1 Introduction

Bronchial carcinoma is an ever-increasing health problem, smoking habits being responsible for a major increase in incidence in recent decades, and with five-year survival rates reaching only 10 - 12% during the last 20 years.

Only 20 - 30% of all patients presenting with bronchial carcinoma are operable at diagnosis and only 40 - 50% of them can be resected for cure. Local recurrences after external beam radiotherapy to 50 -70 Gy occur in 60% of patients, and are responsible for 60% of the mortality due to respiratory failure, obstructive pneumonia and sepsis.

Brachytherapy plays an important role in the palliative treatment of obstructive disease, sometimes in conjunction with endobronchial laser therapy. Brachytherapy plays a limited but specific role in definitive treatment with curative intent in selected cases of early endobronchial disease or in the postoperative treatment of small residual peribronchial disease.

The most common symptoms in those patients suffering from endobronchial obstructive disease are: coughing (45 - 75%), haemoptysis (25 - 35%), dyspnea due to atelectasis (40 - 60%) or retro-obstructive pneumonia (25%).

2 Anatomical Topography

The tracheo-bronchial system is a tree-like tubular structure (Fig 26.1), divided into anatomical

![Fig 26.1: The tracheal-bronchial tree and incidence of non small-cell lung cancer (Fraser, Paré, Fraser and Genereux. Diagnosis of Diseases of the Chest, Saunders, 1989: 1368).](image-url)
sub-units with progressively narrowing lumen diameter and wall thickness. Lumen diameters take up 90% and wall thickness 5% of the whole diameter. The trachea has a lumen diameter of 18 mm, the right and left primary bronchus of 14 mm, the secondary bronchi of 11 mm, the tertiary bronchi of 9 mm (Fig 26.1).

The walls consist of a fibro-muscular skeleton, reinforced by cartilaginous rings in the trachea and primary bronchi and covered by respiratory mucosa endobronchially. The wall thickness (5% of the diameter) decreases from 1 mm in the trachea, to 0.8 mm in primary, 0.6 mm in secondary and 0.5 mm in tertiary bronchi.

3 Pathology

The most common primary malignant tumours occurring in the respiratory tract arise from the endobronchial epithelium. They are subdivided into small cell lung cancers (+/- 25%) and non-small lung cancers (+/-75%). These are further subdivided into squamous cell carcinoma, adenocarcinoma, and undifferentiated large cell carcinoma. The cancer growth frequently leads to endobronchial obstruction, which represents the classical indication for palliative endobronchial brachytherapy. In selected early cases cancer growth is very limited and superficial and is confined to the dimensions of the bronchial wall. These cases may be considered for definitive treatment with curative intent with brachytherapy playing a major role, often in combination with photodynamic therapy.

Lung metastases from other primary sites such as e.g. renal cell carcinoma, breast cancer, soft tissue sarcoma, osteosarcoma, or malignant melanoma only represent an indication for intraluminal brachytherapy if there is endobronchial obstruction caused by intraluminal tumour growth, which is rather rare.

4 Work Up

The definitive decision for brachytherapy, which is mainly palliative, is taken jointly by the pneumologist and radiation oncologist. It is based on clinical examination, flexible bronchoscopy with precise documentation of the location and the amount of obstruction, and X-ray of the chest, which in some cases is supplemented by computed tomography or sometimes still by conventional tomography. Each case should be biopsy proven. It is important to determine tumour extent as clearly as possible.

The tumour dimensions should be noted in mm, along the axis of the tracheal-bronchial tree and in the radial axis, always related to reproducible topographic landmarks. In addition, the minimum and maximum diameter of the involved part of the bronchial tree is measured and recorded in mm. If possible, the thickness of the bronchial wall should also be indicated.

To evaluate the response to treatment objective criteria should be used before and after treatment. Assessment of the grade of dyspnea, haemoptysis, pneumonia and the amount of obstruction by using for example Speiser’ scale (24) and lung function tests is helpful to obtain quantitative information on the functional impact of the obstruction (see Table 26.1). It makes quantitative assessment of functional improvement after brachytherapy or after a combined approach possible.

For curative treatments a comprehensive work up as usual for lung cancer should be performed, including in each case CT of the chest and appropriate investigations to exclude distant metastases.
### Table 26.1: Speiser and Spratling Scale for assessing palliative response in endobronchial brachytherapy (24).

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<th>Score 0</th>
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<th>intermittent: no medication necessary</th>
<th>Score 2</th>
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### 5 Indications, Contra-indications

* The main indication is for palliative treatment of dyspnea, obstructive pneumonia or atelectasis, cough or haemoptisis resulting from endobronchial or endotracheal tumour growth, usually by primary lung cancer but occasionally also by metastatic disease. Extrabronchial tumour extension cannot be adequately treated by intraluminal brachytherapy.

If obstruction is severe, endobronchial brachytherapy is usually preceded by endobronchial disobliteration techniques e.g. laser, cryo coagulation, electrocautery or endobronchial stenting in selected cases (3,15). This may induce rapid relief from symptoms. The combination with brachytherapy aims to achieve long lasting intraluminal tumour control. Intraluminal treatment may be combined with external radiotherapy, particularly as almost all tumours are too large for brachytherapy alone. Nevertheless, as this is mainly a palliative treatment, brachytherapy alone may be justified, if disappearance of symptoms can be achieved by these means long enough for the patient's remaining life span.
* Intraluminal brachytherapy alone can also be considered for the palliative treatment of endobronchial or endotracheal recurrent tumour growth in previously irradiated areas (9,26).

* Postoperative external radiotherapy plus intraluminal brachytherapy of the bronchial stump after resection with positive resection margins.

* Endobronchial brachytherapy with curative intent is considered as a boost for minor residual disease within a combined non-surgical radical approach. This may apply to small cell lung cancer after remission induction by chemotherapy and external radiotherapy or for non-small cell lung cancer as a boost after remission induction by external beam radiotherapy (with or without chemotherapy) (12,26).

* Definitive radiotherapy and brachytherapy (8,21) or brachytherapy alone for small tumours (T1 - T2) (1,11,16,19,27,28,29)

Contraindications for endobronchial brachytherapy are obstruction by extra-bronchial or extratracheal tumour growth, and peripherally located tumours not visible and accessible by bronchoscopy.

### 6 Target Volume

The intraluminal target volume is usually determined by bronchoscopy findings. Proximal and distal margins of the intraluminal gross tumour volume must be carefully assessed and the distance from both margins to the tracheal carina measured. In completely obstructing lesions, assessment of the distal margin may not be possible by endoscopy. Additional information from chest X-ray or CT imaging may be helpful then to estimate the length of the obstruction.

Since in palliative brachytherapy the extraluminal part of the tumour is usually rather large, and therefore not treatable by brachytherapy, there is only limited need for a precise assessment of the extraluminal tumour dimensions for target definition.

In contrast, in curative brachytherapy the whole area at risk must be included. This is the wall in superficial spreading tumours, and tumour depths of a few mm in limited T1- tumours. Autofluorescent bronchoscopy is very helpful in this situation, determining exactly the margins of the infiltrating tumour. The same applies for adjuvant treatment after radical resection with positive margins and for minimal residual disease after chemotherapy and/or external beam therapy. CT scans with the applicator in place allow a better estimate of the tumour topography in relation to the applicator (16,23).

In the longitudinal direction, a safety margin of 2 cm is usually added to both sides of the macroscopic tumour to define the target volume. If there is doubt about the distal margins an extra 2 to 3 cm should be added to be sure to cover the whole endobronchial tumour extension.

### 7 Technique

The technique for introducing the applicator depends on the size of the endobronchial applicator. Small applicators (5 to 6 french) which are nowadays most often used can be introduced directly via the working channel of the bronchoscope. Larger applicators (beyond the size of the working channel) are introduced using a flexible guide wire (Seldinger Technique) through the bronchoscope or via an extra tube introduced by the bronchoscope.
In a widely open tracheal or bronchial lumen (e.g. after laser-photo resection) a precise central and fixed position can be achieved using a specific applicator with an expanding outer cover which fixes the tube to the walls without obstruction of the respiratory system (7). This expansion is mechanically achieved after introduction and positioning. Using this applicator can reduce high contact doses to the mucosa.

With decreasing size of the available sources and catheters (5 to 6 french i.e. 1.7 to 2 mm-outer diameters) it is possible to take tighter bends and to enter tertiary bronchi (Fig 26.2). It has also become possible to treat lesions at the carina or on a bronchial division by sandwiching the tumour between two or even three inserted applicators (Fig 26.3). Using this technique a much larger tumour volume can be treated with adequate doses.

However in most cases the target is covered by a single endobronchial catheter that can cover up to 25-cm target length.

Fig 26.2 : Endobronchial brachytherapy with a small (<2mm, 5 to 6 french) endobronchial applicator, entered in a tertiary bronchus for treatment.
Fig 26.3: Intraluminal technique with two tubes in bronchus brachytherapy:

A. Schematic anatomical diagram showing the ideal situation with two tubes encompassing a small tumour located in the carina of two tertiary bronchi in the left lower lobe.

B. Anterior-posterior localisation radiographs in an extensive tumour growing into both main stem bronchi including the main carina. The two intraluminal tubes diverge at the main carina. Overlay of isodoses indicating also the dwell positions of the stepping source. Note the significant gap for dwell positions in the left tube at the carina to avoid significant overdose to this region.

C. Anterior-posterior localisation radiograph in a tumour growing around the carina of the intermediate and lower lobe bronchus with two intraluminal tubes introduced into the intermediate and lower lobe bronchus.

D. Dose distribution in case of a fork application with a stepping source afterloader. Individual dwell times should be programmed in such a way that the dose at 1.5 cm from the fork will not exceed the dose prescribed at 1 cm from the individual source lines.

7.1 Patient preparation and monitoring

The application can usually be performed on an outpatient basis.

The patient must have an empty stomach and an intravenous access must be prepared. To minimise applicator movement a neck collar must be ready to wear after application and during treatment of the patient.
Ideally, the whole procedure should be performed in the brachytherapy room, since it is easy for the pneumologist to bring along and return the instruments for flexible bronchoscopy there and difficulties may arise, if the patient has to be taken after placement of the brachytherapy application from the department of pneumology to the brachytherapy department. If major acute complications are expected (bleeding), the application is performed in an operating room, maybe using a rigid bronchoscope.

The application itself is performed under local anaesthesia, supplemented by sedatives and vagolytic drugs. It is important to suppress coughing and prevent displacement of the inserted applicator. Specific drug contraindications should be documented before the procedure. If indicated, cardiac function is monitored using ECG. Oxygen saturation is measured e.g. by a pulse oxymeter.

### 7.2 General application procedure

Flexible bronchoscopy and insertion of the brachytherapy applicator is performed with the patient in a sitting or supine position. The bronchoscope is usually advanced through the nose or mouth. Local anaesthesia to the nasal cavity and the nasopharynx is given before inserting the bronchoscope and then continuously via the dedicated channel of the bronchoscope.

Direct application through the working channel of the bronchoscope is possible in applicators with a small diameter. In applicators with a large diameter but with an open end, the Seldinger technique is used. An oral route of intubation is necessary for applicators with a large diameter and a closed end (see below).

The tumour is inspected by the chest physician and radiation oncologist and localised. The distance from the carina to the proximal and distal edges of the macroscopic tumour is measured by moving the bronchoscope. It can also be accurately documented on two anterior-posterior X-rays in the treatment (supine) position with the tip of the bronchoscope at the distal and proximal end of the GTV. If the tumour obstruction does not allow passage of the bronchoscope, a flexible guide wire, which is introduced through the biopsy channel, can be used to radiologically mark the distal end.

### 7.3 Specific applicators with different diameters

#### Small 5 to 6 french applicators

These small applicators can be placed under direct view via the working channel of the bronchoscope. It should be pushed several centimetres beyond the tumour using endobronchial friction to anchor. The bronchoscope can then be withdrawn over the applicator with the applicator remaining in the defined position. If the position is unsatisfactory (e.g. wrong lobar or segmental bronchus), the bronchoscope may be introduced again through the opposite side of the nose and the adequate position can be controlled and corrected if necessary. Using this procedure, several catheters can fairly easily be introduced. If there is difficulty in placing the applicator in the right place - in particular in the right superior bronchus – a special pigtail like ended guide wire may be used to take tight bends.

Finally, the catheters are carefully taped to the patient’s nose and a fixation neck collar is applied.

#### Applicators (> 3 mm)

Applicators with a larger diameter than the diameter of the working channel, cannot be introduced through the bronchoscope. Two possibilities of introducing these larger applicators into the tracheobronchial tree can be chosen:
Open tip applicators with a large diameter can be inserted using a modified Seldinger technique. First, a flexible guide wire is introduced through the working channel of the bronchoscope and placed with its tip at least at the distal end of the tumour obstruction or further beyond, if possible under direct bronchoscopy vision. The long guide wire is fixed and then the bronchoscope is withdrawn leaving the guide wire in place. The applicator is then advanced using the guide wire as a glide path and positioned correctly. If there are uncertainties in accurate positioning, the bronchoscope can be introduced again parallel to the applicator and the final placement can be performed under direct bronchoscopic vision. At the end of the procedure the applicator is taped to the patient's nose.

In both techniques using the bronchoscope channel, the catheter should be more than twice as long as the bronchoscope to allow withdrawal of the bronchoscope over the catheter. If the catheter is not long enough, at least the flexible guide wire should have the sufficient length to withdraw the bronchoscope over it without losing its end.

Applicators with a large diameter and a closed end have to be introduced beside the bronchoscope. After oral intubation of the bronchoscope (continuously injecting local anaesthesia via the dedicated channel) a tube is advanced over the bronchoscope. The tube is placed within the glottis and into the proximal part of the trachea and the bronchoscope is then withdrawn. The applicator is advanced through the tube into the trachea and then the tube is removed. Parallel to the applicator the bronchoscope is introduced again and now the applicator can be precisely placed at the tumour obstruction under direct bronchoscopic view. At the end of the procedure the applicator is carefully taped to the patient's nose.

8 Dosimetry

For final radiographic evaluation a flexible calibrated guide wire or a set of radiographic markers is inserted into the brachytherapy applicator. Orthogonal localisation films with or without a reference frame are taken for documentation and dose planning. The position of the applicator on these radiographs must be checked and compared with the clinical and/or radiographic documentation of the tumour extent at bronchoscopy at the beginning of the application. The tip of the visible guide wire should always pass at least 2 cm beyond the distal tumour edge. On the radiograph, the target is drawn taking into account all diagnostic findings from bronchoscopy and X-ray examinations (computed tomography) as well as the X-ray documentation of the tumour extent during the bronchoscopy.

Appropriate (20 mm) safety margins are indicated proximally and distally from the tumour (see definition of target volume)

The dose, as well as the depth at which the dose is prescribed is at the discretion of the brachytherapist. It may depend on whether the tumour is central or peripheral, on the endobronchial radial extent and the treatment policy. In curative situations the prescription isodose should encompass the target volume completely. CT localisation may help to define the exact target depth. In palliative treatments intraluminal brachytherapy cannot encompass the whole large tumour extent and the dose is prescribed at a certain distance (10 mm) from the source axis as recommended for small applicators, or at a fixed distance (5 mm) from the applicator surface as recommended for large size applicators. Usually when stepping source technology is available, the dose is prescribed either at a fixed distance, or at a varying distance from the source axis or the applicator surface, taking into account the diminishing bronchial diameter along the target. The reference points that indicate the target volume must then be drawn on the orthogonal radiographs and entered into the planning system.
For a curved source the dose at 1 cm will vary depending on the direction of the curvature: the dose will be higher at 1 cm at the concave side than at the convex side. This problem is solved by taking the mean of the doses at 2 points situated in the central plane at 1 cm and perpendicular to the plane of the main curvature (5) (Fig 26.4).

![Diagram](image)

**Fig 26.4:** Dose prescription for intraluminal brachytherapy with a curved source line in a small sized applicator. Prescription is done at the depth considered to be adequate for curative or palliative treatment purposes. Recording and reporting should also be at 1 cm of the source axis in the central plane. In case of a curved source the recording dose should be the mean of two dose points perpendicular to the curvature. Dose points at 1 cm at the convex site underestimate the dose, at the convex site overestimate it. (After Bucciarelli 1993 (5)).

However, according to the ICRU recommendations (ICRU report 58), the dose should, for reasons of comparability, be reported in the central plane at 1 cm from the source for small applicators, and at 5 mm depth from the applicator surface in large diameter applicators (> 5 mm diameter). For eccentric applicator positions, the maximum and minimum values, if available from sectional imaging, should also be reported. In addition, the dose at the applicator surface should be reported, indicating the maximum dose at the lumen/tumour surface (Fig 26.5A and B).

For 2 or 3 diverging sources dwell times should be adjusted in such a way so that the dose at 1.5 cm from the intersection does not exceed the prescribed dose at 1 cm around the single sources. (Fig 26.3D)
Fig 26.5A: Dose distribution and reporting for different applicator diameters (2 and 6mm). The prescribed dose (PD), the reference depth (RD) and the applicator surface dose (AS) are indicated beside the Applicator Diameter (AD) and the radius (r) of the applicator (1 and 3 mm). The Reference Volume Length (RVL) is defined as the length of the 90%-isodose at the reference depth of 5 mm. The Active Source Length (ASL) is also given, which is always longer than the RVL. The RVL is to enclose the PTL as tightly as possible.

Fig 26.5B: Dose distribution and reporting for centred (B1) and non-centered (B2) applicators. As in bronchus brachytherapy the lumen and the applicator are often non identical, the doses for both should then be recorded separately. In case of differences, the respective maximum and minimum values should be given with regard to the prescribed dose, reference depth dose and the lumen dose.
9 Dose, Dose Rate, Fractionation

For the patients’ comfort and to minimise source displacement during treatment, HDR brachytherapy is nowadays the preferred treatment for intraluminal bronchial brachytherapy and is considered superior to LDR brachytherapy. Only a few minutes are required for the treatment because of the high specific activity of the source. However, with adequate cough suppression, extended irradiation over 1 to 4 hours is possible with MDR treatment. This is possible either using 3 to 5 Iridium wire sources combined in a single double lumen tube (for endotracheal or proximal endobronchial lesions only) or using continuous irradiation from a PDR stepping source afterloader.

The total dose depends on the aim of treatment and - if previous radiotherapy has been given - on the dose already delivered. There is some variation in dose specification and diameters of applicators in the literature. Taking a lateral distance of 10 mm from the axis of the source, the dose per fraction varies between 5 - 10 Gy. Larger doses per fraction may lead to adverse side effects (ulcer, necrosis, haemorrhage), in particular as the volume of overdose is significant. This applies in particular for small diameter applicators (e.g. 2 mm) where the mucosal surface dose can be extremely high (17). This effect becomes even more pronounced as central positioning of the applicator is often difficult.

The total dose of HDR brachytherapy usually does not exceed 25 to 30 Gy.

The treatment interval between the single fractions should be least about one week. The treatment time for one fraction is several minutes with a single catheter application using an Ir 192 HDR source with an activity between 5 and 10 Ci. The treatment time may be longer in MDR treatment with combined LDR sources or continuous irradiation with a 0.3 to 1 Ci PDR source.

Intraluminal brachytherapy can be performed simultaneously with external beam radiotherapy with 1 fraction given by brachytherapy and 4 fractions by external beam therapy in one week (12).

10 Monitoring

Besides the standard monitoring during the bronchoscopy procedure described earlier in paragraph VII, the main issue afterwards is cough suppression as this may lead to displacement of the applicator during brachytherapy. This problem mainly occurs during longer treatments with MDR or PDR brachytherapy. Cough suppression is achieved by administration codeine or derivatives and by sedative drugs.

Oxygen tension is continuously monitored. ECG may also be recorded, if necessary.

11 Results

11.1 Palliative effects

As symptom relief is the main endpoint in palliative treatment, results should be described accordingly. There are subjective and objective methods (Speiser and Spratling scores, (Table 26.1) (24) for assessing the efficacy of endobronchial brachytherapy. According to several large series published (6,10,13,14,24,) overall symptom relief is achieved in more than two thirds of the patients. For example in Kohek’s series (13) relief from cough was obtained in 51/73, from dyspnea in 42/63, from haemoptysis in 6/8 patients. Improvement in general condition (Karnofsky scale) was noted in 69.5 to 76.5%.
Partial remission as assessed by objective measurements was achieved in 101/188, minor response in 25/188, no change in 29/188, progressive disease in 33/188 patients. Speiser and Spratling found a change in mean obstruction score (from bronchoscopy findings) before and after brachytherapy in 65 to 71% of the treated subgroups (curative, palliative, recurrent)(24).

A special indication for endobronchial brachytherapy is recurrent endobronchial disease after EBRT in selected patients. Speiser and Spratling (24) reported the same palliative effect and survival outcome in these recurrences as was seen in patients treated primarily with palliative intent. Gauwitz (9) reported on 24 patients with recurrent disease after external beam RT of at least 55Gy. All patients had an ECOG performance less than 2. Treatment consisted of 2 HDR fractions of 15 Gy at 6mm (corresponding to 9 Gy at 10 mm). Symptomatic relief was obtained in 21/24 (88%), and relief from atelectasis in 15/18 (83%), lasting for 26 weeks on the average (7 - 40 weeks). Only 1/24 died of haemoptysis.

In selected small primary tumours, palliation may be more successful and long term survivors have been described. At Manchester's Christie Hospital, 37 patients with small tumours less than 2cm, were treated with a single dose of 15 - 20 Gy delivered at 1 cm from the source (10). Symptom relief lasting for up to 12 months after treatment was obtained for haemoptysis in 96%, relief of pulmonary collapse in 69%, relief of cough in 55% and of dyspnea in 52%. The median survival was 709 days, 2-year survival 49.4 % and 5-year survival 14.1%.

11.2 Side effects

Acute side effects related to the treatment procedure itself are reported in 3 % of applications (10,25) consisting of pneumothorax, bronchospasm, haemoptysis, pneumonia, cardiac arrhythmia, cardiac arrest or hypotension.

Some problems arise in assessing the incidence of late complications occurring weeks to months after brachytherapy, as it is sometimes difficult to differentiate between complications due to tumour progression or from radiotherapy.

The rate of fatal haemoptisis reported in the literature varies from 0% to 32% (Table 26.2). However, it is recognised by most authors that most fatal haemorrhage is not due to brachytherapy, but to tumour progression (4,11) and the rate is comparable to the incidence of haemoptysis after laser coagulation alone. Hennequin (11) found no correlation with site of the treatment, technical factors, fraction size or association with external beam therapy as has been reported by others (10), but only with the length of endobronchial tumour spread. In the randomised trial conducted by the Munich group (12) however, fatal haemoptysis occurred more frequently after 2 x 4.8 Gy HDR boost than in patients who did not receive a boost after 60 Gy external beam RT (18.9% versus 14.2% fatal haemoptisis), but results were not statistically significance ( p=0.53)

The rate of tracheo-oesophageal fistula leading to death in the Macha (14) series is 5.3% (mean 3.5 months after start of radiotherapy). To prevent fistula, it seems to be important to examine the bronchial wall (e.g. flat ulceration) and the oesophageal wall (oesophagoscopy) carefully in central tumours growing in this area. Oesophageal tumour infiltration carries a higher risk of developing fistula.

Late effects such as chronic radiation bronchitis, bronchial stenosis and tracheomalacia are of course only seen in long term survivors, most of them with lesions of the trachea or primary stem bronchus (11). The incidence rates reported in the literature vary between 4 and 13%. Speisser and Spratling (24) related chronic bronchitis to dose and dose rate. (9% in MDR and 13% in HDR). Hennequin et al (11) found a relation between chronic bronchitis and trachea and main stem sites (p=0.002), total
dose (p= 0.04) and irradiated volume (p=0.02), the latter being the only significant parameter in multivariate analysis.

Table 26.2: Incidence of massive haemoptysis after HDR endobronchial brachytherapy:

<table>
<thead>
<tr>
<th>Author</th>
<th>n</th>
<th>HDR-Dose (Gy)</th>
<th>Ref.Point</th>
<th>Previous EBRT?</th>
<th>Massive hemoptysis (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Seagren 1985 (22)</td>
<td>20</td>
<td>1 * 10 Gy</td>
<td>@ 10 mm</td>
<td>Yes</td>
<td>28 %</td>
</tr>
<tr>
<td>Mehta 1989 (18)</td>
<td>31</td>
<td>4 * 4 Gy</td>
<td>@ 10 mm</td>
<td>Yes</td>
<td>3 %</td>
</tr>
<tr>
<td>Roach 1990 (20)</td>
<td>17</td>
<td>30 Gy LDR</td>
<td>@ 5 mm</td>
<td>Yes</td>
<td>0 %</td>
</tr>
<tr>
<td>Bedwinek 1992 (4)</td>
<td>32</td>
<td>3 * 6 Gy</td>
<td>@ 10 mm</td>
<td>Yes</td>
<td>32 %</td>
</tr>
<tr>
<td>Aygun 1992 (2)</td>
<td>60</td>
<td>4 * 5 Gy</td>
<td>@ 10 mm</td>
<td>Yes</td>
<td>15 %</td>
</tr>
<tr>
<td>Sutedja 1992 (26)</td>
<td>31</td>
<td>3 * 10 Gy</td>
<td>@ 10 mm</td>
<td>Yes</td>
<td>32 %</td>
</tr>
<tr>
<td>Gollins 1996 (10)</td>
<td>402</td>
<td>1 * 15-20Gy</td>
<td>@ 10 mm</td>
<td>No (324)</td>
<td>8 %</td>
</tr>
<tr>
<td>Hennequin 1998 (11)</td>
<td>149</td>
<td>4-6 * 7Gy</td>
<td>@ 10 mm</td>
<td>Yes</td>
<td>7.4 %</td>
</tr>
<tr>
<td>Speiser and Spratling (24)</td>
<td>295</td>
<td>3 * 10 Gy</td>
<td>@ 10 mm</td>
<td>Yes</td>
<td>6.3 %</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3 * 7.5 Gy</td>
<td>@ 10 mm</td>
<td>Yes</td>
<td>8.6 %</td>
</tr>
</tbody>
</table>

In the Manchester series (10) fatal haemoptysis (5pts at 9 to 11 months) was seen in long term survivors (4pts) treated with a single dose of 20 Gy. The authors concluded that a single dose of 17.5 Gy might be more appropriate to obtain long-term local control and acceptable complication rates.

A way to improve the therapeutic ratio could be with fractionated dose delivery. In another series, 34 medically inoperable patients with early stage non small cell bronchial cancer, were treated at Institut Gustave Roussy (16) with 6 times 5 Gy (at 1cm in 50% of patients) in six weeks. CT scan and spacer catheters were used to optimise the target volume cover and to spare critical (vascular) organs. Survival at 2 years was 78%, with a local control rate of 85%. No acute toxicity was found except for one pneumothorax.

11.3 Survival

Survival after palliative treatment in M0 patients seems to be dependent on the degree of remission achieved. Macha (14) reported a mean survival of 7.5 months in M0 patients ranging from 8.5 months in PR to only 2.5 months (NC+ PD). However, the impact of endobronchial brachytherapy on survival is still debatable. Speiser and Spratling (24) reported that patients treated with curative intent with external beam radiotherapy and a brachytherapy boost did not have a significantly longer survival than patients treated with external beam radiotherapy alone.

The Munich group (12) conducted a prospective randomised trial on central lung tumours. Patients received 60 Gy with external beam therapy and received either no further treatment or a boost of two 4.8 Gy endobronchial HDR fractions at 10 mm from the source axis. The median local control in these advanced cases was increased with the boost from 12 weeks to 21 weeks (p=0.052). In the 68 patients with squamous cell carcinoma the impact of the boost was more important with a significant increase in local control (p=0.007) Survival time seemed to be longer (40 versus 33 weeks), but did not reach statistical significance (p=0.09).

A specific subgroup to be considered is radiographically occult endobronchial tumours (ROEC) in medically inoperable patients. Although these cases are rare, they could be the best indications for endobronchial BT with curative intent, because in these cases brachytherapy might be able to cover the whole ROEC target volume. The reported outcome in this selected group of patients is encouraging (Table 26.3)
Table 26.3: Endobronchial BT for radiographically occult endobronchial carcinoma (ROEC)

<table>
<thead>
<tr>
<th>Author</th>
<th>n</th>
<th>T size</th>
<th>EBRT</th>
<th>BT schedule</th>
<th>Ref. Point</th>
<th>CR</th>
<th>Loc Rec</th>
</tr>
</thead>
<tbody>
<tr>
<td>EBRT + LDR BT</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fuwa 1997 (8)</td>
<td>17</td>
<td>Chest Xray neg</td>
<td>50 Gy (30 - 77)</td>
<td>22 Gy (10 – 42)</td>
<td>3-9mm</td>
<td>100%</td>
<td>12%</td>
</tr>
<tr>
<td>Saito 2000 (21)</td>
<td>68</td>
<td>Chest Xray neg</td>
<td>40 Gy</td>
<td>25 Gy</td>
<td>@10mm</td>
<td>NA</td>
<td>13%</td>
</tr>
<tr>
<td>HDR BT alone</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tredaniel 1994 (29)</td>
<td>14</td>
<td>Limited to wall</td>
<td>-</td>
<td>3 * 7 Gy</td>
<td>@10mm</td>
<td>84%</td>
<td>14%</td>
</tr>
<tr>
<td>Ardiet 1994 (1)</td>
<td>28</td>
<td>&lt; 10mm CTneg</td>
<td>-</td>
<td>3-5 * 7 Gy</td>
<td>@10mm</td>
<td>84%</td>
<td>24%</td>
</tr>
<tr>
<td>Perol 1997 (19)</td>
<td>19</td>
<td>&lt;10 mm CTneg</td>
<td>-</td>
<td>3-5 * 7 Gy</td>
<td>@10mm</td>
<td>83%</td>
<td>5%</td>
</tr>
<tr>
<td>Taulelle 1998 (28)</td>
<td>22</td>
<td>Limited to wall</td>
<td>-</td>
<td>3-5 * 7 - 10Gy</td>
<td>@10mm</td>
<td>96%</td>
<td>18%</td>
</tr>
<tr>
<td>Hennequin 1998 (11)</td>
<td>73</td>
<td>&lt;20mm CTpos</td>
<td>-</td>
<td>5-6 * 7 Gy</td>
<td>5-15 mm</td>
<td>NA</td>
<td>41%</td>
</tr>
<tr>
<td>Marsiglia 2000 (16)</td>
<td>34</td>
<td>2 - 40mm</td>
<td>-</td>
<td>6 * 5 Gy</td>
<td>5-10 mm</td>
<td>94%</td>
<td>27%</td>
</tr>
</tbody>
</table>

Fuwa et al (8) treated 17 cases of ROEC with the combination of EBRT and intraluminal LDR brachytherapy. Although doses of EBRT and LDR BT varied considerably, no severe late toxicity was observed and 5-year cause specific survival was about 90%.

In a larger Japanese series reported by Saito (21) 64 patients with ROEC (68 lesions) were treated with external beam RT to 40 Gy followed by 25 Gy LDR intraluminal brachytherapy. Five year survival was 72.3%, and disease free survival 87.3% with acceptable acute toxicity with 6% grade 2 pneumonitis and 29% grade 1 late stenosis, but without any grade 2 or greater deterioration of respiratory function due to radiotherapy. Nine (14%) local recurrences were seen, five of them rescued by surgery and EBRT.

In Europe studies were performed on medically inoperable patients with HDR-brachytherapy alone (1,11,16,19,28,29). Most patients received 3 - 6 fractions of 7 - 10 Gy at 10 mm from the source axis. Over 80% had a complete response and a good survival outcome. Local recurrences were noted in 5 - 40% of cases (Table 26.3). Acute toxicity was tolerable, but fatal haemoptysis and bronchial necrosis were reported, especially in those patients who received more than 35 Gy HDR brachytherapy. (11,16,19,29).

11 REFERENCES


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