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Review Article

American Brachytherapy Society Task Group Report: Combined external beam irradiation and interstitial brachytherapy for base of tongue tumors and other head and neck sites in the era of new technologies

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ABSTRACT Irradiation plays an important role in the treatment of cancers of the head and neck providing a high locoregional tumor control and preservation of organ functions. External beam irradiation (EBI) results in unnecessary radiation exposure of the surrounding normal tissues increasing the incidence of side effects (xerostomy, osteoradionecrosis, and so forth). Brachytherapy (BT) seems to be the best choice for dose escalation over a short treatment period and for minimizing radiation-related normal tissue damage due to the rapid dose falloff around the source. Low-dose-rate BT is being increasingly replaced by pulsed-dose-rate and high-dose-rate BT because the stepping source technology offers the advantage of optimizing dose distribution by varying dwell times. Pulsed-dose and high-dose rates appear to yield local control and complication rates equivalent to those of low-dose rate. BT may be applied alone; but in case of high risk of nodal metastases, it is used together with EBI. This review presents the results and the indications of combined BT and EBI in carcinoma of the base of tongue and other sites of the head and neck region, as well as the role BT plays among other—normal tissue protecting—modern radiotherapy modalities (intensity-modulated radiotherapy, stereotactic radiotherapy) applied in these localizations. © 2016 Published by Elsevier Inc. on behalf of American Brachytherapy Society.

Keywords: Brachytherapy; External beam; Tongue

Introduction

Irradiation, alone or combined with chemotherapy (ChT) or biological therapy, as an organ-preserving modality plays an important role in the treatment of cancers of the head and neck (H&N) providing—besides retaining speech and swallow functions practically completely as well as yielding good cosmetic results—a high locoregional tumor control (LRTC). However, delivering maximal doses with external beam irradiation (EBI) to the target volume for better local control (LC) results in unnecessary radiation exposure of the surrounding critical organs (salivary glands, mandible, masticatory muscles, and so forth) thereby increasing the incidence of side effects (xerostomy, osteoradionecrosis [ORN], fibrosis, trismus, and so forth). Intensity-modulated radiotherapy (IMRT) can decrease toxicity, but brachytherapy (BT)—although it is an invasive method requiring special skills and interdisciplinary co-operation with the (H&N) surgeon—seems to be the best choice for dose escalation over a short treatment period and for minimizing radiation-related normal tissue damage,

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due to the rapid dose falloff around the source (1, 2). Low-dose-rate (LDR) BT was the gold standard until the end of the 20th century. Extensive experience with LDR BT has been described in the literature (1–3). Nowadays in several institutions, HDR and pulsed-dose-rate (PDR) BT have replaced LDR BT, because these stepping source technologies offer the advantage of optimizing dose distribution by varying dwell times (2, 3). Although the application of HDR BT is growing worldwide, it is still not widely used because of lack of experience and biological concerns. The potential radiobiological "disadvantage" of HDR can be compensated with twice-a-day (a minimum interval of 6 hours) fractionation schedule and limited fraction doses ≤ 6 Gy (3–5). For these reasons, the Groupe Européen de Curiethérapie and the European Society for Radiotherapy & Oncology (ESTRO) recommend using fraction dose <3–4 Gy and the American Brachytherapy Society (ABS) ≤6 Gy per fraction (3, 4).

On the basis of relevant results from the literature, HDR appears to yield LC and complication rates equivalent to those of LDR (2, 6–10).

BT may be applied alone or combined with surgery in early stage lesions of the oral cavity (OC), where the risk of regional metastases is low. In advanced cases or if there is a high risk of nodal metastases, it is used together with EBI. BT is also a reasonable treatment choice in previously irradiated recurrent cancer, due to tumor extension precluding complete resection with clear surgical margins. In the literature, the most frequently applied isotopes are ^{226}Ra, ^{125}I, ^{222}Rn, ^{131}Cs, ^{198}Au, and ^{192}Ir. The latter is nowadays the most commonly used worldwide.

This review presents the results and indications of combined EBI and BT in carcinoma of the base of tongue (BOT) and other sites of the H&N region and deals with the role of BT among other radiotherapy modalities (IMRT, stereotactic radiotherapy [SRT]) in these localizations.

Methods

For this review, the literature search was performed in MEDLINE (via Pubmed) and limited to articles dealing with BOT, OC, oropharynx (OP), nasopharynx (NP) cancer, and perioperative and intraoperative cases treated with the combination of EBI and BT. Relevant articles with higher number of patients and with appropriate statistical analyses were assessed, but for BOT, we applied a more detailed analysis. Using this method, we selected 83 articles.

EBI + BT in BOT cancer

In the treatment of BOT tumors, the "organ-preserving" modalities have become more and more important, because unlike surgery, which often results in significant morbidity and poor quality of life (QOL) due to impairment of speech and swallowing, they provide a practically complete retaining of functions as well as good cosmetic results and a high LRTC. In a retrospective comparison of outcomes of surgery and RT from different medical centers in the United States, it was found that severe complications occurred in 32% vs. 3.8% in those who underwent upfront surgery vs. radiation (11). So RT with/or without ChT is the most important tool of this kind of treatment (12–24). Local tumor control can be increased without unnecessary radiation to the surrounding normal tissues by local dose escalation using interstitial BT (IBT) boost after EBI (13–19, 25–36). EBI is an essential component in the treatment of the OP because of the propensity of the disease to spread to the lymphatics (37).

In the OP region, the BOT is the most frequent site for BT. LDR BT has been applied for a long time in the treatment of BOT tumors with a good effectivity (13–19, 25–33), but only a few analyses can be found in the literature on the application and efficacy of HDR BT (7, 33–35).

Earlier, it was more common to treat BOT cancer exclusively with EBI. Five-year LC has been reported in the range of 28–70%. Based on tumor (T) size, LC was 72–100% for T1, 54–89% for T2, 32–67% for T3, and 11–20% for T4. Five-year overall survival (OS) was between 22% and 44% (27, 31, 38–44). As to the incidence of grade 4 toxicities, soft-tissue necrosis (STN) and ORN occurred in 0–20% and 0–16%, respectively (26, 44–46).

Authors using LDR BT boost after EBI reported an improved 5-year LC (Table 1) of 64–89%. Five-year OS (Table 1) was reported in the range of 26% and 87% (13–16, 18, 19, 25–33). The time interval between the end of the EBI and the start of the LDR boost varied between 1 and 69 (mean 21) days. As severe (grade 4) side effect, STN occurred in 2.5–27% and ORN in 0–6% (13–16, 18, 19, 25–34, 47).

There are only few data available about the role of HDR BT boost in the treatment of BOT tumors (Table 1). van de Pol *et al.* (33) treated 30 patients with EBI and LDR, PDR, or HDR BT boost. LDR and HDR (24–35 Gy) treatment was carried out in 16 and 5 cases, respectively, while PDR (20–28 Gy) in 9 cases. Cano *et al.* (34) presented 88 patients with LDR (n = 11) or HDR (n = 77) boost. Local recurrence rate was 18.9%. In these studies, LDR and HDR results were not analyzed separately. Results are summarized in Table 1.

In the analyses of Takacsi-Nagy *et al.* (7) with HDR boost, the dose of EBI was 60 Gy and the BT dose was 12–30 Gy. Implantations for BT were carried out 2–6 (mean 3) weeks after completing EBI. The 5-year actuarial LC by T-status was100% for T1, 75% for T2, 61% for T3, and 52% for T4, whereas in the LDR series on average, it was 85–100% for T1, 50–100% for T2, and 46–100% for T3-T4 (13–16, 18, 19, 25–33).

Johansson *et al.* (36) published results with PDR BT. EBI dose was 1.7 Gy, twice daily to 40.8 Gy or 46–50 Gy used with conventional fractionation. BT dose was 30 or 35 Gy. The median time interval between the end of the EBI and