1 Introduction

Localised cancers of the tongue are an ideal indication for brachytherapy because there is a major requirement for local control while maintaining structure and function. (8)

The most common etiological factor is tobacco, which can be compounded by alcohol intake. Men are more commonly affected than women. (21)

The most important prognostic factor is the extent of disease as indicated by TNM staging. (23,16)

The microscopic form of tumour may also have a bearing on outcome. Exophytic tumours do better than ulcerating and infiltrating tumours. (16) As for malignant melanoma, there is a correlation between the depth of tumour penetration and the probability of lymph node involvement. (28)

Radical surgery will provide acceptable cure rates in patients with tongue cancer but often at the expense of poor function; brachytherapy is therefore preferable for T1 and small T2 tumours. (21)

2 Anatomical Topography

The anterior two thirds of the tongue lie in the oral cavity (mobile tongue). The posterior third (base of tongue) is in the oropharynx and the junction between the two is at the insertion of the anterior faucial pillar and the line of the circumvallate papillae. Eighty-five per cent of tumours arise on the lateral border of the oral tongue, 10 to 15% on the ventral surface and 5% or less from the dorsal surface. (21)

Tumours spread through the muscle of the tongue to the floor of mouth and mandible.

Lymphatic drainage is to the jugulo-digastric nodes. The submental, submandibular and upper and lower cervical nodes may also become involved. Thirty to 40% of patients may have palpable lymph nodes on presentation. Of those who are clinically node-negative, approximately 30% may harbour subclinical disease. The risk of node involvement is increased by increasing size of tumour and depth of penetration into muscle. (28)

3 Pathology

The vast majority of tumours are squamous carcinomas (see chapter on head-and-neck general aspects).

4 Work Up

Accurate staging is essential before planning treatment. This is achieved by careful clinical examination
of the primary and lymph node regions. CT and MRI scans are helpful to assess local infiltration and to more accurately stage the neck.

The patient is assessed for fitness to undergo the procedure, which will often require a general anaesthetic.

Blood clotting factors should be checked. Teeth should be examined and receive dental attention if required. A specially made perspex gum shield containing lead protection can be helpful in reducing the risk of osteoradionecrosis.

Patient must be advised to stop smoking and drinking. Those with alcoholism may need extra support and treatment to get through the implant period. (See also chapter on head-and-neck generalities).

5 Indications, Contra-indications

5.1 Indications:

For T1 N0 and T2 N0 patients where the tumour is less than 30 mm in size, brachytherapy can be given as the sole treatment for primary tumour. For larger tumours or those with positive nodes, combined surgery and post operative radiation may be preferable but if this is not feasible patients should have external beam radiation to the primary and node areas with brachytherapy as a boost to the primary.

5.2 Contra-Indications:

- Patient unfit for the procedure.
- T4 disease with bone involvement.

6 Target Volume

The aim should be to treat the gross tumour volume which is usually palpable plus a margin of at least 5 mm all around it. It should be remembered that the lower end of hairpin and loop implants have no crossing sources as they do at the top and the length of the limbs need therefore to be long enough to ensure the volume is adequately covered.

7 Technique

7.1 Pre-planning:

Before going ahead with the implant it is necessary to measure the tumour carefully and plan the exact number of radiation sources to be used with their length and separation. This will allow a provisional dosimetry to be performed so that a source activity can be chosen to deliver a dose rate of 40 to 50 cGy/h during the implant.
The two commonest techniques used for brachytherapy in the oral tongue are:

the guide-gutter technique (8,21)
the plastic-tube loop technique (8,21)

7.2 Guide-gutter technique:

Iridium wire hairpins are prepared with a fixed separation of 12 mms. This limits the width of volume which can be treated to approximately 15 mm and the technique can therefore only be used for smaller tumours (no more than 30 mm in length).

The implant can be performed with the patient sitting upright under local anaesthesia and sedation (Fig. 9.1) or rarely under general anaesthesia. The number and length of hairpins to be used will already have been decided from the provisional dosimetry. The aim is for the sources to be equidistant, parallel and straight and to cover the target volume.

The first phase of the implant is performed with inactive guide gutters (inactive device). These are introduced into the tongue with the help of fluoroscopy which ensures that they are parallel and equidistant.

For tumours that are near the tip of the tongue the anterior needle will be reflected backwards by the mandible. This should be accounted for before beginning the implant so that there is no divergence or convergence of the needles at depth. (Fig 9.1)

The guide gutter is first inserted angled towards the mid line of the tongue but once within the muscle it is straightened out so that the lateral limb of the hairpin runs 3 to 4 mms below the mucosa of the lateral border of tongue (Fig 9.2).

The separation between the hairpin guides should be 10 to 15 mm.

Once fluoroscopy has confirmed that the hairpin guides are parallel and equidistant, a black silk suture is run under the bridge of each one (Fig 9.3).
When the guide gutters are in position, the radioactive hairpins can be cut to the desired length; it is usual to use 4 to 5 cm for implantation of the lateral border of tongue.

The active hairpin is introduced into the guide gutter starting with the most posterior and slotted down the stainless steel guide (Fig 9.4). Once in position the hairpin is held in position in the tongue with a Reverdin needle and the inactive stainless steel guide withdrawn from the tongue (Fig 9.5). The pre-prepared suture is then tied over the bridge of the hairpin to secure it within the tongue.

The procedure is repeated for the other needles working from posterior to anterior (Fig 9.6).

After the implant is completed, AP and lateral radiographs (Fig 9.7,8) are taken, which will be used for computerized dosimetry (Fig 9.9-10).

Another example is given for a patient presenting a long infiltrating tumour implanted with four hairpins: three in a frontal and one in a sagittal position (Fig 9.11, 12, 13, 14).
Fig 9.7: AP X-ray

Fig 9.8: Lateral X-ray

Fig 9.9: Computerized dosimetry: sagittal plane.

Fig 9.10: Computerized dosimetry: reference volume (PTV).

Fig 9.11: MRI scan, showing the GTV. Two brachytherapy-procedures can be used: plastic tube technique or guide gutter technique. Guide gutter technique was chosen, using three guide gutters in a frontal plane and one in a median sagittal plane.

Fig 9.12: Tomography showing the position of the different iridium hairpins.
The “classical” guide-gutter technique as modified by J.P. Gerard and his team [15] is shown in figures 9.15, 16, 17.

Bleeding can sometimes occur on insertion or removal of a guide gutter; this nearly always stops after 3 to 4 minutes of pressure.

7.3 Plastic-Tube Loop Technique:

The loop technique allows a wider separation between the sources than the fixed 12 mm separation of a hairpin. It therefore can be used to treat larger volumes. It also has the advantage that iridium wire can be inserted into the plastic tubes with a remote afterloading machine that reduces the risk of exposure; in case of local oedema inducing the risk of displacement of the plastic tubes, it offers the advantage that one can wait for an acceptable local status before loading the iridium wire.

As for the guide-gutter technique, the number of loops, their separation and length should have been planned before performing the implant following the rules of the Paris system. Loop techniques are performed under general anaesthesia.

It is helpful before starting to outline on the skin of the under surface of the jaw the projection of the tumour to be implanted and the position of the mandible.
The implant is performed by creating a loop of plastic tubing which goes from the skin up over the tongue and down through the skin again.

The loop is formed by passing a hollow stainless steel needle through the skin into the tongue (Fig. 9.18). A parallel stainless steel needle forms the other limb of the loop.

A nylon cord is passed up the stainless steel needle where it exits into the oral cavity and is then passed down the other needle to form a loop. The stainless steel needles are then removed. A length of plastic tubing with a 1.6 mm outer diameter is threaded over the nylon cord and clamped over the cord at its end. The plastic tube is then pulled into the mouth by the nylon cord so that it reforms a loop passing from the skin over the tongue and back out of the skin (Fig 9.19).

![Fig 9.18: Implantation of the two posterior steel needles](image1)

![Fig 9.19: After Nylon cordlet introduction inside the Needles, the needles are removed and replaced by the plastic tube, pulled with the cordlet.](image2)

The clamp is then removed and the nylon cord extracted to leave a hollow plastic tube looped over the tongue (Fig 9.20)

![Fig 9.20: The goal is achieved: Three loops are inserted.](image3)

Three or four loops are inserted into the tongue depending on the volume to be treated with a separation between each loop which should ideally be between 15 to 18 mm. To respect the rules of the Paris system and to assure a better homogeneity of dose distribution, the distance between the “legs” of each loop is the same as the distance between the different loops.
An inert marker wire is passed up the loop so that the position can be identified on radiographs for dosimetry.

The plastic tubes are rinsed with a heparin solution (Fig 9.21). A nylon ball and lead washer are passed over the ends of the plastic tube in preparation for fixing the implant once it is loaded.

Two shielding devices are systematically used in oral-cavity cancers: the first one is a radiotransparent device for radiograph control (Fig 9.22), the second one, identical to the previous one, is made of lead (Fig 9.23) in order to decrease the dose to the critical organs.

After check radiographs have confirmed that the loops are equidistant and parallel the implant can be loaded by passing a pre-encapsulated iridium wire up the pre-implanted plastic tube to form a loop of iridium wire over the tongue (Fig 9.24, 25). The radioactive wire is maintained in place by clamping the inert ends of the plastic inner tubing to the hollow plastic tube loop to fix their position.
7.4 Remote Afterloading:

It is difficult for a remote afterloading device to negotiate the radioactive source around the tight curve of a plastic tube loop. The implant therefore has to be done with straight line (27) sources. Care needs to be taken to avoid a cold spot at the top of the implant at the surface of the tongue where retraction of the isodoses can result in a cold spot at the tongue surface which may be involved by tumour. This is achieved by allowing the plastic tube to protrude 4 to 5 mms above the tongue surface where it is maintained in place with one or two plastic buttons. (27) The afterloading machine also must be programmed to double the dwell time at the top three source positions in order to achieve a source distribution similar to the old Manchester Indian Club needle with increased activity at the uncrossed top end.

Brachytherapy may also be indicated as postoperative treatment; in this case only the plastic-tube technique should be used. (12)

8 Dosimetry

On completion of the implant orthogonal radiographs are taken to show the position either of the hairpins or the plastic tube loops. Spatial data from the radiographs are digitised into a treatment planning computer together with details of the source lengths and activities used for the implant (Fig 9.26, 27). The dose distribution is calculated according to the Paris-system rules. (8)
9 **Dose, Dose Rate, Fractionation**

For continuous low dose rate radiation where the implant is the sole radical treatment, a dose of 65 Gy is prescribed to the 85% reference isodose using the Paris System. A dose rate of 40 to 50 cGy/h should be aimed for in order to achieve the best compromise between local control and complications.

When the implant is being used as a boost it is usual to give 45-50 Gy in 2 Gy fractions with external beam radiation and 20 to 25 Gy with the implant. (4,22,23)

Remote afterloading can be performed either with pulsed dose rate brachytherapy or fractionated high dose rate. (11,13) If pulsed brachytherapy is used with hourly pulses the dose rate and fractionation should be the same as that for continuous low dose rate. (22) For fractionated high dose rate brachytherapy there is insufficient data to provide clear guidelines on the minimum number of fractions and fraction size to be used for radical treatment. (19) The vast majority of these treatments are given as a boost after external beam radiation. (11,13,22)

For continuous low dose rate brachytherapy the mean parameters for brachytherapy in the oral cavity are: (18,29)

- separation 14 mm
- dose rate 40 to 50 cGy/hr
- total dose 65-70 Gy

10 **Monitoring**

Patients will get an acute mucosal reaction which reaches a peak 7 to 10 days after the implantation and then settles over the succeeding 10 to 20 days. Patients will require adequate analgesia during that period.

Following implantation patients should be seen monthly for the first year to evaluate both control of the primary and the adjacent neck nodes. In the second year they should be seen two monthly. The risk of recurrence after two years is slight and follow up intervals may be longer.

(see also chapter on head-and-neck generalities)

11 **Results**

With regard to prognostic factors arising from tumour characteristics, (16,17,25) therapeutic management and more particularly the different brachytherapy techniques, (18,20) there are many similarities between cancer of mobile tongue, floor of mouth (see chapter on floor of mouth cancer) and consequently cancers of the oral cavity. These different points will be described focusing on oral tongue carcinomas.

11.1 **Prognostic factors:**

As has already been mentioned, tumour size is one of the most important prognostic factors. For Lefebvre (14) in a study including 429 patients with oral cavity cancer, the local failure rate is 12%, 17% and 38% (p=0.002) respectively for T1, T2 and T3 tumours. The largest retrospective analysis was done by Pernot (25) of 448 patients with tongue carcinoma and showed the critical role of
tumour volume on local control as well as on loco regional control and survival rate. Hareyama [10] comparing the local control for T1, T2 and T3, also found a significant difference (p<0.05). In the Gustave Roussy experience (7,9) for patients treated by brachytherapy alone, tumour size also plays a role in local control: in 269 patients with mobile tongue carcinoma, the local control rate was 93%, 86%, 69% for T1, T2, T3 lesions respectively.

Other publications have demonstrated the role of tumour size for patients treated with brachytherapy; Mazeron (16) studying the influence of other tumour characteristics, showed (in a series of 166 patients with cancer of the mobile tongue treated by iridium implant alone), that infiltrating tumours recurred in 22% of cases, whereas only 9% of superficial ones did (p<0.001).

11.2 Therapeutic management:

Primary tumour of the mobile tongue can be treated by brachytherapy alone (A) or by a combination of EBRT plus brachytherapy boost (B). During the three last decades many studies have compared these two treatment options and in all of them, local control was better for brachytherapy alone. Gerbaulet (7) and Haie [9] in a total of 269 patients reported local-control rates of 87% and 49% respectively for treatment A and B; Mazeron (17), in a series of 166 patients reported control rates of 88% and 36% respectively; Pernot (24) in 147 patients had control rates of 90% and 51% respectively, while Shibuya (28) reported local-control rates of 75% and 48% respectively in 370 patients.

These results are confirmed by those published in other series (Table 9.1).

11.3 Brachytherapy modalities:

11.3.1 LDR brachytherapy

- Brachytherapy reference dose:
  Mazeron showed in 166 patients treated for tongue carcinoma that the local control increases with dose. (17,18) He recommends a dose of 65 Gy to the CTV, depending on the PVT and the distance. The dose to the mandible can reach up to 70 Gy. For Wendt, (30) local control rises when the proportion of brachytherapy is higher in a combination of EBRT combined with BT.
- Duration of treatment:
  If EBRT and BT are given in combination, the time between these two treatments must be less than 20 days. (25)
- Dose rate LDR
  In a study of 279 patients with T1, T2 tongue carcinoma treated by brachytherapy alone, Mazeron (18) showed a significant effect of the dose rate (according to the delivered dose) on local control:

<table>
<thead>
<tr>
<th>Dose rate</th>
<th>Dose</th>
<th>Local control</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥0.5 Gy/h</td>
<td>≥62.5 Gy</td>
<td>93%</td>
</tr>
<tr>
<td>&lt;0.5 Gy/h</td>
<td>≥62.5 Gy</td>
<td>87%</td>
</tr>
<tr>
<td>≥0.5 Gy/h</td>
<td>&lt;62.5 Gy</td>
<td>79%</td>
</tr>
<tr>
<td>&lt;0.5 Gy/h</td>
<td>&lt;62.5 Gy</td>
<td>52%</td>
</tr>
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</table>
The comparison between the four groups showed that local control was related to the dose when adjusted for dose rate ($p<0.001$) and also related to dose rate after the adjustment for dose ($p<0.01$). Necrosis was related to the dose only below a dose rate of 0.5 Gy/h.

11.3.2 HDR Brachytherapy

Conflicting results are available concerning the efficacy of high dose rate brachytherapy in definitive treatment of squamous cell carcinoma of the mobile tongue. (19)

Lau et al. (31) in a retrospective analysis, reported a loss of therapeutic ratio with 6.5 Gy twice daily for 7 fractions and cautioned against the use of this schedule until further studies are performed. Local failure rate was 5/8 in T1 patients, 8/15 in T2 patients, and 0/2 in T3 patients; overall there were 17 grade 1 late side effects, 7 grade 2, and 1 grade 3. They concluded that the standard radiation treatment for early stage tongue cancer continues to be low dose rate brachytherapy.

In a randomized trial including 29 patients presenting with T1-2N0 of mobile tongue, Inoue et al (11) compared HDR treatment at 60 Gy in 10 fractions over 6 days with low dose rate interstitial brachytherapy at 70 Gy in 4 to 9 days. They reported two-year local control rates of 100 % and 86 %, respectively ($p = 0.157$). They concluded that high dose rate fractionated interstitial brachytherapy could be an alternative to traditional low dose rate brachytherapy for early stage cancer of mobile tongue. The validity of the conclusions of this trial has been challenged, because the number of patients included in this randomized trial was too low for allowing definitive conclusions to be drawn. (20)

11.3.3 PDR Brachytherapy

With pulsed dose rate afterloaders, optimization facilities can be used for solving practical difficulties in the performance of loop implants which arise when remote afterloading is being used, due to limits on the degree of curvature of the applicators. Sethi et al. (27) proposed a replacement of hairpin and loop implants by differentially loaded straight parallel catheters. The PDR afterloaders enable equivalent continuous low dose rate treatments to be given with all the advantages of a stepping source. Clinical studies of feasibility are in progress. First clinical results are encouraging. (22)

11.3.4 Relation PTV/GTV

A very interesting study was done by Pernot (25) in 448 patients with mobile tongue cancer, showing the crucial importance of a safety margin around the tumour surface. When the relation between PTV and GTV is $\geq 1.2$ the local control is 75%, when it is less than 1.2, 52 %.

In conclusion, for T1 and small T2 tumours ($\leq 30$ mm) of the tongue treated by brachytherapy alone the local control rate is 80 to 90%. If T2 tumours are treated by external beam radiation with brachytherapy as a boost, the local control rate has been shown to fall to 40 to 50% and it is preferable, therefore, to deliver the full dose with brachytherapy if possible and to treat the neck with selective neck dissection.

Approximately 20% of patients may develop soft tissue necrosis within the implant volume (Fig 9.27,28). Most heal spontaneously provided that the patient can be persuaded to stop smoking and drinking and pay close attention to oral hygiene.

Osteoradionecrosis may occur in 5 to 10% of cases. Provided the area of exposed bone is less than 1 x 1 cm the majority also heal with conservative management.
<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>
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<td>Akine [1]</td>
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<td>Bolla [3]</td>
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<td>B</td>
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<td>LDR</td>
<td>T1 83, T2 69</td>
<td>T1 93, T2 77</td>
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<td>A 194, B 75</td>
<td>LDR</td>
<td>T1 T2 T3 A 62, B 30</td>
<td>T1 T2 T3 A 87, B 49</td>
<td>STN 11, ORN 13</td>
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<td>A 194, B 75</td>
<td>LDR</td>
<td>T1 T2 T3 A 62, B 30</td>
<td>T1 T2 T3 A 87, B 49</td>
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<td>A 99, B 31</td>
<td></td>
<td></td>
<td>T1-2 92, T3 71</td>
<td>STN 20, ORN 13</td>
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<td>15/14</td>
<td>86/100</td>
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<td>T1 87, T2 84, T3 62</td>
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<td>A 181B 267</td>
<td>LDR</td>
<td>T1 69, T2 41, T3 25</td>
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<td>Shibuya [28]</td>
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<td>A, B</td>
<td></td>
<td>I 84, II 75</td>
<td>Spf 85, exoph 79, infiltr 45</td>
<td>Gr2 38, Gr3 4</td>
</tr>
</tbody>
</table>

Legends:
- Treatments: A: Brachytherapy (BT) B: EBRT + brachytherapy (BT) C: EBRT D: surgery (S) + radiotherapy (RT)
- Complications: STN: soft tissue necrosis ORN: osteoradionecrosis
- Aspects of Tumour: spf: superficial exoph: exophytic infiltr: infiltrating
12 References


