Sanchez R, Celada-Alvarez FJ et al. Clinical implementation of a new brachytherapy system for skin brachytherapy. *J Contemp Brachytherapy* 2015; 6: 417-423.
2. Pontoriero A, Iati G, Conti A et al. Treatment of periocular basal cell carcinoma using an advanced stereotactic device. *Anticancer Res* 2014; 34: 873-875.

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