HIGH DOSE RATE BRACHYTHERAPY IN HEAD AND NECK TUMOURS

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SUMMARY

Introduction: Brachytherapy (BT) is a type of radiation therapy, which consists of placing a radioactive source directly in or close to the tumour, by the insertion of guide needles, rods, probes and radioactive wires or the implantation of "seeds". High-dose-rate brachytherapy (HDR-BT) makes use of a radioactive substance that releases a large amount of radiation in a short time, generally high-dose-rate iridium-192, which has very little volume and so enables very fine tubes to be automatically introduced and controlled from a computer. Unlike low-dose-rate brachytherapy (LDR-BT), its administration does not require the patient to be immobilised and isolated for long time periods; moreover, irradiation of healthcare staff during the introduction of radioactive isotopes is avoided.

Objectives: The principal aim of this report was to assess the effectiveness and safety of high-dose-rate brachytherapy in treatment of tumours of the head and neck. The specific objectives were twofold: 1) to assess the benefits in terms of loco-regional control, distant metastasis, survival, safety, and costs with respect to conventional treatments (external radiotherapy, surgical excision, chemotherapy and low rate brachytherapy); and 2) to assess the benefits with respect to new treatment modalities (intensity modulated radiation therapy, stereotactic radiotherapy, etc.).

Methods: In April 2012, we conducted a systematic search, with no time limit, of the scientific literature contained: in the leading computerised biomedical databases, namely, PubMed, Embase, ISI Web of Knowledge, Centre for Reviews and Recommendations, Cochrane, etc.; and in databases of ongoing studies (ClinicalTrials.gov, Current Controlled Trials, etc) and clinical practice guidelines (National Guideline Clearinghouse, Scottish Collegiate Guideline Network, etc.). In addition, a general Internet search was made to locate grey literature. Papers were selected on the basis of pre-established inclusion criteria, excluding, among others, studies that jointly assessed different brachytherapy techniques and those that had fewer than 50 patients. The data were collected and summarised in evidence tables, with quality being assessed using the SIGN scale.

Results: The study covered a total of 33 publications, which reported on 24 studies: a breakdown of the latter showed that 8 addressed oral cavity and oropharynx (grouped, tongue, lip and floor of the mouth), 10 nasopharynx, 2 recurrences, and 4 costs. Save for one clinical trial on tongue cancer, all comparison studies were retrospective case series based on historical controls. In the analysis of the application of HDR-BT in grouped tumours of the oropharynx, local control at 5 years was 83% and no significant differences were found in terms of the severe late complications with respect to LDR-BT (ulcers: 31% vs. 29%; erosions: 21% vs. 21%). In

a joint analysis of tumours of the oral cavity and oropharynx coming from the same health centre (n=55), loco-regional control was 87% (T1-T2) and 47% (T3-T4) respectively. In the randomised clinical trial conducted on tongue cancer (n=51), the local control rate at 7 years was slightly higher with HDR than with LDR, though this difference was not significant (87% vs. 77%). A retrospective analysis of the complications recorder at this institution during periods of application of HDR (1991-1999) and LDR (1967-1996) also found similar complication rates. In another series from a different institution, local control in patients with tongue cancer was significantly greater with surgical resection (94%) than with LDR (83%) or HDR (65%), and the mandibular osteonecrosis rate was significantly higher in the HDR-BT group (20% vs. 8.4%). In lip cancer, only study furnished results on effectiveness (n=103 patients) and this reported that neither local-relapse free survival at 5 years nor acute- and late-complication rates varied when LDR was replaced by HDR (94%).

Insofar as the nasopharynx was concerned, the 12 case-series analyses (10 health centres) concluded that the local control rates were higher with HDR-BT boost plans than with external beam radiation therapy (EBRT) plans alone (86%-97.5% vs. 60%-90%). Overall disease-free survival at 5 years was also higher in the group treated with HDR-BT boost (71%-92% vs. 60%-90%). In one of the series, the severe complication rates were very high, i.e., auditory loss/deafness (84%), osteonecrosis/osteolysis of the jaw (82%), cranial neuropathies (47%) and fibrosis of the neck (13%). In one analysis that compared three-dimensional conformal radiation therapy (3D CRT) boost to HDR boost, the overall and cause-specific 5-year survival rates were slightly higher in the 3D-CRT group (64% and 70% vs. 56% and 60%). In another study, local control at 3 years was observed to be greater during the period in which fractionated stereotactic radiosurgery replaced HDR-BT as a boost to EBRT (86% vs. 71%).

Discussion: Since only one small-sized clinical trial was identified and all the remaining comparative studies were retrospective analyses of highly biased time series, there is no way of knowing to what extent the above results furnish valid and applicable information. Aspects such as the lack of comparability in terms of patient characteristics, study period, treatment protocol and follow-up time, as well as the lack of information on patients' progress and complications mean that these results serve solely for postulating possible hypotheses, and not for inferring conclusions or specific recommendations.

Conclusions and recommendations: The results of the studies reviewed leave important doubts as to the application of HDR-BT as a definitive treatment for primary tumours of the head and neck. The results are not consistent in terms of their equivalence for controlling relapses in tumours of the tongue, and there are studies which show a clear trend towards an increase in late grade III or IV toxicity. The nasopharyngeal studies indicate that local control may be greater with fractionated stereotactic radiosurgery or three-dimensional conformal radiation therapy, and there are many authors who feel that these and other tumours of the head and neck could be more effectively treated with treatment plans and/or modalities other than HDR-BT. An evidence-based, clinical practice guideline should be drawn up to address the various alternatives for treatment of cancer of the head and neck, including different plans, guidelines and radiation dosage. In view of the

lack of quality studies, this is admittedly the only way of drawing up recommendations for the treatment of these tumours.