

Appendix III

Radiotherapy Guidelines

Radiation therapy for head and neck cancer is extremely complex. Optimal results can be achieved only by a specially trained team consisting of a radiation oncologist, physicist, dosimetrist, and radiation technologist. In addition, modern radiotherapy equipment and techniques should be used. Anatomic, tumour and clinical circumstances dictate the use of radiation as primary treatment or as an adjuvant to surgery in combination with chemotherapy for head and neck cancer.

Radiation Doses:

Selection of radiation doses depends on the tumour and neck node size, location of the tumour, and clinical circumstances. In general, primary and gross adenopathy require a total of 70 Gy or more at a dosage of 2.0 Gy/day. In contrast, radiation to low risk nodal stations in the neck requires a total of 50 Gy, also at a dosage of 2.0 Gy/day. Postoperative irradiation is recommended based on the tumour stage, tumour histology and surgical findings following tumour resection. In general, adverse postoperative risk factors that call for adjuvant RT include T4 tumours, close or positive margins, multiple positive nodes, perineural/lymphatic/vascular invasion, or extracapsular nodal spread. Due to interruption of the normal vasculature, scarring and relative hypoxia in the tumour bed, higher doses of radiation (60 to 65 Gy) are required for microscopic disease to decrease the chances of locoregional failure.

Fractionation:

No single fractionation schedule has proven to be best in all tumours. Historically, most radiation oncology departments in Canada deliver treatment once per day, 5 days per week, at 1.8 to 2.0 Gy/fraction. In recent years, data strongly indicate some squamous cancers can grow rapidly, especially in the face of cell depletion. The upper dose of 2.0 Gy/fraction, delivering greater than 1,000 cGy per week, is now most commonly used. Thus, the guidelines have been revised to suggest the dose of 2.0 Gy/fraction is preferred, with the exception of salivary gland tumours, which may have slower cell kinetics (Harwood et al, 1981; Amornmarn et al, 1985; Schwaibold et al, 1988; Kim et al, 1992; Parson, 1994). External radiation doses exceeding 75 Gy at conventional fractionation of 1.8 to 2.0 Gy/day may lead to unacceptable normal tissue injury. Altered fractionation includes accelerated treatment delivering more than 1,000 cGy per week and hyperfractionation. The biological rationale for using hyperfractionation is based on the discovery by Withers and colleagues (Thames et al, 1982; Withers et al, 1982) of a large, consistent difference in repair capacity of late and early responding tissues. Accelerated schedules attempt to compensate for rapid tumour proliferation by compressing the time-dose schedule. During the last decade, a number of phase II trials have suggested an advantage to the use of altered fractionation schemes in various head and neck cancers (Bourhis et al, 1997). Two large, randomized clinical trials have reported improved locoregional control using altered fractionation. The European Organization for Research and Treatment of Cancer (EORTC) protocol 22791 compared hyperfractionation (1.15 Gy twice daily, or 80.5 Gy over 7 weeks) with conventional fractionation (2 Gy once daily or 70 Gy over 7 weeks) in the treatment of oropharyngeal carcinoma. At 5 years, there was a 19%

increase in local control in the hyperfractionation arm (40% versus 59%; = .02) and no increase in late complications (Horiot et al, 1992). A recent long-term follow up analysis has demonstrated a small survival advantage as well for hyperfractionation. Another EORTC protocol (22851) compared accelerated fractionation (1.6 Gy three times daily, or 72 Gy over 5 weeks) with conventional fractionation (1.8 to 2.0 Gy once daily or 70 Gy over 7- 8 wk) in various intermediate to advanced head and neck cancers (excluding cancers of the hypopharynx). Patients in the accelerated fractionation arm did significantly better with regard to locoregional control (= .02), resulting in a gain of 13% at 5 years. Disease-specific survival showed a trend (= .06) in favor of the accelerated fractionation arm. Acute and late toxicity were increased in this fractionation arm, however, raising questions about the net advantages of accelerated fractionation (Horiot et al, 1997). In the United States, the Radiation Therapy Oncology Group (RTOG) has reported results of a large phase III clinical trial (protocol 90-03) comparing hyperfractionation with two variants of accelerated fractionation (Fu et al, 1999). After 2 years of follow-up, both accelerated fractionation with a concomitant boost and hyperfractionation were associated with improved locoregional control and disease-free survival compared with standard fractionation. However, acute toxicity was increased. There was no significant difference in the frequency of grade 3 or worse late effects reported at 6-24 months after treatment start among the various treatment groups. Altered fractionation with concomitant boost or hyperfractionation for stage III or IV may be considered standard therapy for oral cavity, oropharynx, supraglottic larynx, and hypopharyngeal squamous cell cancers.

Brachytherapy:

With the development of afterloading techniques and the availability of artificially produced radioisotopes, radioactive implants have become an integral part of head and neck radiotherapy. Brachytherapy can be used as a definitive treatment for early superficial lesions, with the expectation of good local control and cosmetic function. When a radioactive implant is combined with external irradiation, excellent results have been achieved in selected head and neck tumours in uncontrolled trials. Several European and American medical centers have had extensive experience with brachytherapy (Fu et al, 1976; Pigneux et al, 1979; Mendenhall et al, 1981; Puthawala et al, 1981; Wang, 1983; Goffinet et al, 1985; Puthawala et al, 1985; Vikram et al, 1985; Crook et al, 1988; Mazon et al, 1993). The success of brachytherapy techniques is partly dependent upon the training, experience and skills of the implant team. The technique can be used as an alternative or adjunct to resection or external beam radiotherapy.

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