10
Floor of Mouth Cancer
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1 Introduction

Carcinoma of the floor of mouth represents 8% to 12% of all head and neck cancers. Eighty-five to 95% of patients are males; the mean age is 58 years for men and 65 years for women. (15,19)

Classical clinical symptoms can be discomfort or pain under the mobile tongue, difficulty with protraction or swallowing, speech impairment, but more frequently, the dentist or the family physician discovers the disease. (15)

Prognostic factors (8,11,16,19,21) are tumour size, nodal involvement and age, but the topography of the tumour in relation to the oral tongue and to the mandible must also be considered as well as the macroscopic appearance of the tumour (infiltration, ulceration). (9)

Brachytherapy plays an important role in the conservative approach of T1 and T2 cancers of floor of mouth. (16)

On the other hand, brachytherapy combined with external beam irradiation is not a good therapeutic approach in advanced disease because in this case, the brachytherapy target volume would be by definition identical for a primary brachytherapy and/or for a brachytherapy boost. (8,11) For any tumour size, the combination of external beam irradiation and brachytherapy boost yields worse results than those obtained by brachytherapy alone to the primary tumour plus or minus surgical neck node dissection. (2,8)

If there is very limited disease (10-20 mm) or for very advanced cancers, surgery alone may be indicated. Advances in reconstructive surgery have increased the surgical indications for large tumours when they involve the mandible. (15,19)

2 Anatomical Topography

The floor of mouth constitutes one of the soft tissues of the oral cavity. It is a semilunar space of 40-50 mm in length and 20-25 mm in width, extending from the mandible to the undersurface of the tongue. The genioglossus, the myelohyoid, and geniohyoid muscles form its bottom. The posterior boundary is the base of the anterior pillar of the tonsil. (15)

The limit between floor of mouth and mobile tongue is the pelvilingual sulcus. Several cancers can involve this anatomical site, resulting in a tumour which can be described as leaf of a book or “feuillet de livre”. Usually, when the larger part of the tumour mainly affects the floor of mouth, the tumour will be considered as floor of mouth cancer.

Lymphatic drainage is to the submental and submandibular nodes in the case of anterior sites, or in the case of lateroposterior sites directly to the jugulodigastric nodes. Cross-over of lymphatic drainage is common in the case of anterior lesions. (15)
The critical organ is the mandible because of its close anatomical relationship, with a high risk of osteoradionecrosis. The extreme fragility of the floor of mouth mucosa must be taken in consideration at the time of the therapeutic decision, particularly if brachytherapy is indicated. (16,20,24)

3 Pathology

Squamous cell carcinoma represents 90 to 95% of the malignant tumours of the floor of mouth. Other very rare types are adenocarcinoma, adenoid cystic carcinoma, melanoma, sarcoma. (15)

The most frequent premalignant lesions are leukoplakia, erythroplakia, and lichen; in about 20% of cases they are associated with carcinoma at the time of diagnosis. (19)

The site of the primary tumour is, in decreasing order of frequency, in the anterior, lateral or posterior part of the floor of mouth. Tumours may extend to the lower part of the mobile tongue, to the mandible, or rarely to the oropharynx. (15)

Different macroscopic forms are exophytic, superficially spreading, infiltrating, ulcerative; these different forms are often mixed, and associated with local infection, making the determination of the tumour volume difficult.

The place of nodal involvement depends on tumour site and the frequency of involvement on size. Nodes are positive in 35% to 40% of patients, with bilateral involvement in 10% to 15%. (15,19)

4 Work Up

After evaluation of the general status, a very careful head and neck examination is carried out to establish as accurately as possible: tumour site and volume, macroscopic features, locoregional extension and node involvement. The final result of this examination must be documented with a topographical drawing of the tumour with its dimensions and its relation to critical structures. In all cases, possible bone extension must be investigated.

Dental assessment is essential. If dental status is poor, specific measures must be taken. A protective individual device should be prepared. (9,11,16)

Different complementary examinations are prescribed:

- For the primary tumour: biopsy, radiography of the mandible, ultrasonography, CT-scan, MRI-scan (systematic search for bone involvement).
- For the nodes: ultrasonography, CT-scan, MRI-scan, fine needle aspiration for cytological examination.
- Distant metastasis or second malignant tumours: head and neck examination and endoscopy, chest radiography, oesophagoscopy, bronchoscopy.
## 5 Indications, Contra-indications

The indications for brachytherapy (Table 10.1) must take into account different parameters: (15,19,21)

- General status, age, biological parameters, dental status;
- For the tumour: size, macroscopic appearance, site, distance to the mandible;
- For the nodes, the presence or absence of palpable adenopathy;
- Experience of the team.

For brachytherapy to be possible, the tumour must be accessible by hand to be implanted with a satisfactory technical approach respecting the rules of a system.

Table 10.1: Indications for treatment cancer of the floor of the mouth

<table>
<thead>
<tr>
<th>Tumour</th>
<th>T1, T2 &lt; 30 mm (&gt; 5 mm distant from the mandible): brachytherapy</th>
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<tr>
<td></td>
<td>T2 ≥ 30 mm (≥ 5 mm distant from the mandible): surgery or brachytherapy</td>
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<tr>
<td></td>
<td>T1, T2, T3 (close to the mandible, &lt; 5 mm): surgery; postoperative irradiation may be indicated</td>
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<tr>
<td></td>
<td>T3: surgery and/or radiotherapy; combination of external beam radiotherapy and brachytherapy is rarely indicated</td>
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<td></td>
<td>T4: radical surgery and/or external beam radiation therapy.</td>
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</tbody>
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<table>
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<tr>
<th>Nodes</th>
<th>Tumour managed with brachytherapy:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>T1N0: wait and see, if effective follow-up is possible</td>
</tr>
<tr>
<td></td>
<td>T2N0: elective node dissection*</td>
</tr>
<tr>
<td></td>
<td>T1T2/N1N2: functional or radical node dissection*</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Tumour treated with external beam radiation therapy</th>
<th>Nodes areas irradiated at the same time</th>
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</table>

<table>
<thead>
<tr>
<th>Tumour treated with surgery</th>
<th>Node dissection at the same time*</th>
</tr>
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</table>

* cervical postoperative radiation therapy in case of pathological nodal involvement
The risk of radionecrosis depends on the irradiated volume and dose to the mandible. These parameters depend on the number of lines in contact with or close to the mandible, their spacing, contact length, and angulation. If only one source is in limited contact with the mandible, the risk of osteoradionecrosis is minimal (<5%); with two lines this risk is still acceptable (10% to 15%), but with three lines this risk becomes too high (40% to 50%), and brachytherapy is consequently contraindicated. These rules are essential for establishing the indications and contraindications for brachytherapy. (8,9)

Involvement of the mandible (T4) is an absolute contraindication for brachytherapy. Extension to the gingiva does not represent an inevitable contraindication to brachytherapy: if infiltration of the gingiva is limited, and no more than two radioactive lines have to be implanted in direct contact with the gingiva, brachytherapy may be indicated.

When external beam irradiation is combined with brachytherapy, it is necessary to implant the initial infiltrating tumour volume. The number of radioactive sources required is consequently the same as for definitive brachytherapy and based on most published results (table 2 – see end of chapter) this combined treatment is not recommended. (8,10,17,22)

6 Target Volume

As it often occurs in oral-cavity malignant tumours, the delineation of the macroscopic tumour volume (GTV) is difficult because of the inflammatory reaction. Some additional information is offered by sectional imaging, in particular MRI.

In defining the CTV, a safety margin is chosen, which is at least 5 mm in all directions, except towards the mandible, which forms a natural barrier.

The topographical relation between the target (CTV) and the mandible must be assessed carefully.

After determination of the target volume (PTV), the technique and geometry of implantation are decided (afterloading system, number of radioactive lines, length, space between them and distance to the mandible), and a provisional dosimetry is performed.

7 Technique

7.1 Plesiobrachytherapy:

Moulds can be used only for very superficial lesions (up to 5-mm target depth). The applicator must be adapted to the topography of the tumour. This is achieved by an appropriate choice of moulds, either standard or customised. Fixation and immobilisation are crucial.

7.2 Interstitial Brachytherapy:

Both guide-gutter and plastic-tube techniques are applicable (8,17,23). Specific guidelines for floor-of-mouth cancer include the following: in order to decrease the dose to the mandible and consequently the risk of osteoradionecrosis, the contact of radioactive lines with the mandible should be minimised. Moreover, the radioactive lines must be inclined or bent according to the internal surface of the mandible, reducing even more the dose to the bone.
Guide gutters as well as plastic tubes are therefore implanted parallel to each other (Fig 10.1-7). To determine the distance between the lines and the length of the radioactive lines, three parameters must be considered: the target volume, the situation of the tumour in relation to the mandible, and the rules of the Paris system. Too large intersource spacing should be avoided, to limit the dose delivered to the mandible. With the guide-gutter technique, the distance between the two parallel lines is fixed by the dimensions of guide gutters: 12 mm. Ideal separation between the double pins is consequently 12 mm. When it is not achievable, this spacing should be kept, as far as possible, between 8 and 14 mm. (25) With the plastic tube technique, there is of course more flexibility, but again intersource spacing should not exceed 14 mm.

### 7.2.1 Guide-gutter technique

*Fig 10.1 Local anaesthesia*

*Fig 10.2: Implantation of the guide gutter and insertion of the silk suture*

*Fig 10.3: Loading of the iridium hairpin*
**Fig 10.4, 5: Removal of the guide gutter replaced by the iridium hairpin**

**Fig 10.6, 7: X-ray control: AP and lateral view**

**Fig 10.8: Shielding System**
The length of the radioactive lines is crucial. There is a clear relationship between this length and the risk of osteoradionecrosis and, while the target volume should be adequately covered (including the 5 mm safety margin), it is advised to avoid too long radioactive lines, particularly in contact with the internal surface of the mandible. With the guide-gutter technique, 2 to 3 cm long hairpins are often chosen. (8,11,17)

Tumours situated on or close to the midline are often implanted with five radioactive sources, two anterior, and three posterior (see figure), forming a trapezium, which can easily be divided into three equilateral triangles, thus respecting the rules of the Paris system. (8)

Anterolateral or posterior tumours are in most cases implanted with two or three guide gutters or two or three plastic loops, in a plane perpendicular to the mandible.

### 7.2.2 Plastic-tube technique

Tumours of the pelvilingual sulcus are implanted with two or three loops perpendicular to the mandible, according to a technique similar to that described for mobile tongue cancers (see this chapter) (Fig 10.9,10). The external branches of the loops are as far as possible angled away from the inner table of the mandible so that just the apex of the loop is close to the bone, reducing the dose to this critical organ. If the tumour does not involve the ventral surface of the tongue, it is not necessary to load the bridge of the loop with radioactive wires, and two parallel wires then replace the loop.

Tumours superficially extending to the gingival mucosa, when not suitable for surgery because of age or poor health status, are implanted using the plastic tube technique (see figure) or with the crossing technique used for post operative implants. (13,23)

Postoperative implants, with or without external beam radiation therapy, may be indicated when surgical margins are positive or close to tumour. Large tumours of the floor of mouth that do not reach the gingiva but infiltrate the sulcus and the ventral surface of the tongue are often treated by wide resection using a myocutaneous flap. In this case, the implantation is not performed in the flap, but in the residual disease. (13,23)
The plastic tubes are then implanted along the insertion of the flap; the anterior branch can also be implanted at a few millimetres from the suture, with the posterior branch in the flap. Tumours adhering to the gingiva are more difficult to treat, especially when the surgeon has resected the superior part (rim) of the mandible arch, leaving the inferior rim. In this case, the mucosa of the tongue is used for covering the rim, and is sutured to the lip and/or the cheek. This mucosa is furthermore at high risk of local recurrence, and the plastic loops have to bridge the rim. To achieve this, the spacing of the external branches of the loops has to be greater than that of the internal branches, with regard to the mandible, and optimisation is consequently highly recommended. (23)

A shielding system is always employed in order to decrease the dose to the teeth and the mandible and also to maintain the sources in good position throughout irradiation (Fig 10.8). This shielding system must be tested during the implantation procedure and may need modification according to the geometry of the implant and the tolerance of the patient. (9,16,17,20)

8 Dosimetry

Dosimetry is based on two orthogonal films of the implant and/or CT-scan cuts (or MRI) perpendicular to the parallel radioactive lines. 3-D imaging is highly recommended since it permits accurate estimation of the dose delivered to the mandible. The images should be taken with the shielding system in place to reproduce exactly the conditions of treatment. For this purpose and to obtain high quality images, an acrylic radiotransparent copy of the shielding system is used. (16)

For plesiobrachytherapy, the reference dose is calculated according to the thickness of the tumour. With interstitial implants, the dose calculation is based on the Paris System. Dose is prescribed to an isodose representing 85% of the basal dose rate. Dose distribution is checked in the central plane (see Physics chapter) as well as on the 3D representation of the source isodoses, the tumour volume (if visible on the CT-scan and/or MRI) and the mandible (Fig). Dose-volume histograms are also useful.

9 Dose, Dose Rate, Fractionation

With definitive low dose rate brachytherapy, a total dose of 65 Gy is prescribed at the reference isodose and delivered at a dose rate of 0.3-0.6 Gy/h. (8,18,19)

For pulsed dose rate brachytherapy, a dose of 65 Gy should be delivered in 130 x 0.5 Gy hourly pulses.

For implants delivered as a boost after 45-60 Gy external beam irradiation, a dose of 20-30 Gy LDR-PDR is recommended. The interval between external beam irradiation and brachytherapy boost should be kept as short as possible. (9,21,22)

For salvage implants in a previously irradiated area, a dose of 60 Gy LDR-PDR is adequate. For HDR brachytherapy, total dose and fraction size should aim at radiobiologically equivalent radiation doses (see radiobiology chapter). While no specific scheme is currently recommended, the dose per fraction should ideally be less than 3 Gy.

10 Monitoring

See chapter on Head and Neck General Aspects
11  Results

Local control obtained with definitive brachytherapy of limited stage carcinoma of the floor of mouth series ranges from 75% to more than 90% (Table 10.2).

Tumour size is the most important prognostic factor for local control (Table 10.2). For example, in the Institut Gustave Roussy experience, (9,11,16) for 206 patients with floor of mouth carcinoma, the local control rate was 97%, 91%, 69% for T1, T2, and T3 tumours, respectively.

Tumours extending to the mobile tongue and/or to gingiva are associated with poorer local control than those limited to the floor of mouth. For this reason patients presenting with pelvigingival tumour may be referred to the surgeon. (19)

As we saw, primary tumours of the oral cavity can be treated by a combination of external beam radiation therapy with a brachytherapy boost, or by brachytherapy alone. (5) In the last three decades, several studies have compared these two treatment options and have shown results better with definitive brachytherapy (Table 10.2). The local control rate ranges from 72% to 92% (average 85%) with definitive brachytherapy, and from 50% to 62% (average 55%) with the combination. (10,16,20).

Both soft tissue and bone necroses observed after interstitial implantation are more frequent in tumours of the floor of mouth than in those of the mobile tongue. Soft tissue necrosis (Fig 10.11) rate ranges from 20% to 30% and bone necrosis (Fig 10.12) from 5% to 10% (Table 10.2). However, most of these necroses were grade 1 (not severely interfering with patient comfort and healing spontaneously in a few weeks or months) or grade 2 (requiring hospitalisation for medical management, mainly with antibiotics and steroids) and only a few grade 3 (requiring minor or major surgery). The incidence of necrosis increases with increasing tumour volume and decreasing distance between the edge of the tumour and the mandible. (16,24)
<table>
<thead>
<tr>
<th>Authors</th>
<th>N Pts</th>
<th>TNM – Stage</th>
<th>Treatment</th>
<th>Brachy</th>
<th>Survival %</th>
<th>Local control %</th>
<th>Complications %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aygun (1)</td>
<td>116</td>
<td>I 22, II 26, III 32, IV 36</td>
<td>A, B</td>
<td>LDR</td>
<td>AS I 61, II 50, III 23, IV 14</td>
<td>I 83, II 85, III 42, IV 21</td>
<td>17</td>
</tr>
<tr>
<td>Bachaud (2)</td>
<td>94 +MT</td>
<td>I 52, II 42</td>
<td>A 26, B 68</td>
<td>LDR</td>
<td>OS 43, CSS 53, DFS 45</td>
<td>I 75, II 45, A I 100, II 70, B I 64, II 45</td>
<td>17</td>
</tr>
<tr>
<td>Baillet (3)</td>
<td>966</td>
<td>T1 211, T2 389, T3 230, T4 136</td>
<td>A 233, B 294, C 264, D 38</td>
<td>LDR</td>
<td>T1 55, T2 43, T3 25, T4 22</td>
<td>T1 91, T2 78, T3 64, T4 53</td>
<td></td>
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<tr>
<td>Bolla (4)</td>
<td>239</td>
<td>T1, T2, T3</td>
<td>B</td>
<td>LDR</td>
<td>T1 65, T2 58, T3 30</td>
<td>T1 81, T2 59, T3 37</td>
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<tr>
<td>Cole (6)</td>
<td>162</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>89</td>
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<tr>
<td>Decroix (7)</td>
<td>490</td>
<td>T1 88, T2 237, T3 137, T4 28</td>
<td>A 160, B 114</td>
<td>LDR</td>
<td>T1 50, T2 35, T3 16, T4 18</td>
<td>T1 95, T2 79, T3 57, T4 57</td>
<td></td>
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<tr>
<td>Inoue (12)</td>
<td>41</td>
<td>T1, T2, T3</td>
<td>LDR/HDR</td>
<td>16/25</td>
<td>32/36</td>
<td>69/94</td>
<td></td>
</tr>
<tr>
<td>Lefebvre (14)</td>
<td>146</td>
<td>T1 53 T2 76 T3 17</td>
<td>A</td>
<td>LDR</td>
<td>46</td>
<td></td>
<td>T1 91, T2 79, T3 53</td>
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<td>Marsiglia (16)</td>
<td>206</td>
<td>T1 87, T2 102, T3 14, T4 3</td>
<td>A 179, B 27</td>
<td>LDR</td>
<td>A 74, B 30</td>
<td>A: T1 97, T2 91, T3 69, A 89, B 59</td>
<td>A: STN 16 ORN 12</td>
</tr>
<tr>
<td>Gerbaulet (8)</td>
<td>117</td>
<td>T1 N0 47, T2 N0 47, T2 N1-3 23</td>
<td>A</td>
<td>LDR</td>
<td>T1 N0 93, T2 N0 61, T2 N1-3 28</td>
<td>T1 N0 94, T2 N0 74, T2 N1-3 65</td>
<td>STN T1 9, T2 24, ORN T1 6, T2 14</td>
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<tr>
<td>Decroix (7)</td>
<td>207</td>
<td>T1 84, T2 100, T3 17, T4 4</td>
<td>A 102, B 105</td>
<td>LDR</td>
<td>T1 71, T2 42, T3 35</td>
<td>T1 97, T2 72, T3 51</td>
<td>Gr1 17, Gr2 12, Gr3 4</td>
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<td>Pernot (22)</td>
<td>15</td>
<td>T1 T2 N0</td>
<td>A</td>
<td>LDR</td>
<td>84</td>
<td>100</td>
<td>12</td>
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<tr>
<td>Thomas (26)</td>
<td>175</td>
<td>T1 47, T2 87, T3 19, T4 22</td>
<td>A 92, B 8, C – D 75</td>
<td>LDR</td>
<td>44</td>
<td>T1 90, T2 82, T3-4 36</td>
<td>ORN 27</td>
</tr>
</tbody>
</table>

Legends:
- Treatments: A: Brachytherapy alone B: EBRT + brachytherapy C: EBRT D: surgery + radiotherapy
- Complications: STN: soft tissue necrosis ORN: osteoradionecrosis
- Results: AS: Actual Survival OS: Overall Survival CSS: Cancer Specific DSS: Disease Specific Survival
- Aspects of the tumour: spf: superficial exoph: exophytic infiltr: infiltrating
Many attempts have been made during the last decade to improve the therapeutic ratio. The probability of both local control and necrosis are significantly correlated with total dose, dose rate, and intersource spacing (see chapter on oral tongue cancer). To maximise the local control rate while minimising the necrosis rate, we now recommend delivering 65 to 70 Gy at a 0.3-0.5 Gy/h dose rate, while keeping the intersource spacing below 15 mm. (18,25) In addition, it has been proven that wearing a custom-made lead gutter moulded to the mandible throughout the course of the interstitial treatment dramatically reduces the risk and severity of bone necrosis. (16,24)

12 References