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Review article

Endoluminal brachytherapy: Bronchus and oesophagus

Curiethérapie endoluminale : cancers bronchique et de l'oesophage

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ABSTRACT

Endobronchial brachytherapy could be proposed in case of endoluminal tumours either as a palliative or a curative treatment. As a curative treatment, endobronchial brachytherapy could obtain a high local control rate in case of limited disease. In palliative setting, endobronchial brachytherapy improved thoracic symptoms in more than 80% of cases, but it is less efficient than external beam radiation therapy for palliation. It could be also proposed to maintain the airway open after laser therapy. Oesophageal brachytherapy is a valuable option as a palliative treatment, underused at this time. It causes less side effects and a better quality of life compared to self-expanded metallic stents. For a curative aim, there is today no demonstration that a combination of external beam radiotherapy and oesophageal brachytherapy give better results than external beam radiotherapy alone in locally advanced tumours. For superficial diseases, the combination of external beam radiotherapy and oesophageal brachytherapy seems, on the contrary, promising.

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RÉSUMÉ

La curiethérapie endobronchique peut être proposée pour les tumeurs endoluminales, soit dans une optique curative, soit à visée palliative. Pour les lésions limitées à la bronche, elle permet d'obtenir le contrôle local pour un nombre élevé de patients. À visée palliative, elle améliore les symptômes thoraciques dans plus de 80 % des cas, mais son effet palliatif est moindre que celui de la radiothérapie externe. Elle peut être aussi proposée après désobstruction par laser pour prolonger la perméabilité des voies aériennes. La curiethérapie endo-œsophagienne est une option intéressante à visée palliative actuellement sous-utilisée. Elle donne moins d'effets secondaires que la pose de prothèses métalliques auto-expansibles avec des résultats en qualité de vie meilleurs. À visée curative, il n'y a aujourd'hui pas de démonstration qu'elle apporte un bénéfice dans la prise en charge des tumeurs localement évoluées. Pour les tumeurs superficielles, l'association d'une radiothérapie externe et d'une curiethérapie apparaît prometteuse.

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1. Introduction

Despite the advent of high-dose rate brachytherapy, the indications of endoluminal brachytherapy remain rare and are still

controversial issues. High-dose rate iridium192 sources allowed a short treatment time, with a dose-rate around 1 Gy/min. For both localizations, three types of indications have been evaluated: palliative, curative and in combination with external beam radiotherapy. In fact, most of the clear indications are palliative and many other techniques (laser, cryotherapy, prosthesis, etc.) have been developed in this indication, competing with high-dose rate brachytherapy. In this review, we summarized the literature and try to define the best indication for both localizations.

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2. Endobronchial brachytherapy

2.1. Technique

The endobronchial brachytherapy procedure involves the placement of a catheter in close proximity to an endoluminal malignancy to deliver local irradiation. The catheter is inserted during a routine flexible bronchoscopy and is thereafter connected to the remote afterloading device containing the irradiation source. Usually, steps of 5 mm are used. Treated length could be as long as 8 to 10 cm. Dose is prescribed 1 cm away from the source, covering not only the bronchial mucosa but also the wall of the bronchus. Margins of 2 cm around the visible tumours are usually applied to define the target volume. All the procedure can be performed on an outpatient basis.

Endoscopy is the first step of the procedure and probably the most important. Visualisation of the tumour and careful determination of its situation into the bronchial tree is of great importance for the success of the treatment. Distance between carina and the outset of the tumour must be evaluated, as the tumour length. Two catheters could be placed if the tumour is situated at the carina or at a bronchial branching.

High-dose rate brachytherapy has the physical characteristics of brachytherapy but the radiobiology of external beam treatments: fractionation of total dose is required to minimize normal tissues complications: a subtle balance must be made between the number of fractions (and endoscopies) and the late tolerance. The small treated volume allowed a dose per fraction higher than external beam treatments. Dosimetry can be performed on orthogonal radiographic films or on CT-scan.

Different fractionation protocols (usually, one to three sessions of 5 to 15 Gy) have been used in clinical treatment without a clear consensus regarding the best schedule. In a randomized study comparing two fractionation schedules, two fractions of 7.2 Gy were equivalent to four fractions of 3.8 Gy, for efficiency and tolerance [1,2]. In a retrospective study, Muto et al. observed less radiation bronchitis and stenosis when the dose per fraction was low and recommended three fractions of 5 Gy [3]. For palliation, in a large randomized study, one single fraction of 10 Gy gave the same results as 3 fractions of 7.5 Gy [4].

Most of the authors prescribed the dose at 1 cm from the source. In a study dealing with superficial cancers, the point of prescriptions varies according to the type of bronchus: 10 mm for trachea, 7 mm for main bronchus and 5 mm for lobar or segmental bronchi [5]. In practice, 3 to 6 fractions of 5 Gy were usually prescribed. A Cochrane database review concluded that a variety of fractionation schedules may have similar effectiveness [6].

2.2. Toxicity

Acute toxicity is usually mild. Late complications were mainly fatal haemoptysis and radiation bronchitis. The incidence of fatal haemoptysis ranged from 0 to 32% [7–10]. Most of them result from tumour progression and were not directly related to endobronchial brachytherapy. It seems that location of the tumour in the upper right lobe is a predictive factor of this fatal event, maybe because of the close proximity of the pulmonary vessels and the right main bronchus.

Radiation bronchitis is often observed after endobronchial brachytherapy but was unusually symptomatic [8,11,12]. This complication is probably related to the dose and the volume treated.

2.3. Curative treatment

Surgery remains the cornerstone of the treatment of early stage on-small cell lung cancer. However, some patients, such

Table 1
Results of curative endobronchial brachytherapy.

Study	Number of patient	Follow-up (months)	Local control (%)	Survival (%)
Tauelle et al. [43]	22	30	84	46
Pérol et al. [44]	19	12	75	78
Peiffert et al. [45]	33	14	90	53
Marsiglia et al. [46]	34	24	85	78
Hennequin et al. [13]	106	60	51.6	24
Aumont-Le Guilcher et al. [11]	226	60	63	29

as heavy smokers, may have an impaired baseline pulmonary function. Therefore, very early endobronchial disease justifies the consideration of a minimally invasive technique. In the same way, medically unfit patients for surgery could also be treated with intraluminal techniques. After surgery or external beam radiotherapy, sometimes recurrences could be detected as a pure endobronchial disease and are then amenable to a new local treatment.

In these situations, accurate staging with high resolution computed tomography and/or (¹⁸F)-fluorodeoxyglucose PET-CT is clearly needed to eliminate nodal involvement. Different intraluminal techniques are available: photodynamic therapy, cryotherapy and brachytherapy.

Different types of curative indications have been proposed for endobronchial brachytherapy:

- local relapses after external beam radiotherapy are in some cases purely endobronchial, without nodal or visceral metastases. Endobronchial brachytherapy could be performed after a previous irradiation and so could be proposed to these patients with the aim of cure;
- microinvasive or in situ carcinomas, uni- or multifocal, were also candidates for endobronchial brachytherapy.

Few data have been reported in this indication (Table 1). Our team reported the results of 106 patients with a limited endobronchial lesion: complete response was observed in 81.2%; local control rate was 60.3% and 51.6% at 3 and 5 years respectively [13]. The 5-year cancer-specific survival rate was 48.5%. However, overall survival was only 24% because most of the deaths were due to intercurrent diseases.

Endobronchial brachytherapy have also been combined with photodynamic therapy [14] for extensive endobronchial tumours (1 to 6 cm): in a series of 32 patients, 28 patients were controlled with combination of photodynamic therapy followed six weeks later by five fractions of 4 Gy of high-dose rate brachytherapy.

For locally advanced tumours, the combination of endobronchial brachytherapy and external beam radiotherapy improved local control but not survival [15,16].

2.4. Palliative care

Because of its delayed effect, endobronchial brachytherapy is not indicated in case of complete bronchial obstruction and imminent suffocation. Partial bronchial obstruction is often observed outside the context of major dyspnoea. In these cases, according to the life expectancy of the patient, some endobronchial treatment could be considered to prevent complete bronchial obstruction and its distressing symptoms. After laser recanalization of an obstructive tumour, the risk of reobstruction is high [17,18]. To maintain the air passage, complementary techniques could be proposed. A palliative treatment must be quickly efficient, without major toxicity and not expensive. Validated scales must be used to evaluate the palliative effect: this is not often done in most of the studies.

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