Original article

GEC-ESTRO ACROP recommendations for head & neck brachytherapy in squamous cell carcinomas: 1st update – Improvement by cross sectional imaging based treatment planning and stepping source technology

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A B S T R A C T

The Head and Neck Working Group of the GEC-ESTRO (Groupe Européen de Curiethérapie – European Society for Therapeutic Radiology and Oncology) published in 2009 the consensus recommendations for low-dose rate, pulsed-dose rate and high-dose rate brachytherapy in head & neck cancers. The use of brachytherapy in combination with external beam radiotherapy and/or surgery was also covered as well as the use of brachytherapy in previously irradiated patients. Given the developments in the field, these recommendations needed to be updated to reflect up-to-date knowledge.

The present update does not repeat basic knowledge which was published in the first recommendation but covers in a general part developments in (1) dose and fractionation, (2) aspects of treatment selection for brachytherapy alone versus combined BT + EBRT and (3) quality assurance issues.

Detailed expert committee opinion intends to help the clinical practice in lip-, oral cavity-, oropharynx-, nasopharynx-, and superficial cancers. Different aspects of adjuvant treatment techniques and their results are discussed, as well the possibilities of salvage brachytherapy applications.

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Locoregional failure is the predominant pattern of failure in head and neck (H&N) cancer [1] and the majority of local failures are identified in the high-dose areas of modern radiochemotherapy series [2,3]. Hence, local dose intensification is an unmet need in H&N cancer, especially taking into account that large cohort analysis data showed that local control was the most significant variable affecting the development of distant metastasis [1–4].

Brachytherapy (BT) alone or in combination with external beam (EBRT) and chemotherapy leads to local dose escalation over the possibilities of up-to-date EBRT technologies. Major advantages of modern brachytherapy are the use of imaging in BT target and organ of risk definition, the implementation of stepping source technology with the potential for intensity modulation and the developments in medical and physics quality assurance (QA).

The GEC-ESTRO Head & Neck Working Group published the first recommendations in 2009 [4]. In this update the recommended standards of H&N BT by the use of stepping source technology and cross sectional imaging based treatment planning are considered; however, without discussing recommendations regarding the use of imaging technology. Generally, we advice to use MRI for definition of tumor extension and CT for investigating bone involvements. PET could be useful for staging procedures and for differentiation between scar and biologically active tumor tissue as well for information on hypoxic regions.

General aspects of treatment planning: dose and fractionation

Target definition of the Gross Tumor Volume (GTV) and Clinical Target Volume (CTV) are usually performed by clinical examination aided by imaging and intraoperative findings. In brachytherapy, typically no additional margin is required to ensure that the
CTV receives the planned dose and therefore, unlike external beam irradiation, CTV and PTV (Planning Target Volume) are considered equivalent. The classical Paris system rules combined with cross sectional imaging offers useful help in preimplant determination of the number of planes, the number of catheters and the spacing depending on the CTV characteristics.

Brachytherapy in the H&N area is usually delivered through fixed applicators (plastic tubes or steel needles) inserted with a margin of 5–10 mm around the CTV. An appropriate implant geometry to the CTV is essential to provide an adequate target coverage and a favorable dose non-uniformity ratio (V_{100}/V_{50} = DNR). The optimal spacing between applicators is ≤15 mm [5]. Surface mold applications are sometimes useful for superficial tumors of the head and neck region.

Dose planning and dose calculation should be based on 3D studies from a CT or MRI scan. The prescription dose is usually the minimum dose received by the CTV or a CTV surrogate (i.e., the D_{90} > 100, V_{50} > 90%). Dose inhomogeneities need to be minimized following general rules such as those derived from the Paris system [6,7] with additional optimization if needed, mainly by geometrical and graphical methods [8] which is possible in stepping source systems. A cautionary measure is to keep the hyperdose sleeves (200% isodose volumes) as thin as possible and not confluent with other applicator sleeves [6]. DNR should be equal or lower than 0.36 and in IMRT (intensity modulated Brachytherapy) 0.42 [9]. However, in small GTVs (few cm³ and applicator spacing of less than 10 mm), the DNR may be as high as 0.50–0.52. Dose through the skin should be avoided if possible – except when using surface molds or at the skin involving cancers.

Standardized Organ at Risk (OAR) dose–volume constraints in H&N brachytherapy are lacking. It is wise, however, to keep the dose in bone, nerves, vessels and other dose-limiting organs as low as possible provided that the CTV coverage is adequate (i.e., D_{95} is at least 90% of the prescribed dose). The use of lead sheats or plastic spacers is encouraged to reduce the dose to the ipsilateral mandible in oral cavity implants.

The dose administered in H&N brachytherapy depends on the actual indication for therapy and given type of fractionation. Due to lack of large cohort randomized data retrospective series with long term follow-up has to be relied on. Most available outcome data come from the LDR Ir-192-wire era and should be used as a reference when proceeding to modern fractional schedules of PDR and HDR. The LQ (Linear-Quadratic) model with an α/β ratio of 10 Gy and a repair half-time of 1.5 h could be used to calculate iso-effective doses of different fractionation schedules [4]. Recommendations from ICRU report 58 should be used when reporting brachytherapy [10].

When moving from LDR to PDR it must be taken into account that the original PDR schedule with 0.5 Gy/pulse every hour during both day and night was designed to be biologically equivalent to LDR [11]. It has also been postulated that pulsing every second or third hour would be equivalent [12]. Long term clinical outcome data with PDR 24 pulses per day and 12 pulses per day are now available [13–16]. In contrast, when moving from LDR to HDR the total treatment dose has to be reduced depending on the dose per fraction. To be able to deliver the HDR brachytherapy in a short overall time most institutions use 2 fractions per day with a minimum of 6 h interval that is the time required to allow complete repair of sublethal damage. A meta-analysis did not reveal significant differences in outcome compared to LDR, but the data need to be interpreted with caution [17]. Table 1 gives an overview of proposed fractionation schedules for PDR and HDR.

**General aspects of treatment selection: BT alone versus BT + EBRT**

**Brachytherapy alone**

Brachytherapy alone has been nowadays replaced by surgery in the treatment of most T1 and T2 tumours due to advances in surgical and anesthetic procedures that have been proven safe and effective even in frail patients; however, no randomized trial has ever compared surgery versus brachytherapy in primary tumours. In addition, surgery provides a complete pathological documentation of the extent of disease that allows an individualized adjuvant treatment plan for subsequent radiotherapy.

However, brachytherapy alone remains an acceptable mode of treatment in intact T1 and small T2 tumours with low risk of lymph node involvement that meets at least one of the following criteria: 1/Patient decision; 2/Tumor location in areas of functional importance (lip commisure, etc.); 3/Tumor location in areas of cosmetic relevance such as the periorificial zone (eyelids, pinna, ears, etc.); 4/Medical contraindication for radical surgery. Ninety percent of the cases described above are locally controlled after LDR/PDR doses of 60–70 Gy with hourly doses in the 0.4–0.7 Gy range [18]. These results underline the equal effectivity of brachytherapy compared to surgery in nodal negative T1-T2 cancers.

Finally, patients with 5/Small tumors of 3 cm or less arising in previously irradiated areas not suitable for surgical salvage are also potential candidates for primary brachytherapy alone with dose and volume adjustments aimed to minimize potential complications derived from cumulative dose. Ten years local control rates of salvage brachytherapy with simultaneous chemotherapy are by 75%.

**Combined EBRT + brachytherapy**

The combination of external beam irradiation and brachytherapy for H&N cancers follows the same principles applied in other tumor sites treated with combined modality therapy such as advanced cervical cancer. Brachytherapy is used as a boost 1–2 weeks after the completion of EBRT, usually in the form of IMRT (Intensity Modulated Radiation Therapy) or VMAT (Volumetric Arc Therapy). Cisplatin-based chemotherapy is commonly added in the more advanced cases. Attempt should be made to keep the overall treatment time similar to EBRT alone.

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Table 1: Different PDR and HDR schedules for H&N BT proposed in literature.

<table>
<thead>
<tr>
<th>Brachytherapy schedule</th>
<th>Mono (Gy)</th>
<th>Boost (Gy)</th>
<th>Surgery + BT (Gy)</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>PDR 0.4 Gy</td>
<td>24 pulses/d</td>
<td>70</td>
<td>30</td>
<td>50–70</td>
</tr>
<tr>
<td>PDR 0.8 Gy</td>
<td>12 pulses/d</td>
<td>60</td>
<td>30–35</td>
<td>50–60</td>
</tr>
<tr>
<td>HDR 2.5 Gy</td>
<td>2 fx/d</td>
<td>5d/w</td>
<td>34–36</td>
<td>10–20</td>
</tr>
<tr>
<td>HDR 3 Gy</td>
<td>2 fx/d</td>
<td>5d/w</td>
<td>18</td>
<td>54</td>
</tr>
<tr>
<td>HDR 4 Gy</td>
<td>2 fx/d</td>
<td>5d/w</td>
<td>36</td>
<td>–</td>
</tr>
<tr>
<td>HDR 5 Gy</td>
<td>2 fx/d</td>
<td>5d/w</td>
<td>45</td>
<td>–</td>
</tr>
<tr>
<td>HDR 6 Gy</td>
<td>2 fx/d</td>
<td>5d/w</td>
<td>48</td>
<td>21</td>
</tr>
</tbody>
</table>

* Depends on the implant inhomogeneity.
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