1 Introduction

The vermilion of the lip forms a transition zone between skin and oral mucosa and therefore the risk for cancer is related both to sun exposure and classical etiological factors for oral cancer such as tobacco, alcohol and bad oral hygiene.

Farm labourers and fishermen have a higher risk of lip cancer, as they are likely to be exposed to these risk factors.

2 Anatomical Topography

Histologically the lip can be divided in three different parts. The cutaneous lip (see chapter on skin cancers) goes over the vermilion or dry mucosa of the lip, which forms a transition zone between the skin and the wet oral mucosa.

Its lateral limits are about 1cm from the lip commissures: the upper limits are the naso-labial groove at the skin and the gingivo-labial groove at the mucosa side; the lower limits are the mento-labial and the lower gingivo-labial groove.

Its lymphatic drainage goes to the sub-mental, sub-mandibulary and sub-digastric lymph nodes. The submandibular nodes are the most frequently involved.

All patients affected with tumours reaching the median line are at high risk for bilateral nodal involvement.

3 Pathology

Most lip cancers are squamous cell cancers (90%). The remaining 10% are basal cell cancer (starting from the cutaneous area). Sarcomas, cylindromas, melanomas are very rare.

Pre-cancerous conditions, such as actinic cheilitis, leucoplakia, Bowen’s disease, are frequently associated. They often constitute a diagnostic and an additional therapeutic problem. In general these associated lesions can be adequately treated by radiotherapy but form rather a contraindication to limited surgery.

4 Work Up

The mean age of a patient suffering from lip cancer is over 65 years; patients are often in poor general condition, contraindicating major surgical excision and flap reconstruction.

An accurate medical examination should always include a systematic examination of the head-and-neck region, of the skin and teeth as well as X-rays of chest and mandible when indicated.
It is mandatory to carefully inspect and palpate the tumour area and the whole affected lip, the other lip and the commissural areas. The tumour itself may be exophytic, ulcerated, or infiltrating. These three forms can sometimes co-exist.

The size (in mm) and site of the tumour: (cutaneous lip, vermilion, wet mucosa), invasion of lip muscles or commissural invasion should be carefully assessed and noted. Any infiltration of the wet mucosa significantly increases the risk of nodal metastases.

Lip cancers are often poorly defined. Associated lesions are far from rare and should actively be sought for and noted as well. Detailed drawings or photographs will help to document the exact size and localisation. From every tumour and any suspected extension adequate biopsies should be taken.

Lymph node involvement is rare but can be frequently bilateral. A bi-digital palpation with a finger inside the mouth is necessary to better estimate the nature of submandibular lymph nodes. In case of clinical doubt, fine-needle aspiration is a simple procedure to assess involvement. Lymph nodes have been reported in 2% of T1, 6% of T2 and 15-30% of T3 cases (8). Lymph node involvement is more frequent when there is tumour extension to the wet mucosa (6, 7).

Tumour must be staged, according to the TNM staging system. (See appendix)

5 Indications, Contra-indications

Brachytherapy is indicated in over 90% of lip cancers.

A simple surgical wedge excision is only indicated for very superficial, small tumours less than 0.5 cm in their major axis. However the local recurrence rate, varying between 10 and 30% according to different authors should be used (1, 6, 9) in any case suggests systematic postoperative brachytherapy.

Larger tumours (over 5 cm in their major axis) are treated by external beam radiation followed by brachytherapy, or surgical excision followed by reconstruction surgery with an Abbe- Estlander lip flap rotation or derived techniques. Tumours invading adjacent bone usually require surgery if feasible.

6 Target Volume

The clinical target volume includes all visible and palpable tumour extensions with a safety margin of 5 - 10 mm according to the different directions. Because there is little movement of interstitial implanted sources when adequately fixed with templates or plastic tubes, the PTV usually corresponds very closely to the CTV.

7 Technique

Over 90% of cases can be treated by brachytherapy alone (6). It is nowadays classically performed with Iridium$^{192}$, applied in small source carriers. These are usually hypodermic needles but also guide needles, classic nylon tubes, silk threads, small vascular catheters, guide gutters, or a combination of more of these afterloading techniques in the same patient.

Whenever possible a custom made protection device should be prepared to shield the upper lip and
the lower gum (fig 8.1). The protector consists of a 2mm lead shield placed between both lips and the mandible, contained in an acrylic mouthpiece. This reduces the dose to the upper lip and lower gum by a factor of two. It must be made by an experienced colleague in the stomatology or dental department and tested for comfort before the patient starts brachytherapy.

To make exact dosimetry possible an identical dummy protector without lead shielding or removable lead plate can be made and used for dosimetry. However this procedure with a dummy protector is not so important as for intra-oral implants where the presence of the protector really disturbs the position of the implanted nylon tubes.

7.1 Hypodermic needles

These are hollow, bevelled needles with small outer diameter (0.8mm) and variable length (4 to 8 cm), open at both ends. They cause little trauma and can be directly inserted in the tissues. This technique is the optimal technique for lip carcinoma (Fig 8.2).

The rigid fixed steel and template system avoids collapse of the sources due to the elasticity of the soft tissues.
Templates with predrilled holes (0.6 mm) in a triangular configuration and with spacing of 10 to 15 mm should be available in the department.

Hypodermic needles can be used in lip tumours of less than 3cm in largest diameter, not involving the lateral commissurae. The inner diameter is 0.5 mm and can be afterloaded with 0.3mm iridium wires.

7.2 Classic plastic tubes

They have a diameter which is larger (1.6 to 1.9mm) than hypodermic needles. They are more flexible, allowing a better adaptation to round surfaces (Fig 8.3). However it is more difficult to keep good parallelism between tubes over the whole length of the treated volume Large plastic tubes are therefore indicated for larger masses, or when the lateral commissurae or cheek are involved.

Their loading has sometimes to be delayed as long as necessary for regression of the post brachytherapy trauma and oedema.

Fig 8.3: Interstitial implant in three planes: the deep and middle plane with plastic tubes, the superficial with hypodermic needles.

7.3 Silk threads

They are seldom used for the brachytherapy of lip cancer, unless it is a very small lesion preferentially in the upper lip (Fig 8.4). They can be used in the completion of a plastic-tube implant, or in combination with hypodermic needles. For example when a part of the tumour bulges out of the implanted area and a sub-optimal dosage is achieved, this can be corrected by an additional silk thread that can “warm up” the under-treated area.

Fig 8.4: Basal cell cancer of the upper lip implanted with the silk thread technique (4A) and cosmetic result two years later (4B).
7.4 Small vascular catheters

Their indications for lip cancer are similar to the indications for silk thread and small plastic tubes.

7.5 Guide gutters

Guide gutters are only exceptionally used. They are reserved to treat lesion with limited lateral commissura involvement.

8 Dosimetry

Orthogonal projection images are taken to register the source positions. Usually computer dose calculations are done. Mean Central Dose is determined. The prescribed dose to the Minimal Target Dose usually corresponds to 85% of the MCD (Paris System).

9 Dose, Dose Rate, Fractionation

The prescribed dose is 60-75 Gy at the 85% reference isodose, at dose rates between 30 to 90 cGy/h. Usually a dose rate at 45 to 80 cGy/h should be aimed at. Therefore, the linear activity of iridium sources should be in the range of 5.5 to 7.7 cGy/hr linear Air Kerma rate at 1 meter. Depending on the linear activity and the source spacing and length this will take 4 to 6 days to deliver the aforementioned dose. A dose of 60-65 Gy for T1 and 65-70 for T2 is advocated. Although doses up to 70-75 Gy can be given in some large tumours, without unacceptable sequels (6,7) the raise in cosmetic radiation damage is higher than the gain in local control expected from a dose increase above 70 Gy (13).

10 Monitoring

Daily control of the position of source carriers and protector device is mandatory. Minor analgesics may be indicated.

Acute side effects as mucositis (in the second week) and epidermitis (in the third to fourth week) can be mild (Fig 8.5A) to severe (Fig 8.5B) and have to be treated symptomatically with topical applications.

Fig 8.5A: Mild mucositis in a patient with a small (3mm source length) implant and having worn the protection device. Fig 8.5B: Severe mucositis of both lips and tip of the tongue four weeks after implant in a patient treated with high dose (75 Gy) without protection device.
11 Results

Lip cancer is a common malignancy in the head and neck region, and is very often diagnosed at an early stage. Surgery as well as external radiotherapy, and interstitial implants with radioactive sources are very successful in treating these lesions. Modern brachytherapy (BRT) with Iridium wires is a simple and effective treatment modality leading to excellent local control rates and cosmetic and functional results.

11.1 Local control

Overview of the literature shows local control rates of 90 - 95% at 5 years (table 8.1) for Ir-192 brachytherapy following the Paris system implantation rules. The results are somewhat better in T1 (0% - 5%) five year failure rates than in T2 disease: 2.1% - 8.2% (3 - 6,9,12,14).

Table 8.1: Local control results after interstitial brachytherapy for lip cancer.

<table>
<thead>
<tr>
<th>Author</th>
<th>Cases</th>
<th>BT-Dose</th>
<th>5 year (10y)*Local Failure Rates</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gerbaulet et al.</td>
<td>316</td>
<td>Ra\textsuperscript{206} Ir\textsubscript{192}</td>
<td>All 0% 0% 2.1% 7.7% 4/6</td>
</tr>
<tr>
<td>Pigneux et al.</td>
<td>93</td>
<td>Ir\textsuperscript{192} 65-75Gy</td>
<td>4.5% 2.2% 4.3% 5.2%</td>
</tr>
<tr>
<td>Mazeron et al.</td>
<td>1896</td>
<td>Ra\textsuperscript{206} Cs\textsuperscript{137}</td>
<td>10.9% 8.3% 10.8% 10% 7/12</td>
</tr>
<tr>
<td>Cowen et al.</td>
<td>248</td>
<td>Ir\textsuperscript{192} 60-81 Gy</td>
<td>4% 3.4% 5.4% 3.7% 6/9</td>
</tr>
<tr>
<td>Orrechia et al.</td>
<td>47</td>
<td>T1-T2</td>
<td>6.4% 6.4%</td>
</tr>
<tr>
<td>Van Limbergen</td>
<td>2794</td>
<td>Psr\textsuperscript{40-90Gy Cs\textsuperscript{137}}</td>
<td>6% 10% 5% 8.2% 19% 0/24</td>
</tr>
<tr>
<td>Cerezo et al.</td>
<td>117</td>
<td>XRT (+-surgery)</td>
<td>4% 4% 6%</td>
</tr>
<tr>
<td>Gerbaulet et al.</td>
<td>231</td>
<td>Ir\textsuperscript{192} 70-85 Gy</td>
<td>5.6% na Na Na na</td>
</tr>
<tr>
<td>Beauvois et al.</td>
<td>237</td>
<td>Ir\textsuperscript{192} 65-68 Gy</td>
<td>5% 12% 8%*</td>
</tr>
<tr>
<td>Farrus et al.</td>
<td>72</td>
<td>T1-T3</td>
<td>11% 10% 7% 25%</td>
</tr>
<tr>
<td>De Visscher</td>
<td>108</td>
<td>Ir\textsuperscript{192} 48-70 Gy</td>
<td>4.6% 1.1% 23.5% 0/2</td>
</tr>
<tr>
<td>Tombulini</td>
<td>57</td>
<td>Ir\textsuperscript{192} 62 Gy</td>
<td>10% na Na na</td>
</tr>
</tbody>
</table>

PSR: post surgical recurrences
They seem to be slightly worse with old radium or Cesium needle technique (9), or when Paris system implantation rules are not followed. In the Barcelona study (5) local recurrences were 1/21 (4.8%) when active source lengths were long enough for covering the PTV and were 7/51 (13.7%) when source lengths were shorter than prescribed by Paris System rules. Beauvois (1) reported even that when the entire lip was treated (this was the treatment policy in Nancy after 1985) no heterolateral lip recurrences were seen.

In the large 1993 GEC-ESTRO brachytherapy for lip cancer study (brachytherapy for lip cancer study 224 recurrences in 2794 patients were noted over a long follow up time (up to over 15 years) with an annual probability for recurrence rate of less than 1% (13). The local disease free survival probability (DFS) at 5, 10 and 15 years follow-up were respectively 94%, 90% and 89%. Significant higher local control rates were seen in lower lip cancers, and worse in commissura lesions (P=0.00001). A highly significant difference was noted between the local control rates according to T-stage (P=0.00001). For T1 tumours, the 5, 10 and 15 years DFS were respectively 95%, 91% and 90%; for T2, they were 91%, 89% and 86%; and for T3 in 82%, 78% and 78%. Local control rates were worse in poorly differentiated tumours: the 5 and 10 year local control rates being 97% and 95% for WHO I lesions, 95% and 80% for WHO II, and 80% and 77% in WHO III lesions. There were no differences in local control rates for patients treated with combined surgery and brachytherapy versus patients treated with brachytherapy alone.

Besides T size, the brachytherapy dose delivered is the major predictor for local control. In the GEC-ESTRO (13) in field recurrences decreased with increasing doses in T1 and T2 lesions (table 2) excepted in a small subgroup of 38 T2 patients treated at very high doses, 26 of them in the same institute, suggesting that technical performance might be responsible for the 8 - 11% local failures rates in the over 80 Gy dose group.

<table>
<thead>
<tr>
<th>GEC-ESTRO 1993 Lip CA study</th>
<th>5 year True Local Failure rate in function of Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>T1</td>
</tr>
<tr>
<td></td>
<td>n</td>
</tr>
<tr>
<td>40-50 Gy</td>
<td>9</td>
</tr>
<tr>
<td>50-60 Gy</td>
<td>56</td>
</tr>
<tr>
<td>60-70 Gy</td>
<td>300</td>
</tr>
<tr>
<td>70-80 Gy</td>
<td>482</td>
</tr>
<tr>
<td>80-90 Gy</td>
<td>70</td>
</tr>
<tr>
<td>&gt; 90 Gy</td>
<td>18</td>
</tr>
</tbody>
</table>

Excluding this subgroup the data suggest that 60 - 65 Gy is optimal to treat T1 (2 - 3% local failure at 5 years) and 65 - 70 Gy optimal to treat T2 lesions (3.1-4% local failure rate at 5 years). There was no obvious influence of brachytherapy dose rates on local tumour control within the range of 20 cGy/hour to 239 cGy/hour.

These local control rates compare favourably with surgical series (6 - 30% local failures) (1,6,8). In addition, local recurrences can be salvaged in 80 % of cases by surgery (3 - 6, 10 - 12) or brachytherapy (1,6,9,11) (Table 8.3).
Table 8.3: Results of salvage treatment for local recurrences of lip cancer after initial brachytherapy*, or external beam RT**.

<table>
<thead>
<tr>
<th>Author</th>
<th>N</th>
<th>N lip rec</th>
<th>Salvage treatment</th>
<th>Local Salvage Ratio</th>
<th>Ultimate LC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gerbaulet</td>
<td>316</td>
<td>24</td>
<td>Surgery, salvageBT</td>
<td>14/22 64%</td>
<td>97.4%</td>
</tr>
<tr>
<td>Pigneux</td>
<td>91</td>
<td>4</td>
<td>Surgery, salvageBT</td>
<td>4/4 100%</td>
<td>100%</td>
</tr>
<tr>
<td>Nguyen</td>
<td>na</td>
<td>31</td>
<td>Salvage BT</td>
<td>28/31 90%</td>
<td>na</td>
</tr>
<tr>
<td>Cowen 1990</td>
<td>248</td>
<td>18</td>
<td>Surgery</td>
<td>15/18 83%</td>
<td>98.8%</td>
</tr>
<tr>
<td>Orrechia</td>
<td>47</td>
<td>3</td>
<td>Surgery</td>
<td>2/3 66%</td>
<td>98%</td>
</tr>
<tr>
<td>Beauvois</td>
<td>237</td>
<td>12</td>
<td>Surgery, salvageBT</td>
<td>11/12 91%</td>
<td>99%</td>
</tr>
<tr>
<td>Farris 1996</td>
<td>72</td>
<td>8</td>
<td>Surgery, salvageBT</td>
<td>7/8 87.5%</td>
<td>98.6%</td>
</tr>
<tr>
<td>De Visscher</td>
<td>108</td>
<td>5 <em>/</em>*</td>
<td>Surgery</td>
<td>5/5 100%</td>
<td>100%</td>
</tr>
<tr>
<td>Tombolini</td>
<td>59</td>
<td>6</td>
<td>Surgery</td>
<td>3/6 50%</td>
<td>95%</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>111</td>
<td></td>
<td></td>
<td>89/111 80.2%</td>
<td></td>
</tr>
</tbody>
</table>

11.2 Complications

Since the lip is rather radioresistant; severe complications are rare. Superficial necroses occur in 2.8 - 10.1% (3,6,10,13). They heal spontaneously in 70% before six months and require surgery in less than 5% of cases (3) Lip ulceration depends strongly on total dose and dose rate. In the Gec-Estro overview (13) there was no incidence of lip ulceration in 0% with doses under 50 Gy, 4.8% for 50 - 60 Gy, 6.3% for 60 - 70 Gy, 7.3% for 70 - 80 Gy, 7.7% for 80 - 100 Gy and in 3/8 patients treated with doses over 100 Gy. Ulceration also is dose rate dependent since present in 2.5% at dose rates under 40 cGy/h, in 6% between 40 - 80 cGy/h, 6.9% between 80-120 cGy/h and 15.2% at dose rates over 120 cGy/h.

Cosmetic outcome is good to excellent in 80%-95% (Fig 6A and 6B) (3,6,8,13) with usually only mild depigmentation in 2.5 - 17.3% (3,6,13), telangiectasia in 15.2% (13), light oedema in 4.4% (3), dyskeratosis in 4.8% (3) or fibrosis in 8%) (3). In the GEC-ESTRO review good to excellent cosmesis was seen in 94.9% of T1, 84.3% of T2, 72.5% of T3 and 60% of T4. Poor outcome was noted in 1.3% of T1, 4.1% of T2, 10.1% of T3 and 20% of T4 (13).

Lip deformation and retraction is seen in 6% (3) of cases and is seen more frequently after treatment of larger lesions (3,8,13) and commissura lesions (3,13) (Fig 7); Functional loss due to lip deformation was noted in the GEC-ESTRO overview in 0/126 upper lip, 0.5% of 1199 lower lip, and in 4.2% of 92 commissura cases (13). Mazeron (8) reported grade 3 cosmetic and functional sequelae in 1% of 393 T1, in 5% of 363 T2 and 9 % of 78 T3 lesions.
Fig 8.6: Squamous cell lip cancer (6A) and cosmetic outcome (6B) five years after 75 Gy LDR brachytherapy.

Fig 8.7: Bulky lip cancer at the lateral commissura extending in both upper and lower lip (7A) and cosmetic outcome after 10 years (7B).

Cosmetic outcome has also been related to dose and dose rate. In the GEC-ESTRO study cosmetic outcome was excellent or good in 96.5% under 50 Gy, 91% between 50 - 70 Gy and 85% for doses over 70 Gy. In T1 cases (when cosmetic damage due to T size is minimal) bad cosmesis was seen in 0% when dose was lower than 60cGy, 1.5% between 60-80 Gy, and 8.6% over 80 Gy.

12 References


