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EDITORIAL

Intensity-modulated Radiotherapy — A New Standard for Treating Nasopharyngeal Carcinoma?

Regarding target volume dose coverage for nasopharyngeal carcinoma (NPC), plans generated from intensity-modulated radiotherapy (IMRT) were compared with those of 3-dimensional conformal radiotherapy (3DCRT) and conventional 2-dimensional radiotherapy (2DRT).[1-6] After the use of IMRT, Hunt et al reported an escalation of the mean planning target volume (PTV) dose, an improved dose coverage of the skull base and the medial aspect of the cervical nodes, and a significant reduction of dose to the critical normal organs including the spinal cord, temporal lobes, and mandible, when compared with the radiation plans of 2DRT and 3DCRT.[2] Superior dose coverage for the neck nodes by IMRT plans was also shown by Cheng et al.[1] In addition, the primary tumour's clinical target volume (CTV) was more completely circumscribed in high dose (≥95% of prescribed dose) in the IMRT plans than in others.[7] A larger volume of the parotids can be spared high dose IMRT,[1,6,8,9] especially when there is no parapharyngeal tumour infiltation.[3,4] The principal benefits of an IMRT plan were parotid gland and middle/inner ear dose-sparing for early T-stage and improved target dose coverage (with critical neural organ dose-sparing as a secondary benefit) for advanced T-stage.[3,4] Recent experience has shown that IMRT can be used safely with concurrent chemotherapy[8-11] and that chemo-IMRT can accommodate the practice of accelerated fractionation with the concomitant boost technique.[11,12] Radiobiological advantage can also be gained through a special form of accelerated fractionation — simultaneously modulated accelerated radiation therapy (SMART) — in which the gross tumour volume (GTV) is given a higher total radiation dose within the same treatment period (hence a higher biological equivalent dose) than the volume at risk of microscopic tumour invasion.[13]

A 3-year actuarial local control rate as high as 98% was reported by Lee et al[8] in an updated series of 76 patients with NPC using IMRT as the primary radiotherapy technique, with a substantial proportion of patients also receiving Intergroup chemotherapy[14] and/or a brachytherapy boost), after a median follow-up period of nearly 3 years. Wolden also reported a 2-year actuarial locoregional control rate of 97% with IMRT in 39 patients at the Memorial Sloan-Kettering Cancer Centre (with/without dose-acceleration using the concomitant boost technique and with/without chemotherapy using the Intergroup's regimen).[14] Although the benefit of IMRT on local tumour control in these studies[10,11] cannot be disassociated from the effects of the other treatments, including chemotherapy, brachytherapy boost, and accelerated fractionation with concomitant boost, such a high level of local control has never been previously reported using 2DRT.[15-17] Moreover, 98% of patients had either none or only mild (grade I) chronic xerostomia 2 years after completion of IMRT.[8,9] Therefore, it is apparent that the dosimetric advantage of IMRT over 3DCRT or 2DRT[2-4] has translated into significant clinical benefits with enhanced therapeutic ratio.[7-9,11]

Based on both the physical dosimetric advantages and the early superior clinical results, one can argue that a randomised clinical trial comparing the efficacy of IMRT versus other treatments is unnecessary and may even be unethical. The situation appears analogous to the historical case in which the linear accelerator replaced the cobalt machine without a randomised clinical trial. The caveat, however, is that the present clinical data for IMRT for NPC has come from highly specialised centres with superb physicist and paramedical support, and certain IMRT software such as inverse planning with the feature of 'dose-painting', which enables differential dose delivery to different parts of the target (PTV versus CTV versus GTV), are not yet widely available. More importantly, the number of patients successfully treated with IMRT is too small and the follow-up periods are too short[10-12] to form a solid foundation for the recommendation of a global change in the radiotherapy standard for all patients with NPC. It is mandatory to confirm the excellent IMRT results in a much larger population of patients with NPC and wait for the results to mature given adequate follow-up before one can confidently abandon 2DRT and adopt IMRT as the new standard for NPC. Lastly, IMRT

often leads to 'dose-sharing' where an excessive dose to the target and the organs-at-risk (OARs) is redistributed to non-OAR healthy organs which are irradiated more than during 2DRT. The biological phenomenon of enhanced radiosensitivity with increased normal cell-kill in the low fractional dose range may result in enhanced late complications and so subtract from the therapeutic ratio of IMRT. Indeed increased irradiation to the minor salivary gland in the oral cavity and oropharynx can be counter-productive for the preservation of saliva production. Late carcinogenesis affecting the organs that receive a low but significant radiation dose is also a potential hazard.

In conclusion, confirmatory data from larger series with longer follow-up periods are necessary to completely document the superior efficacy and safety of IMRT over that of 2DRT. For the time-being, however, based on the very promising preliminary results,[8,9,11,12] IMRT should be used, where resources allow, throughout the complete course of primary radical radiotherapy for both early and advanced T-stages. Subject to confirmation with additional data, IMRT should be tentatively regarded as the new standard for NPC radiotherapy.

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