

Evolution in the management of skin malignant lesions using new radiotherapy techniques

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Abstract

Introduction

Radiotherapy plays an important role in the treatment of skin tumours. For skin carcinomas, external irradiation (kilovoltage X-rays or electrons according to clinical characteristics) is more preferable than interstitial brachytherapy, which is recommended for tumours of the lip and nasal vestibule. Electrons are usually used for treating superficial lesions and skin cancers, as well as in the orthovoltage radiotherapy. In order to treat mycosis fungoides, total cutaneous electron beam radiation therapy is efficient for patients with limited superficial plaques. In the treatment of classical form of Kaposi's sarcoma, radiotherapy can achieve local control, whereas it gives good palliative results in the epidemic form. New radiotherapy techniques, such as helical tomotherapy, showed increased advantages, including dose escalation to the target tumour volume and the best protection of adjacent organs at risk. The aim of this work is to accurately evaluate the efficiency and tolerance of old and new radiotherapy techniques in the treatment of different skin tumours and to review the already existing techniques.

Conclusion

With all these new treatment modalities, the modern radiotherapy technique becomes a highly adapted treatment for different tumour types,

which is a part of the multidisciplinary management.

Introduction

Radiotherapy plays an important role in the treatment of skin tumours, such as those arising from non-melanoma skin cancer and primary cutaneous lymphoma. For non-melanoma skin cancers, including basal cell carcinoma (BCC), cutaneous squamous cell carcinoma (CSC), Merkel cell carcinoma (MCC) and adnexal carcinoma (AC), complete surgical excision with a security margin is still the reference therapy. But, the choice of the treatment technique depends on various factors, such as the size of the tumour, the general condition of the patient, cosmetic considerations and recurrence. Radiotherapy is an effective option to control tumour growth and to improve quality of life of the patient. Histological confirmation is essential before radiotherapy initiation.

For BCCs, radiotherapy is an alternative option if surgery is not preferred due to recurrence, incomplete excision, nodules of >2 cm in the head, or bone or cartilage involvement¹. In such cases, 5–10-mm security margins are maintained depending on the tumour size, and superficial X-rays and electron beams are usually employed. A randomised controlled trial was conducted to compare radiotherapy with surgical excision of facial BCC of <4-cm diameter with 4-year failure rates of 7.5% and 0.7%, respectively ($P = 0.003$). Cosmetic outcomes significantly favoured surgical excision at 4 years in 87% of the surgery-treated patients, whereas 69% of the radiation-treated patients opined the cosmetic results to be

satisfactory ($P < 0.01$). The study used different techniques of radiotherapy, including interstitial brachytherapy, contact therapy and conventional radiotherapy². Despite these results, radiotherapy is still an option for BCCs that occur in areas where surgery would be technically difficult or would result in unacceptable tissue destruction, or for patients who would not be able to tolerate surgery³. In a study, the efficacy of electron beam radiotherapy for BCCs was evaluated; and 3-year local recurrence-free survival rates were found to be 97.6% for tumours treated with 54 Gy in 18 fractions and 96.9% with 44 Gy in 10 fractions⁴. Radiotherapy has also been compared with treatment with imiquimod 5% cream for nodular BCCs on the eyelid; in this study, remission rates were equivalent in both the groups, but tolerability was better in the radiotherapy group during the treatment⁵.

For CSCs, radiotherapy is recommended when surgery is not possible, or it is used as an adjuvant in the treatment of high-risk tumours with 10–15-mm security margins⁶. The 3-year freedom from local recurrence was 97% with 54 Gy in 18 fractions, whereas it was 93.6% with 44 Gy in 10 fractions in a study about electron beam therapy⁴. Radiotherapy is particularly an option for CSCs overlying cartilage⁷, those with perineural invasion^{8,9}, or with recurrence¹⁰. Adjuvant radiotherapy is also indicated if there is regional lymph node involvement^{11,12}.

For MCCs, radiotherapy is applied to the cavity of the excised primary or recurrent tumour¹³. Adjuvant regional radiotherapy on the tumour bed decreases regional recurrence, but

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has no benefit on overall survival^{14,15}. Radiotherapy alone can be a reasonable option for inoperable MCCs with similar overall and disease-free survival rates to combination of surgery and radiotherapy¹⁶. A recent study showed that radiation monotherapy could also be used for lymph node-positive MCC (for both microscopic and palpable lymph node disease), with comparable results to lymphadenectomy with or without adjunct radiotherapy^{17,18}.

With regard to ACs, a few cases have been published about radiotherapy for sebaceous carcinoma. Sebaceous carcinomas have been considered radioresistant for years. But recently, reports of successful treatment of sebaceous carcinoma with radiotherapy have been published. Local control at the primary site after radiation and/or surgery was 90%, as observed in a study including 10 patients¹⁹. An appropriate radiotherapy delivery regimen (>55 Gy) seems to be an effective treatment for sebaceous carcinoma in combination or as an alternative to surgery²⁰⁻²².

In mycosis fungoides, total cutaneous electron beam radiation therapy is efficient for patients with limited superficial plaques. In the classical form of Kaposi's sarcoma, radiotherapy can achieve local control, whereas it gives good palliative results in the epidemic form²²⁻²⁴. Radiation therapy is also a treatment of choice in the low-grade B-cell lymphomas^{25,26}. The aim of this critical review was to discuss the evolution in the management of skin malignant lesions using new radiotherapy techniques.

Discussion

The authors have referenced some of their own studies in this review. These referenced studies have been conducted in accordance with the Declaration of Helsinki (1964) and the protocols of these studies have been approved by the relevant ethics committees related to the institution

in which they were performed. All human subjects, in these referenced studies, gave informed consent to participate in these studies.

Place of helical tomotherapy in the treatment of skin cancers

The choice of the most appropriate irradiation technique depends on tumour localisation and clinical target volume, as much as histology, and the size and thickness of the tumour. Three standard radiation techniques used for skin cancers are low-energy X-rays for tumours of <1 cm thickness, electron beams for thicker tumours, and brachytherapy for lesions of the lower lip and nasal pyramid. Helical Tomotherapy® (HT; Accuray Incorporated, Sunnyvale, CA, USA) is a new technique of radiotherapy and little data have been published on non-melanoma skin cancer. HT is an intensity-modulated radiation treatment using 6 MV photons combined with megavoltage computed tomography (CT) imaging allowing accurate patient positioning. This dynamic therapy has been developed at the University of Wisconsin in late 1980s²⁷. The system is mounted upon a continuous rotating gantry coupled with translation of the patient through the gantry. The helical delivery minimises the risk of significant high- or low-dose deposition in the areas of overlap or junctioning. It is an adaptive radiotherapy with constant possibility to verify a therapeutic plan, that is, patient positioning, target tumour/organ registration and reconstruction of delivered dose. The dose is delivered slice by slice during an axial CT scan²⁸. Advantages of this technique are increase in irradiation dose on the target tumour volume and the best protection of adjacent organs at risk²⁹. Indeed, this technique allows targeting areas of disease while simultaneously minimising the dose to organ at risk³⁰. It is useful for large-size tumours, complex-form tumours and when organs at risk are close or inside

the tumour. Head and neck cancer is one of the best indications for tomotherapy. It has also already been used against sarcomas, gynaecological and lung tumours, and haematologic diseases²⁸⁻³⁰. HT has achieved better target coverage in the treatment of head and neck cancer with better protection of organs at risk by reducing xerostomia compared with step-and-shoot intensity modulated radiotherapy (IMRT)³¹. We have shown that HT to be an effective option of radical treatment for advanced non-melanoma skin cancers as monotherapy or in combination with surgery. In our study, at a median 12-month follow-up, complete remission was observed in 88% of tumours: 100% in BCCs, 85.7% in CSCs, 80% in MCCs and 75% in ACs. This is a promising response rate, especially because our patients suffered from hard skin lesions; indeed, tumours treated in this study had poor prognoses either because of their localisation (face), incomplete surgical excision, recurrent or inoperable nature, or lymph node involvement. Early, late toxicity and cosmetic results were satisfactory. The method facilitates sparing of organs at risk (OARs). These results should be confirmed by larger prospective studies with longer follow-up³¹. To the best of our knowledge, this study is the largest cohort analysis of HT treatment of advanced non-melanoma skin cancer. Currently, only a few case reports have been published about the efficacy of tomotherapy for skin cancer: one case of multiple BCCs was treated simultaneously, one case of extensive BCC of the forehead and the scalp³², one case of sarcomatoid sarcoma of the scalp, one case of recurrent eccrine mucinous adenocarcinoma of the scalp, and three cases of skin malignancies³³⁻³⁶.

A few new indications have been reported about the decreasing tumour mass before stem cell transplantation in aggressive cutaneous lymphomas³⁷.

Conclusion

Radiotherapy plays an important role in the treatment of skin tumours. For skin carcinomas, external irradiation (kilovoltage X-rays or electrons according to clinical characteristics) is more preferable than interstitial brachytherapy, which is recommended for other types of tumours. New radiotherapy techniques, such as HT, have showed increased advantages, including dose escalation to the target tumour volume and the best protection of adjacent organs at risk. With all these new treatment modalities, the modern radiotherapy technique becomes a highly adapted treatment for different tumour types, which is a part of the multidisciplinary management.

Abbreviations list

AC, adnexal carcinoma; BCC, basal cell carcinoma; CSC, cutaneous squamous cell carcinoma; CT, computed tomography; HT, helical tomotherapy; MCC, Merkel cell carcinoma.

References

1. Coulomb A Agence Nationale d'Accréditation et d'Evaluation (ANAES). Recommendations for basal cell carcinoma. *Ann Dermatol Venereol*. 2004 Jun-Jul; 131(6-7 Pt 2):661-756. In French.
2. Avril MF, Auperin A, Margulis A, Gerbaulet A, Duvallard P, Benhamou E, et al. Basal cell carcinoma of the face: surgery or radiotherapy? results of a randomized study. *Br J Cancer*. 1998 Nov;78(9):1257-100-6.
3. Smith V, Walton S. Treatment of facial basal cell carcinoma: a review. *J Skin Cance*. 2011;2011:380371. [Epub 27 Apr 2011].
4. van Hezewijk M, Creutzberg CL, Putter H, Chin A, Schneider I, Hoogveen M, et al. Efficacy of a hypofractionated schedule in electron beam radiotherapy for epithelial skin cancer: analysis of 434 cases. *Radiother Oncol*. 2010 May;95(2):245-9.
5. Garcia-Martin E, Gil-Arribas LM, Idoipe M, Alfaro J, Pueyo V, Pablo LE, Fernandez FJ. Comparison of imiquimod 5% cream versus radiotherapy as treatment for eyelid basal cell carcinoma. *Br J Ophthalmol*. 2011 Oct;95(10):1393-6.
6. French Society of Dermatology. Guide-line for the diagnosis and treatment of cutaneous squamous cell carcinoma and precursor lesions. *Ann Dermatol Venereol*. 2009 Sep;136(Suppl 5):S166-86.
7. Caccialanza M, Piccinno R, Percivalle S, Rozza M. Radiotherapy of carcinomas of the skin overlying the cartilage of the nose: our experience in 671 lesions. *J Eur Acad Dermatol Venereol*. 2009 Sep;23(9): 1044-9.
8. Han A, Ratner D. What is the role of adjuvant radiotherapy in the treatment of cutaneous squamous cell carcinoma with perineural invasion? *Cancer*. 2007 Mar;109(6):1053-9.
9. Waxweiler W, Sigmon JR, Sheehan DJ. Adjunctive radiotherapy in the treatment of cutaneous squamous cell carcinoma with perineural invasion. *J Surg Oncol*. 2011 Jul;104(1):104-5.
10. Wong J, Breen D, Balogh J, Czarnota GJ, Kamra J, Barnes EA. Treating recurrent cases of squamous cell carcinoma with radiotherapy. *Curr Oncol*. 2008 Oct;15(5):229-33.
11. Ch'ng S, Maitra A, Allison RS, Chaplin JM, Gregor RT, Lea R, Tan ST. Parotid and cervical nodal status predict prognosis for patients with head and neck metastatic cutaneous squamous cell carcinoma. *J Surg Oncol*. 2008 Aug;98(2):101-5.
12. Bessède JP, Vinh D, Khalifa N, Rhein B, Clavère P, Orsel S, Sauvage JP. Lymph node metastasis of cutaneous epidermoid carcinomas of the head and neck: prognostic factors and therapeutic strategies. A propos of a series of 13 cases. *Rev Laryngol Otol Rhinol(Bord)*. 2001;122(2):111-7.
13. Guillot B, Boccara O, Mortier L, Bens G, Girard C, Saiag P, et al. Expert consensus on the management of Merkel cell carcinoma. *Ann Dermatol Venereol*. 2011 Jun-Jul;138(6-7):469-74.
14. Jouary T, Leyral C, Dreno B, Doussau A, Sassolas B, Beylot-Barry M, et al. Adjuvant prophylactic regional radiotherapy versus observation in stage I Merkel cell carcinoma: a multicentric prospective randomized study. *Ann Oncol*. 2012 Apr;23(4):1074-80.
15. Ghadjar P, Kaanders JH, Poortmans P, Zaucha R, Krenkli M, Lagrange JL, et al. The essential role of radiotherapy in the treatment of Merkel cell carcinoma: a study from the Rare Cancer Network. *Int J Radiat Oncol Biol Phys*. 2011 Nov;81(4): e583-91.
16. Pape E, Rezvoy N, Penel N, Salleron J, Martinot V, Guerreschi P, et al. Radiotherapy alone for Merkel cell carcinoma: a comparative and retrospective study of 25 patients. *J Am Acad Dermatol*. 2011 Nov;65(5):983-90.
17. Fang LC, Lemos B, Douglas J, Iyer J, Nghiem P. Radiation monotherapy as regional treatment for lymph node-positive Merkel cell carcinoma. *Cancer*. 2010 Apr;116(7):1783-90.
18. Bichakjian CK, Coit DG, Wong SL. Radiation versus resection for Merkel cell carcinoma. *Cancer*. 2010 Apr;116(7): 1620-2.
19. Pardo FS, Wang CC, Albert D, Stracher MA. Sebaceous carcinoma of the ocular adnexa: radiotherapeutic management. *Int J Radiat Oncol Biol Phys*. 1989 Sep;17(3):643-7.
20. Yen MT, Tse DT, Wu X, Wolfson AH. Radiation therapy for local control of eyelid sebaceous cell carcinoma: report of two cases and review of the literature. *Ophthalm Plast Reconstr Surg*. 2000 May;16(3): 211-5.
21. Conill C, Toscas I, Morilla I, Mascaró JM Jr. Radiation therapy as a curative treatment in extraocular sebaceous carcinoma. *Br J Dermatol*. 2003 Aug;149(2): 441-2.
22. Calitchi E, Kirova Y, Le Bourgeois JP. Radiotherapy and skin tumors. *Cancer Radiother*. 1998 Sep-Oct;2(5):556-65.
23. Kirova YM, Belembaogo E, Frikha H, Haddad E, Calitchi E, Levy E, et al. Radiotherapy in the management of epidemic Kaposi's sarcoma: a retrospective study of 643 cases. *Radiother Oncol*. 1998 Jan; 46(1):19-22.
24. Kirova YM, Piedbois Y, Haddad E, Levy E, Calitchi E, Marinello G, et al. Radiotherapy in the management of mycosis fungoides: indications, results, prognosis. Twenty years experience. *Radiother Oncol*. 1999 May;51(2):147-51.
25. Kirova YM, Piedbois Y, Le Bourgeois JP. Radiotherapy in the management of cutaneous B-cell lymphoma. Our experience in 25 cases. *Radiother Oncol*. 1999 Jul;52(1):15-8.
26. Kirova YM, Piedbois Y, Pan Q, Guo L, Le Bourgeois JP. Radiotherapy of cutaneous lymphomas. *Cancer Radiother*. 1999 Mar-Apr;3(2):105-11. In French.
27. Tomé WA, Jaradat HA, Nelson IA, Ritter MA, Mehta MP. Helical tomotherapy: image guidance and adaptive dose guidance.

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- Front Radiat Ther Oncol. 2007;40:162–78.
28. Mackie TR, Balog J, Ruchala K, Shepard D, Aldridge S, Fitchard E, et al. Tomotherapy. *Semin Radiat Oncol*. 1999 Jan;9(1):108–17.
29. Beavis AW. Is tomotherapy the future of IMRT? *Br J Radiol*. 2004 Apr;77(916):285–95.
30. Welsh JS, Lock M, Harari PM, Tomé WA, Fowler J, Mackie TR, et al. Clinical implementation of adaptive helical tomotherapy: a unique approach to image-guided intensity modulated radiotherapy. *Technol Cancer Res Treat*. 2006 Oct;5(5):465–79.
31. Kramkimel N, Dendale R, Bolle S, Zefkili S, Fourquet A, Kirova YM. Management of advanced non-melanoma skin cancers using helical tomotherapy. *J Eur Acad Dermatol Venereol*. 2014 May;28(5):641–50. [Epub 6 Apr 2013].
32. Montgomery L, Macpherson M, Gerig L, Carty K, Fox G, Esche B, et al. Simultaneous treatment of multiple basal cell carcinoma lesions. *Br J Radiol*. 2008 Dec;81(972):e290–2.
33. Murthy V, Master Z, Gupta T, Ghosh-Laskar S, Budrukkar A, Phurailatpam R, Agarwal J. Helical tomotherapy for head and neck squamous cell carcinoma: dosimetric comparison with linear accelerator-based step-and-shoot IMRT. *J Cancer Res Ther*. 2010 Apr–Jun;6(2):194–8.
34. Chatterjee S, Mott JH, Dickson S, Kelly CG. Extensive basal cell carcinoma of the forehead and anterior scalp: use of helical tomotherapy as a radiotherapy treatment modality. *Br J Radiol*. 2010 Jun;83(990):538–40.
35. Sterzing F, Neuhof D, Stroebel P, Debus J, Herfarth KK. Sarcomatoid sarcoma of the scalp—helical tomotherapy as a new radiotherapy option. *Eur J Dermatol*. 2008 Nov–Dec;18(6):731–2.
36. Motta M, Alongi F, De Martin E, Fiorino C, Maggiulli E, Rigoni L, et al. Helical tomotherapy for scalp recurrence of primary eccrine mucinous adenocarcinoma. *Tumori*. 2009 Nov–Dec;95(6):832–5.
37. Servy A, Kramkimel N, Franck N, Park S, Kirova YM. Helical tomotherapy in oncology. Case report of circumferential cutaneous lymphoma treated by this optimized radiotherapy. *Cancer Radiother*. 2014 Mar;18(2):136–8. [Epub 10 Jan 2014].