



GEC-ESTRO recommendations

GEC-ESTRO recommendations for brachytherapy for head and neck squamous cell carcinomas

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ABSTRACT

Both primary and recurrent squamous cell carcinoma of the head and neck are classic indications for brachytherapy. A high rate of local tumor control at the cost of limited morbidity can be achieved with brachytherapy through good patient selection, meticulous source implantation and careful treatment planning. However, no randomized trials have been performed, and there is scant evidence in the literature especially regarding practical clinical recommendations for brachytherapy for head and neck subsites. The Head and Neck Working Group of the European Brachytherapy Group (*Groupe Européen de Curiethérapie*-European Society for Therapeutic Radiology and Oncology (GEC-ESTRO) therefore decided to formulate the present consensus recommendations for low-dose rate, pulsed-dose rate and high-dose rate brachytherapy. The use of brachytherapy in combination with external beam radiotherapy and/or surgery is also covered as well as the use of brachytherapy in previously irradiated patients. Given the paucity of evidence in the literature, these recommendations are mainly based on clinical experience accumulated by the members of the working group over several decades and the respective publications. The recommendations cover in a general part (1) patient selection, the pre-treatment work up and patient care, (2) treatment strategy, (3) target definition, (4) implant techniques, (5) dose and dose rate prescription, (6) treatment planning and reporting, (7) treatment monitoring (8) catheter removal, and (9) post-treatment patient care and follow-up. The recommendations are then specified for the classical brachytherapy tumor sites following an analogue more focussed structure (patient selection, implant technique, target definition, dose and dose rate prescription, results): lip, oral mucosa, mobile tongue, floor of mouth, oropharynx, nasopharynx, paranasal sinuses.

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Experience accumulated over several decades treating head and neck tumors with irradiation has demonstrated that a high tumor dose is required to achieve local control. With external beam irradiation alone, it is difficult to spare adjacent normal tissues such as the salivary glands, the mandible, and mastication muscles which sustain undesirable late effects. The overriding advantages of brachytherapy are a high localized dose with rapid fall-off, and a short overall treatment duration [1]. The primary tumor volume

receives a total dose, which cannot be safely delivered by external beam radiotherapy alone, and rapid fall-off allows relative sparing of critical normal tissues. Interstitial implant therapy is ideal for selectively delivering a high dose exclusively to the primary tumor volume, thus minimizing sequelae. Considerable experience has been accumulated with low-dose rate (LDR) brachytherapy in the treatment of carcinoma of the lip, tongue, floor of the mouth, oral mucosa, base of the tongue, tonsillar region, soft palate, nasopharynx, etc. [2]. It can be applied as the sole treatment, as a complementary treatment with surgery and as a local boost in combination with external beam radiation therapy. The recent analyses of large clinical series show that it is an effective treatment method, but also indicate that LDR brachytherapy modalities should be optimized to increase the therapeutic ratio when treat-

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ing such tumors. LDR brachytherapy is now challenged by high-dose rate (HDR) brachytherapy and pulsed-dose rate (PDR) brachytherapy [3]. HDR and PDR stepping source technology offers the advantage of optimizing dose distribution by varying dwell times [1]. Preliminary results obtained with these two latter modalities are now available [3].

A panel of members of the *Groupe Européen de Curiethérapie* [European Brachytherapy Group] – European Society for Therapeutic Radiology and Oncology (GEC-ESTRO) with clinical expertise in brachytherapy for Head and Neck cancers have formulated recommendations for LDR, HDR, or PDR brachytherapies for newly diagnosed or recurrent head and neck cancer. As no randomised trials have been performed in the field, these general and site-specific recommendations were established through consensus. Experts in head and neck cancer, including some not experienced in brachytherapy, reviewed this report. It was finally approved by the GEC-ESTRO Executive Committee.

Squamous cell carcinomas are the most common head and neck cancers, and will only be considered in this report. Curative brachytherapy alone is usually not indicated for other types of cancer such as adenocarcinomas, lymphomas, melanomas, and sarcomas (with the exception of rhabdomyosarcomas that can be a good indication for brachytherapy).

General aspects

Patient selection, pre-treatment work-up and patient care

Interstitial brachytherapy can be used alone or in combination with external beam radiotherapy and/or surgery. In the case of primary brachytherapy, radioactive sources can be implanted exclusively in well-defined tumors, and the indications are inevitably limited [1]. When combined with surgery (intra-, perioperative brachytherapy applications), it is possible to widen surgical margins by approximately 1.0–1.5 cm. The aim of the combined procedure is to preserve organ function or for cosmetic purposes. Brachytherapy ideally offers local dose escalation in large tumors, and serves as an effective boost therapy. All potential candidates for brachytherapy should undergo a detailed examination of the head and neck region before any treatment by the brachytherapist as well as a thorough general physical examination and a chest radiograph. In most patients, especially for tumors of the posterior part of the oral cavity and the oropharynx, an examination under general anesthesia is necessary, preferably in combination with panendoscopy, in order to rule out synchronous second primary tumors. Panendoscopy includes a bronchial and oesophageal examination with brush cytology and biopsies of any lesion.

Computerized tomography (CT) and magnetic resonance imaging (MRI) are both useful. The CT scan depicts both soft tissue and bone, and is more sensitive than MRI for evaluating lymph nodes. MRI is more sensitive for detecting muscle invasion, because of better tumor-to-muscle contrast. MRI is also more sensitive than CT for depicting invasion of the medullary space of the mandible and tumor spread along the inferior alveolar nerve. 3D delineation of the tumor volume is also easier with MRI. Fluorodesoxyglucose (FDG) Positron Emission Tomography (PET) can sometimes visualize tumor or nodal extension overlooked by CT and MRI.

Brachytherapy alone is contraindicated if the tumor scheduled for implant therapy is not accessible or if the tumor limits are ill-defined (dose distribution is inhomogeneous, and displacement of radioactive sources by a few millimeters creates unplanned hot or cold spots, thus perfect geometry is mandatory) or if the tumor is abutting or has invaded bone.

Oral hygiene and the dental status should always be evaluated. Mandibular panoramic radiographs are required to provide information about the height and the structure of the mandible as well

as radiographic evidence on bone destruction. When radiotherapy is planned, the oral surgeon evaluates the dental and periodontal status completely. When dental extractions are necessary, complete healing is required before brachytherapy to avoid necrosis. When linear sources are used for implant therapy, a prosthesis including lead shielding can be used when brachytherapy of the lips, the mobile tongue, the oral mucosa, and the floor of mouth is planned close to the mandible, to reduce the dose to the mandible and to avoid osteoradionecrosis. This shielding system is made of a 2 mm-thick lead shield encased in a plastic protection. Each patient has a custom-made lead shield adapted to the anatomy and tumor volume where the source is implanted. In fact, two dental shielding systems are made for each patient. The first is made of lead and the second of acrylic resin alone. The radiotransparent gutter is used for X-ray control during the implantation procedure to check any tube displacement, and for dosimetry, in order to reproduce identical conditions as during treatment. The patient wears the lead shielding throughout the duration of irradiation, to protect the teeth, gums, and mandible. It reduces the dose delivered by about 50%. With intensity-modulated brachytherapy (IMBT), the protection of critical structures can be managed by applying different dwell times and source positions.

Treatment strategy

When external beam radiation or neoadjuvant chemotherapy is combined with brachytherapy, the initial tumor volume should always be considered, whatever the subsequent tumor shrinkage is. The placement of radio-opaque markers (e.g., gold seeds) or tattoos can be very helpful in delineating the tumor volume before any shrinkage occurs.

Concomitant chemotherapy during brachytherapy is not recommended for the treatment of primary tumors outside clinical trials, unless relevant clinical data are available. However, concurrent chemotherapy during brachytherapy appears to be useful for the treatment of recurrences [4,5].

The total duration of radiation therapy, including the external beam component and the brachytherapy boost, should be as short as reasonably achievable (within 8 weeks) to limit tumor cell repopulation. This means that the interval between external radiotherapy and brachytherapy should be as short as possible and less than 2 weeks.

Target definition

The Gross Tumor Volume is the primary tumor volume defined by the clinical examination and imaging techniques. The Clinical Target Volume (CTV) is the GTV plus a safety margin taking into account possible microscopic extension, which depends on the tumor situation but should never be less than 5 mm, and is in most cases 0.5–1 cm. The Planning Target Volume (PTV) is not different from the CTV in a “perfect” implant. The Treated Volume is encompassed by an isodose surface corresponding to the minimal target dose, the isodose ideally encompassing the CTV.

The skin should not be included in the CTV unless it is invaded by tumor, and the skin dose should be minimized as much as possible. Markers placed on the skin surface or CT/MRI planning can help identify it and calculate the dose.

Implant technique

Brachytherapy sources should always be implanted in an operating room equipped for anesthesia, with adequate lighting and suction facilities and the means to deal with extensive bleeding. Although arterial hemorrhage is exceptional it should be anticipated. That is why two competent persons should always be present.

The brachytherapy technique should be based on a classic system for interstitial brachytherapy (like those designed in Paris, Manchester or New York), which mainly consists of three parts:

- A set of rules to describe how the radiation sources should be distributed inside a defined volume to achieve acceptable dose homogeneity.
- A dose calculation method and
- A system for dose prescription. These methods should be updated because they were developed before the advent of computers for calculating and displaying isodoses, and before their integration with imaging. It is now possible to better adapt dose distribution to the CTV, especially with remote afterloaders using stepping source technology, which allows the “optimisation” of dwell positions and times. In general, catheters should be parallel and equidistant; they are ideally spaced at 1 to 1.5 cm, while intersource spacing up to 2 cm is acceptable under certain circumstances. Ultrasound or fluoroscopy guidance may be helpful when implanting catheters. Most LDR implant techniques can be used for HDR or PDR treatments. However, some of them, such as the loop technique, are more complicated because it is difficult for the source “to negotiate the bridge”; loops can be replaced by two parallel tubes and dose distribution can be optimized by increasing dwell times at the blind end of the catheter at the tip [6].

Dose and dose rate prescription

The total dose, dose rate, dose per fraction, and overall treatment time are important considerations. Recommendations will be given according to the tumor site. In general, in LDR brachytherapy, delivering a high total dose is recommended to secure local control, and to maintain the dose rate between 0.3 and 0.6 Gy/h in order to minimize late side effects [7,8]. With HDR brachytherapy, a smaller dose per fraction may reduce tissue injury, but a higher number of fractions are required. Doses between 3 and 4 Gy per fraction have been recommended [9]. When irradiation is delivered twice a day, the interval between fractions should be as long as possible, with a minimum of 6 h. With PDR brachytherapy, which offers the biological advantages of LDR brachytherapy with the technological advantages of the HDR-afterloading method, daytime PDR schedules were introduced by some authors to avoid hospitalization and to reduce overall treatment costs. Whether it is possible to restrict PDR irradiation exclusively to office hours, as proposed by some authors [10,11], remains controversial. Until now, no prospective study and no long-term results of any study support the “office hours” schedule. In our opinion, only the complete 24-h treatment schedule (pulse dose 0.3–0.7 Gy/h) guarantees that PDR brachytherapy will preserve all the radiobiological advantages of LDR brachytherapy. The results of clinical studies show that PDR brachytherapy leads to a similar level of success in terms of local control and toxicity, compared with conventional LDR brachytherapy, provided the same basic rules are applied, e.g., delivering the same total dose in the same overall treatment time [4,5,7]. The use of the linear-quadratic model is recommended to calculate iso-effective fractionation schedules, with alpha beta value of 10 Gy and half time of repair of 1.5 h [12].

The optimum time-dose pattern for PDR brachytherapy remains under debate. Some recommend the same total dose as that used for LDR brachytherapy, delivered in the same total time in 24 hourly fractions per day. Others have estimated that treatment can be safely delivered in a smaller number of larger size fractions delivered 3 h apart, with or without a night break [9,11].

Treatment planning and reporting

Dose distribution is calculated by the Treatment Planning System (TPS) based on the images of the implant (using dummy sources). Although this was successfully achieved in the past using two orthogonal fields, dose calculation based on 3D images (CT and/or MRI) is now highly recommended. The use of 3D imaging in head and neck brachytherapy to delineate the GTV and CTV (despite some uncertainties) and the organs at risk including the mandible makes it possible to obtain objective data on dose volume histograms (DVHs). Identifying hot spots on contiguous areas or cold spots in organs at risk also provides elements, which allow the optimization of dose distribution, especially if a stepping source afterloader is to be used (the so-called Intensity-Modulated Brachytherapy – IMBT).

The optimization method should be specified. Quality parameters such as the Dose Non-Uniformity Ratio (DNR), Homogeneity Index (HI) and Uniformity Index (UI) together with other parameters as listed in Table 1 should be documented. However, optimization should not be used as a substitute for poor-quality catheter implantation.

The recommendations for reporting interstitial therapy according to ICRU report 58 are given in Table 1.

Treatment monitoring

During brachytherapy, meticulous patient monitoring is mandatory, in order to detect potential displacement of radioactive sources or catheters. Adequate analgesic and anti-inflammatory coverage is given. Mouthwashes and nutritional support through a nasogastric tube or a gastrostomy (if necessary) are essential. Antibiotics may be useful. The patient must also be taught to watch out for inflammatory reactions, which always occur after the removal of the implants, start about 7 days later, increase until the third week, are stable over one week, and then decrease and finally disappear at the end of the sixth week. The risk of secondary infection is low during interstitial treatments, but it is still necessary to verify the position of the applicator during the irradiation.

Catheter removal

Implant catheters should be removed in the operating room, where management of hemorrhage and airway protection are achieved more effectively. An intravenous access is recommended and the presence of two persons is mandatory. In case of bleeding, bimanual compression for ten minutes is usually effective for stopping arterial bleeding.

Post-treatment patient care and follow-up

Patients should be regularly followed-up. The GEC-ESTRO recommends that patients should be seen by the brachytherapist one month after treatment, every three months during years 1 to

Table 1

Recommendations for reporting interstitial therapy according to ICRU report 58.

Description of the clinical conditions, including GTV and CTV
Description of the technique (is the application performed following a system ?)
Source specification, including RAKR (Reference Air Kerma Rate) and TRAK (Total Reference Air Kerma)
Complete description of the time-dose pattern
Treatment description
Mean central dose (MCD), Minimum Target Dose, Homogeneity Index
Volumes and their dimensions, including PTV, Treated Volume, high-dose regions, low-dose regions, reference volume, irradiated volume (level 2)
Coverage and conformity if possible
Organs at risks

3, then every six months during years 4 and 5, then yearly. The most common complication is soft tissue necrosis. Bone necrosis became uncommon once lead gutters were systematically employed during irradiation or intensity modulation with a stepping source was used. The vast majority of necroses are managed medically with antibiotics, steroids, analgics, mouthwashes, and proper feeding. Hyperbaric oxygen may be useful in severe cases. A clinical examination under general anesthesia is recommended to resect superficial necrotic tissues and to exclude a local relapse. Biopsies are not recommended unless tumor progression is suspected. Surgical excision of necrosis should only be considered after the failure of medical treatment.

Lip

Tumors <5 cm can be treated with brachytherapy alone (Table 2). Larger tumors can be treated with combined external beam irradiation and a brachytherapy boost or brachytherapy alone. Tumors invading bone should be managed surgically if feasible.

The rigid needle technique with a template offers the best geometric conditions for the implant, and it is highly recommended in HDR treatments. Tumors affecting the upper lip and those involving the commissura can be better treated using the plastic tube technique.

A protector device is mandatory for the mandible and the upper lip.

The clinical target volume includes all visible and palpable tumor extension with a safety margin of 5–10 mm.

A (LDR/PDR) dose of 60–65 Gy for T1, 65–70 Gy for T2, and 70–75 Gy or even higher doses for T3 lesions is recommended [1,13]. Experience in HDR treatments for lip cancer is limited, and the scarcity of large series with long-term results makes it difficult to establish definitive conclusions regarding the total dose and optimal fractionation schedule [14].

A simple wedge excision is indicated for superficial very limited tumors (about <5 mm). When surgical excision with primary closure and negative margins cannot be achieved, definitive brachytherapy is an excellent option. Brachytherapy when chosen offers better functional and cosmetic results than surgery or external beam radiotherapy alone. An overview of the literature shows local control rates of 90–95% at 5 years for LDR Iridium 192 brachytherapy [15]. About 80% of the local failures can be salvaged surgically. Superficial necroses occur in 2–10.1% of the cases, 70% of which heal spontaneously before 6 months, and less than 5% require surgery.

Lymph node involvement is rare but frequently bilateral. Elective neck dissection should be discussed in locally advanced N0 tumors.

Oral mucosa

Brachytherapy alone is recommended for tumors that are <4 cm in diameter and <1.5 cm in thickness. It is contraindicated if the tu-

mor extends to the bucco-alveolar sulcus or the intermaxillary commissure.

A one-or two-plane plastic tube technique is the most appropriate. A posterior loop is mandatory in medial and posterior tumors to adequately cover the buccal mucosa of the intermaxillary commissure region [16].

A lead shield can be used to protect the mandible and superior maxilla.

The clinical target volume includes the gross tumor volume with a safety margin of 10 mm at the anterior and posterior parts and 5–10 mm at its lower and upper limits.

A total dose of 65–70 Gy (LDR/PDR) delivered exclusively by brachytherapy yields the best results. If brachytherapy is given as a boost after 45–50 Gy of external beam irradiation, the dose is 25–30 Gy (LDR/PDR).

An overview of the literature shows local control rates of 80–90% for LDR Iridium 192 brachytherapy alone [1,17]. Grade 3 complications (mainly soft tissue necrosis) are observed in less than 10% of the patients.

Lymph node involvement is uncommon. As in lip cancer, elective neck dissection should be discussed in N0 locally advanced tumors.

Mobile tongue

Brachytherapy alone is recommended for T1 N0 and T2 N0 tumors that are smaller than 4 cm. For tumors >3–4 cm or N1 lesions, brachytherapy can be delivered as a boost after 40–45 Gy of external beam irradiation to the neck and oral cavity. In this case, surgery is often preferred. Postoperative brachytherapy is an elegant way to deliver adjuvant irradiation in the case of narrow or positive margins. Contraindications are T4 tumors involving the bone or incomplete coverage of soft tissue over the bones following surgical procedures.

The plastic tube technique (with or without loops) is the most commonly used. Using a spacer on the dorsum of the tongue can improve parallelism. The guide gutter technique can be applied for the smallest tumors, especially in older patients because the procedure can be performed under local anesthesia.

A lead gutter protector is mandatory.

The clinical target volume includes all visible and palpable tumor extension with a 5-mm safety margin.

The recommended dose (LDR-PDR) is 65–75 Gy for the treatment with definitive brachytherapy and 25–30 Gy after 40–45 Gy of external beam radiotherapy [18]. If delivered postoperatively, these doses are reduced to 50–60 Gy and 10–24 Gy, respectively [19]. For salvage implants in a previously irradiated territory, a dose of 60 Gy is adequate. The recommended dose rate/pulse dose is .03–.07 Gy/h/24 h. The results of HDR brachytherapy remain to be validated in prospective studies. If it is the only technique available but not included in a prospective study, treatment should be delivered in fractions of less than 3–4 Gy [20].

Table 2

SCC of the oral cavity and oropharynx: summary of methods and results according to anatomical site. RN, rigid needles; PT, plastic tubes; LC, local control; N, necrosis rate; ERT, external beam radiotherapy.

Anatomical site	Patient selection	Implant technique	Safety margin	Dose	Result
Lip	T1-3	RN	5–10 mm	60–75 Gy LDR-PDR	LC: 90–95% N: 2–10%
Buccal mucosa	<4 cm	PT	5–10 mm	65–70 Gy LDR-PDR (25–30 Gy boost if 45–50 Gy ERT)	LC: 80–90% N: <10%
Mobile tongue	T1-3	PT	5 mm	65–75 Gy LDR-PDR (25–30 Gy boost if 40–45 Gy ERT)	LR: >90% N: 10–20%
Floor of mouth	T1-2N0	RN or PT	>5 mm	65 Gy LDR-PDR (10–25 Gy boost if 46–50 Gy ERT)	LR: >90% N: 10–30%
Oropharynx	< 5 cm	PT	>10 mm	LDR-PDR: 25–35 Gy boost following 45–50 Gy ERT HDR 21–30 Gy/3 Gy fractions or 21–24 Gy/ 4 Gy fractions boost following 45–50 Gy ERT	Base of tongue: LR: T1-2 80–90% T3-4 65–80%. N 25% Faucial arch: LR: T1-2: up to 90%. T3: 67%. N: 20%

The local control rate is higher than 90% for T1, and T2 N0 treated with brachytherapy alone [1]. It is lower in patients treated with external irradiation and a brachytherapy boost. Approximately 10–20% of patients may develop soft tissue necrosis within the implant volume. Osteoradionecrosis may occur in 5% to 10% of cases; the area of the exposed bone is usually less than 1 cm. The vast majority of necroses heal spontaneously or after medical treatment.

Lymph node involvement is frequent and often bilateral. Elective treatment of the neck with surgery and/or radiation is recommended in the majority of the cases. Watchful waiting regarding the neck may be discussed in the case of T1N0 tumors treated with brachytherapy alone.

Floor of mouth

The relative risk of normal tissue injury for lesions near the mandible is greater than for the oral tongue, where the bone is not contiguous. Brachytherapy alone is recommended for T1N0 and T2N0 tumors <30 mm and >5 mm from the mandible. Tumors >30 mm and <40 mm and >5 mm from the mandible may be treated either with brachytherapy or by surgery. Surgery is recommended for tumors >40 mm or <5 mm remote from the mandible. Postoperative irradiation may be indicated. Postoperative brachytherapy may be used to deliver adjuvant irradiation in case of narrow or positive margins or lymphatic invasion or tumor infiltration exceeding 5 mm in the absence of other risk factors such as positive lymph nodes. Involvement of the mandible is an absolute contraindication to brachytherapy. However, if surgery is not suitable because of the patient's age or a poor medical status, extension to the gingiva if limited is not an absolute contraindication to brachytherapy.

Both guide-gutter and plastic tube techniques are applicable. In order to decrease the dose to the mandible and consequently the risk of osteoradionecrosis, contact between the mandible and high dose areas should be minimized (no more than two lines), and they should be inclined or bent according to the internal surface of the mandible.

A lead spacer can be used.

The clinical target volume includes all visible and palpable tumor extension with a safety margin of at least 5 mm.

The recommended dose (LDR-PDR) is 65 Gy in case of definitive brachytherapy and 15–25 Gy after 46–50 Gy of external beam radiotherapy. If delivered postoperatively, these doses are reduced to 50–65 Gy and 10–25 Gy, respectively. For salvage implants in a previously irradiated territory, a dose of 60–65 Gy is adequate [4–5]. For HDR brachytherapy, no recommendations can be proposed until prospective studies have been conducted.

The local control rate is higher than 90% for T1, and T2N0 treated with brachytherapy alone [1] or postoperatively [20]. It is lower in patients with larger tumor treated with external beam irradiation and a brachytherapy boost. Approximately, 10–30% of patients may develop soft tissue necrosis within the implant volume. Osteoradionecrosis may occur in 5–10% of the cases. The vast majority of necroses heal spontaneously or after medical treatment. A surgical intervention is necessary mostly in only 1–2% of patients [20].

Lymph node involvement is frequent and often bilateral. Elective treatment of the neck with surgery and/or radiation is recommended in the majority of cases. Watchful waiting regarding neck surgery may be discussed in case of T1N0 tumors treated with brachytherapy alone.

Oropharynx

Iridium LDR, HDR or PDR interstitial implants may be indicated for the treatment of squamous cell carcinoma measuring <50 mm

in diameter arising in the base of tongue, the soft palate, the tonsillar fossa, and the vallecula.

Implant brachytherapy is rarely used if the primary tumor extends to the retromolar trigone, and contraindicated in the nasopharynx, the larynx, the hypopharynx, or if the primary tumor extends to the underlying structures or invades bone. Implant therapy is usually not performed when the primary tumor is associated with bulky lymph nodes.

Brachytherapy is usually delivered as a boost after 45–50 Gy of external beam radiation therapy to both the primary tumor and cervical node areas. Brachytherapy alone may be used exclusively for purely exophytic tumors measuring 10 mm or less in diameter, and for recurrent cancers or new tumors arising in previously irradiated territory.

The plastic tubes are implanted under general anesthesia with nasal intubation. A temporary tracheostomy might be necessary if the vallecular region is invaded by a large tumor.

A protector device can be used for the mandible if the tumor extends to the oral cavity.

The safety margin should be at least 10 mm. In tumors of the base of the tongue, a larger safety margin may be necessary because delineation of gross disease may be problematic, and the entire organ may have to be encompassed in most cases.

After 45–50 Gy of external beam irradiation, an additional dose of 25–30 Gy of (LDR-PDR) brachytherapy is recommended for tonsillar region tumors, and 30–35 Gy for base of tongue tumors. It may be useful to boost the whole base of the tongue to 65–70 Gy and the macroscopic tumor site to 75–80 Gy in base of tongue tumors. When the source is implanted in a previously irradiated area for a recurrent or a new tumor, a dose of 60 Gy is required. With HDR brachytherapy, the fraction size and number of fractions are varied: a suggestion is that the HDR fraction size should not exceed 4.5 Gy. Typical protocols combine 45–50 Gy of external beam radiotherapy and a 21–30 Gy boost of brachytherapy in 3 Gy fractions (Eq2 Gy: 22.75–32.5 Gy for tumor and 25.2–36 Gy for late responding normal tissues) or 16–24 Gy in 4 Gy fractions (Eq2 Gy: 18.7–28 Gy for tumor and 22.4–33.6 Gy for late responding normal tissues) [9].

With base of tongue cancer, a local control rate of 80–90% can be expected in T1–2 disease and 65–80% in T3–4 lesions, with transient late necrosis of the mucosa occurring in about 25% of the cases [1,21].

With faucial arch squamous cell carcinomas, the local control rate has attained 90% for T1–2 tumors, and 67% for T3 lesions, with soft tissue necrosis occurring in about 20% of the cases [21,22].

Some retrospective analyses compared the results of external beam irradiation followed by interstitial implant brachytherapy and primary surgery followed by external beam irradiation. A better performance status score and improved quality of life were consistently observed with primary radiation therapy [21–24]. Furthermore, it was recently clearly shown that the movement of the target caused by breathing and swallowing during external beam radiotherapy can be a drawback and should be taken into account during the delineation process [25]. Brachytherapy does not face this problem.

The management of palpable cervical nodes after 45–50 Gy of external beam irradiation may consist of neck dissection or higher doses of radiation therapy, depending on the size of the nodes, their response to irradiation, and individual medical practice. A boost to the neck can be delivered by external beam irradiation and/or brachytherapy.

Interstitial implant brachytherapy can also play a special role in salvage treatment. It can be successfully used to treat tumors arising or recurring in previously irradiated territory. The 5 year local control rate is 57–69%, the 5-year overall survival rate is 14–40%, and the necrosis rate is 5–27% [4,5,26,27].

Nasopharynx

As the nasopharynx is deeply situated and surrounded by bone, vessels and nerves, only endocavitary techniques can be performed. The depth of the target volume should therefore not exceed 10 mm. Consequently, only superficial tumors or those exhibiting sufficient shrinkage after external beam radiotherapy and/or chemoradiation and not involving the underlying bone or deeply invading the infratemporal space are suitable for brachytherapy. Brachytherapy indications are therefore restricted to boost doses against minimal residual local disease after external beam irradiation or as salvage therapy for well-circumscribed and superficial local recurrences limited to the nasopharyngeal cavity. Tumors extending into the nasal cavities or the oropharynx should not be accepted for brachytherapy.

An applicator should be used. It can be customized (mould technique) or standardized (e.g., the Rotterdam nasopharyngeal applicator) [1,28]. The applicator should be properly immobilized with good apposition between the applicator and the nasopharyngeal vault.

The CTV is defined based on the information from endoscopy, CT scan and MRI. However, as it is difficult to delineate tumor extension and to define the depth of the GTV precisely, a large safety margin is recommended around the gross disease.

Dosimetry is based on two orthogonal films or CT scan slices. If CT scan slices are available, the dose is usually prescribed to an isodose covering the surface of the underlying bone, which is situated at 5–10 mm from the mucosal surface. Dose distribution is then optimized when possible so that the reference isodose follows the bone surface. Levendag et al. have published a comprehensive method based on the silicone Rotterdam Nasopharynx Applicator (RNA), and on the dose at several anatomical points related to the target and critical organs that are easy to be identified on lateral and AP X-ray films. The dose is prescribed at a reference point situated on the midline of the bony surface of the nasopharyngeal roof [23]. Brachytherapy can be used to deliver an additional dose to a small tumor volume after a full course of external beam radiotherapy. According to Levendag et al., the recommended dose for patients with a T1 tumor is 60 Gy of external beam radiotherapy in 30 fractions and 6 weeks, followed, after a rest period of 1–2 weeks, by HDR brachytherapy, 18 Gy in 6 fractions over 3 days (2 fractions per day, 6 h apart), and for T2–4 tumors, 70 Gy of external beam radiotherapy followed, after a rest period of 1–2 weeks, by HDR brachytherapy, 12 Gy in 4 fractions. TT (tumor tissue) and NT (normal tissue) dose points based on easy to identify anatomical landmarks depicted on lateral and AP X-ray films are used for dose prescription and dose reporting. The dose to the tumor is prescribed to a fixed anatomical bony landmark, the so-called “Na” point. In the recent years, T1–2 tumors were boosted with brachytherapy, while stereotactic radiation was used for T3–4 tumors [28].

When brachytherapy is delivered for a recurrent nasopharyngeal tumor in a previously irradiated area, 60 Gy (LDR–PDR) is delivered in 6 days, or even at a lower dose rate.

The results reported in the literature concern limited patient series and follow-up. The different techniques appear to be safe and effective. With combined therapy delivered upfront, one can expect a >90% local control rate for T1–2 disease [1]. About 50% of local recurrences can be controlled following a dose of 60 Gy or more.

Paranasal sinuses

Cancers involving the nasal cavity and paranasal sinuses represent 3% of all head and neck malignancies. Since the majority of these tumors are at an advanced stage at diagnosis, mutilating surgery often involves exenteration of the orbit. Histologically, the

majority of paranasal cancers are squamous cell cancers. Paranasal sinus cancers have a low metastatic rate (<15–20%), but local recurrences are fatal in the majority of the cases. If neck nodes are not involved (N0), elective neck surgery is unnecessary. Treatment results following surgery and radiotherapy (both used as monotherapy) are poor and the local recurrence rate is high. The limiting factor for successful external beam radiation is the steep dose–response curve for retinal injury as well as that of other structures in the orbit. Therefore, different combined modality methods including brachytherapy have been introduced in the clinical practice. Although early paranasal sinus lesions are often cured by surgery alone, there is still strong evidence for combining surgery and radiotherapy with the advantages of preoperative and/or dose escalated external beam radiotherapy. Brachytherapy is the ideal dose escalation method combined with external beam therapy and surgery. Treatment of the entire orbit is usually required for tumors involving the roof of the sphenoid sinus, involvement of the base of skull and/or orbital invasion. This results in major functional loss and cosmetic damage. Combined surgery and radiotherapy including brachytherapy offer the possibility of organ and function preservation in stages I, II and in some stage III tumors with orbital invasion [30–32]. Brachytherapy is indicated as monotherapy for small lesions after surgery with clear/narrow margins or for superficial recurrences, as a boost to external beam radiotherapy in all other tumor stages, and is combined with surgery in recurrent tumors.

Concerning the brachytherapy technique, the majority of the literature contains information on the use of intracavitary mould techniques. In the early literature, the manual packing method was common while manual afterloading techniques with pre-prepared obturators were used later. Most of the publications are from the 80s and older, with only a few recent papers, mainly case reports.

The target is defined intra-operatively and with preoperative cross-sectional imaging (CT/MRI). In the absence of surgery, target definition should be based on modern imaging methods (CT/MR/PET).

At present, it is not possible to recommend a specific dose using LDR, HDR or PDR given the limited data in the literature [29]. There is a longer experience with conventional moulds and LDR treatment schedules [30,31].

In 81 patients with maxillary sinus cancer having involved margins postoperatively Naszaly et al. reported an 18% higher 5-year survival rate when a brachytherapy boost was used in combination with low dose (40–50 Gy) postoperative external beam irradiation compared to patients who were treated with external beam doses of 55–65 Gy without a brachytherapy boost. They also observed a lower incidence of brachytherapy side effects if the target volume did not include the entire maxillary sinus but was limited to the residual/recurrent cancer regions [33]. Other groups have provided evidence for the feasibility of visual acuity preservation and improved outcome following treatment with interstitial implants using both LDR and HDR techniques [29,32].

Discussion

Both the oral cavity and oropharynx are essential in co-ordinating the complex functions of deglutition, phonation, and airway protection. Preserving this function is a difficult challenge when treating squamous cell carcinoma of this anatomical region. The treatment modalities available include surgery, external beam irradiation, brachytherapy and various combinations of the three [34]. The wide range of results in the literature leaves considerable uncertainty as to the treatment of choice. Despite reconstruction, resections may leave considerable functional deficits. Furthermore,

concern about adequate margins or lymph node involvement often results in the addition of postoperative irradiation, which further increases late morbidity.

Considerable experience in the treatment of head and neck tumors with radiotherapy has demonstrated that a high tumor dose is required to achieve local control. Unfortunately, even with modern imaging and new technologies such as IMRT, it is still difficult to spare adjacent normal tissues with external beam irradiation alone. Interstitial implant brachytherapy is an ideal solution if we want to deliver a high dose exclusively to the primary tumor volume thereby limiting the risks of severe xerostomia or trismus [1–3]. On the other hand, although interstitial brachytherapy is considered a highly effective technique for the treatment of limited-stage squamous cell carcinoma of the oral cavity and oropharynx, no randomized trials have been performed to confirm the superiority of implant therapy over fractionated external beam radiation therapy.

When a limited recurrence or a new tumor develops in a previously irradiated territory, brachytherapy can deliver a curative dose with an acceptable risk of complication.

The majority of the published results were obtained with low-dose-rate techniques and manual afterloading. Stepping source technology allows easier optimization of dose distribution based on 3D imaging. When introducing a 3D image-based approach for GTV and CTV assessment, there is a need for a common language to describe the concepts and to define the terms which are to be used [35,36]. While the use of such technologies is recommended, it is too early for precise recommendations regarding the use of 3-D imaging and optimization in brachytherapy of head and neck tumors. A panel of specialists within the GEC-ESTRO are working on these topics, and will develop recommendations for the use of 3D-imaging-based brachytherapy in patients with head and neck cancer.

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