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Research Article

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# High Dose Rate Endobronchial Brachytherapy: Our institutional experience as an Effective Palliative Treatment Modality in Bronchial Carcinoma

**Jigna Bhattacharya*, R K Vyas, Saheli Saha, U Suryanarayan, Ankita Parikh, Satish Palgade, Parthiv Mehta**

*Department of Radiotherapy, The Gujrat Cancer & research institute, Civil Hospital Campus, Asarwa, Ahmedabad-380 016. Gujarat, India.*

***Corresponding author**
Jigna Bhattacharya, Department of radiotherapy, The Gujrat Cancer & research institute, Civil Hospital Campus, Asarwa, Ahmedabad-380 016. Gujarat, India, Tel: +91-79- 2268 8000, E-mail:jignabhattacharya@gmail.com

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## Abstract

***Background:*** *Treatment of inoperable carcinoma lung poses a challenge both due to the magnitude and local symptoms with resultant worsening of performance status of the patients. Endobronchial brachytherapy is an established modality for palliation of symptoms, namely dyspnoea, haemoptysis and coughthat result from disease infiltration of the airways. This study was aimed at evaluating the role of HDR endobronchial brachytherapy with external radiotherapy for symptomatic improvement and compliance for such patients at our institution.*

***Method:*** *50 patients of inoperable Ca Lung with significant bronchial component, includingnon-small cell and small cell, were assessed. Patients were evaluated with fibre optic bronchoscopy regarding degree of bronchial obstruction. They were randomized into two treatment arms,*
*Arm A: Endobronchial brachytherapy(EBBT) followed by External RT.*
*Arm B: External beam Radiotherapy followed by endobronchial brachytherapy.*
*Endobronchial Brachytherapy was delivered using remote afterloading HDR brachytherapy with $Ir^{192}$ source. Dosefor external RT was 30Gy/10#, on Linear Accelerator or Co-60 teletherapy unit.Endobronchial brachytherapy doserange was 6.5Gy-10Gy in single or two fractions, one week apart. Bronchoscopic assessment was done after one week of each fraction of endobronchial brachytherapy as well as after completion of treatment at every 1 month for 3 months. In some patients with good response, follow up bronchoscopy was performed after 6 months. Response to the therapy was also assessed with the Speiser scoring criteria.*

***Results:*** *Total 50 patients were randomised into two arms according to presenting symptoms and Bronchoscopic feasibility for the catheter insertion. There were 20 patients in arm A and 30 patients in arm B. In short follow up, complete response for haemoptysis was achieved in 98% of patients (n=14), 80% patients showed complete response to dyspnoea(n=46). Symptoms like chest pain and cough showed less improvement after endobronchial brachytherapy. Re-expansion of atelectasis was seen in 100% patients (n=29). Values in both the arms were compared using Pearson Chi-square test. The pre- and post-treatment symptomatic differences were comparable in both the arms and statistically significant for dyspnoea, chest pain, cough, haemoptysis while it was found to be insignificant in patients with change of voice.*

***Conclusion:*** *Endobronchial brachytherapy, as documented, is an important palliative modality to relieve the obstructive symptoms like dyspnoea and hemoptysis, in patients with intrabronchial malignant mass.*

## Introduction

Lung cancer remains the major cause of cancer related death world-wide. In developing countries, like India, despite attempts at standardized screening procedures, most of the patients present at an advanced stage. This might be attributed to the vague symptomatology or lack of awareness. Unresectable carcinoma lung offers poor survival even with best interventions [1]. Along with its metastatic potential, symptoms due to the bronchial growth like haemoptysis, dyspnoea, cough, chest pain results in rapid deterioration of general condition, rendering the patient ever more discordant for aggressive intervention [2-4].

Radiotherapy and chemotherapy is still the mainstay of treatment for inoperable lung carcinomas at present. Local tumour control and symptomatic improvement with external beam radiotherapy is dose dependent. However, the tolerance of normal lung tissue and movement of the organ limits the use of external beam radiotherapy. Endobronchial therapy in the form of brachytherapy, laser therapy, photodynamic therapy, radiofrequency ablation and prosthetic stents have brought about significant improvement in the treatment of malignant airway obstruction [5]. Among these methods, endobronchial brachytherapy alone as well as in conjugation with external beam radiotherapy has been used effectively for palliation of symptoms due to endobronchial disease extension [6,7]. But

technical difficulties hinder this modality from being widely utilized in routine clinical practice.

In this article, we have summarized our experience with this less employed modality of treatment of inoperable ca lung with endobronchial growth.

## Methods and Materials

In this prospective study, 50 patients of carcinoma lung, age ranges from 37 to 83 years, presented in the department of Radiation oncology were assessed on the basis of following features:

1. Bronchoscopic evidence of endobronchial disease,
2. Histological evidence of malignancy,
3. Inoperable disease,
4. Disease limited to central airway.

Speiser's scoring index was used for assessment of degree of airway obstruction. Performance status was noted according to the KP score. Thepatients were enrolled in the study after all routine investigations and metastatic workup, which includes complete blood count, renal function test, liver function test, chest x-ray, ultrasound of abdomen and pelvis, CT scan thorax etc.

**Table 1:** Histopathological distribution:

| SMALL CELL CARCINOMA | SQUAMOUS CELL CARCINOMA | ADENO CARCINOMA |
|---|---|---|
| 6 | 26 | 18 |

The patients were randomized in to two arms according to their presenting complains and Bronchoscopic evaluation of the endobronchial growth extent. Patients who were having significant dyspnoea and in bronchoscopy, catheter insertion was possible without causing bleeding, were taken into arm A. Patients in Arm A were treated with endobronchial brachytherapy followed by external beam radiotherapy.

Patients with 100% lumen occlusion in which there are higher chances of bleeding during the procedure were taken into arm B. Patients in Arm B received external beam radiotherapy prior to endobronchial brachytherapy.

External beam radiotherapy was delivered on 6MV linear accelerator or Cobalt-60 with beam directed AP-PA (antero-posterior) fields. Treatment fields were determined with the help of conventional X-ray simulation. 2 cm margin was given to the gross tumour volume (GTV) and mediastinal lymph nodes. Dose for the external beam radiotherapy was 30 Gy in 10#, as all the patients taken in this study were for palliative treatment intent.

For endobronchial catheter placement, patients were prophylactically pre-medicated with injection atropine (intramuscular), injection ranitidine, injection ondansetron and injection dexamethasone (intravenous). The brachytherapy catheter is a polythene tube of 6Fr diameter and 100 cm long. Trans-nasal fibre optic bronchoscopy was carried out under local anaesthesia. The tumour location, percentage of luminal occlusion and length of airway obstruction was recorded for the purpose of dose prescription.

The catheter along with a metal guide-wire was introduced through the working channel of the bronchoscope. The catheter tip was placed 2 cm beyond the distal extent of the disease, if it was accessible. In patients where the distal end of the bronchial growth cannot be accessed, the length of the tumour was assessed with the help of the CT scan thorax.The placement was done under the fluoroscopy guidance which helped to confirm the position of the catheter after the removal of the bronchoscope. The external end of the catheter was secured with the patients' nose with the adhesive tape. After this, the patients were shifted to the simulator. The metallic guide wire was removed and a dummy source wire was inserted inside the catheter. X ray films were taken in AP and Lateral view. The treatment length was decided on the X-ray and planning was done on the Oncentra- version 4.3 treatment planning system. Treatment was delivered with HDR remote afterloading device (Elekta microselectron) containing Ir192 source. Dose was described at a depth of 1 cm.

All 48 patients received 2 fractions of 6.6 or 7.5 Gy brachytherapy, each at an interval of 1 week. Two out of 50 patients received single fraction of 10 Gy, as these patients were having huge endobronchial growth with grade 3 dyspnoea.

Patients were evaluated after 1 month for response assessment. Bronchoscopy and chest radiographs were used for the purpose. Symptoms were scored using Speiser scoring index at a monthly interval.

### Speiser's symptomatic scoring index

**Hemoptysis:**

0 None
1 Less than 2x/week
2 Less than daily but greater than 2x/week
3 Daily,bright red blood or clots
4 Decrease of Hb/Htc>10%greater than 150cm3, requiring hospitalization or leading to respiratory distress

**Dyspnoea:**

0 None
1 Dyspnoea on moderate exertion
2 Dyspnoea with normal activity, walking on level ground
3 Dyspnoea at rest
4 Requires supplemental oxygen

**Cough:**

0 none
1 Intermittent, no medication necessary
2 Intermittent, non-narcotic medication
3 Constant or requiring narcotic medication
4 Constant, requiring narcotic medication but without relief

**Pneumonia/ elevated temperature:**

0 Normal temperature, no infiltrates, WBC < 10000
1 Temperature > 38.5 and infiltrate, WBC < 10000
2 Temperature > 38.5 and infiltrate and/or WBC > 10000
3 Lobar consolidation on radiograph
4 Pneumonia or elevated temperature requiring hospitalization

## Results

Majority of the patients included in the study were male, with only one being female. The predominant histological type was squamous cell carcinoma (52%), followed by adeno carcinoma (36%) and small cell carcinoma (12%). The disease locations were as follows left upper lobe bronchus (26%), left lower lobe bronchus (22%), left main bronchus (5%), right upper lobe bronchus (20%),right lower lobe bronchus (12%) and right main bronchus (10%). Procedure and treatment were well tolerated in almost all patients

except incidence of post treatment pneumonitis in 3 patients and fatal haemoptysis in 1 patient. The adverse outcome might be due to predisposing poor general condition because of advanced disease or due the brachytherapy procedure.

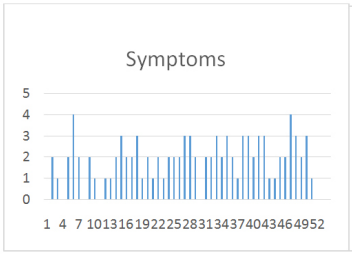
## Response to dyspnoea

Pre-treatment incidence of dyspnoea was as noted in fig 2. As shown in the graph, 2 patients were having grade 4 dyspnoea, 12 patients were having grade 3 dyspnoea.

The response to the treatmentwasremarkable with the $p < 0.005$only one patient in arm A was having grade 2 dyspnoea on follow up, 9 patients were having grade 1 dyspnoea after 3 to 4 months of follow up.

**Table 2:** Response to dyspnoea

| Improvement | No dyspnoea | Gr-1 dyspnoea | Gr-2 dyspnoea |
|---|---|---|---|
| No. of patients | 40 | 9 | 1 |
| percentage | 80% | 18% | 2% |



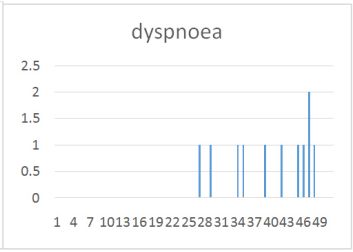




**Figure 1:** pre-treatment dyspnoea **Figure 2:** Post-treatment dyspnoea

## Response in haemoptysis

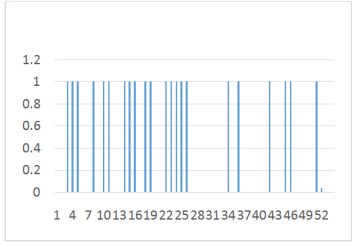
Total 14 (28%) patients were presented with the complain of hemoptysis. 98% ($p < 0.005$) patients responded to treatment completely. Only one patient in Arm A failed to show any response.

## Response to chest pain

Response to chest pain was only moderate in either of the arms, the p value was significant. Total 22 (36%) patients were presented with the complain of chest pain.No response was noted in 30% of these patients who had to be continued onnarcotic medicines for pain control.

**Table 3:** Response to chest pain

| | Pre-treatment chest pain | Post-treatment chest pain |
|---|---|---|
| No. of patients | 22 | 21 |
| Percentage | 44% | 42% |



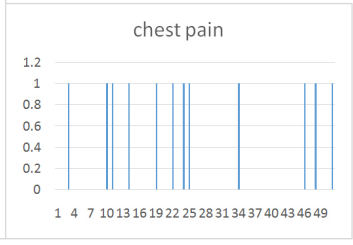
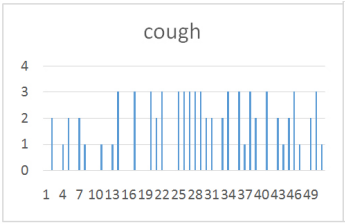




**Figure 4:** Pre-Treatment chest pain **Figure 5:** Post-treatment chest pain

## Response to cough

Response to cough was considerable with the p value < 0.05. 34 (68%) patients out of 50 were presented with the complain of cough. 15 patients were having grade 3 coughing and 11 patients with grade 2 coughing. Moderate response was noted. Out of 34 patients 11(34.4%) patients were having grade 1 coughing only, rest of 23 (67.6%) patients have 100% relief.



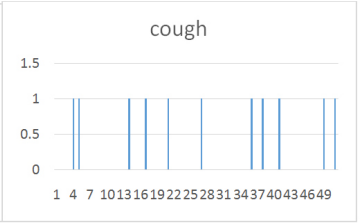
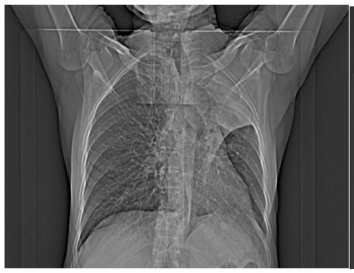




**Figure 6:** Pre-treatment cough **Figure 7:** Post-treatment cough

## Response to pneumonia/atelectasis

Chest X-rays and CT scan thorax were used for assessment of radiological response,evaluation of re-expansion or resolution of atelectasis in the follow-up period. 29 patients out of 50 were presented with different scores of pneumonia/atelectasis. 100% response was seen in atelectasis. Clinical outcome in terms of normalisation of WBC counts,decrease in fever were observed in all the patients (fig of CT scan).



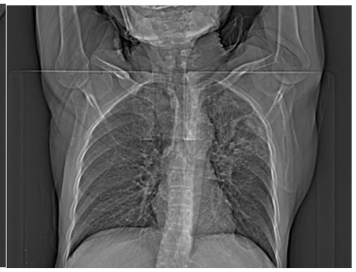
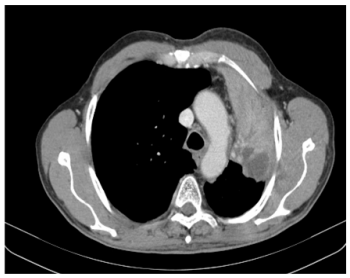


**Figure 8:** Pre treatment-consolidation **Figure 9:** Post EBBT-complete resolution



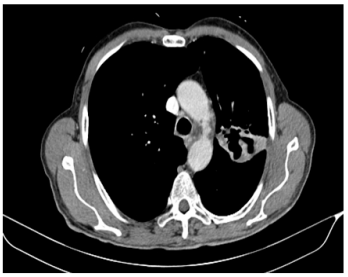


**Figure 10:** Consolidation in CT scan consolidation( Pre treatment ) **Figure 11:** Resolution of (PostTreatment)

## Response to change in voice

3 (6%) patients, 2 in Arm B and 1 in Arm A, had alteration of voice as the presenting complaint. 100% response was achieved post treatment, with significant p value.

## Bronchoscopic improvement

Extent of luminal occlusion was noted at the time of presentation and compared with the Bronchoscopic view during both the sessions of brachytherapy catheter placement and on monthly follow up. 12 (24%) patients presented with the complete luminal occlusion. 100%-90% lumen opening were noted in follow up bronchoscopy.

Patients with squamous cell carcinoma and small cell histology appeared to respond better than those with adenomatous histology.

## Complications

Although the treatment period was uneventful in majority of the patients, 3 patients (6%) developed pneumonitis after the first or second fraction of endobronchial brachytherapy, requiring hospitalization for the same. All the 3 patientsresponded to conservative management. 1 patient (2%) in Arm A succumbed to fatal haemoptysis 24hrs post-procedure. This patient had a huge exophytic endobronchial growth. 2 patients (4%) developed bronchial stenosis during the follow-up period, at 6 months in one patient and at 5 months in the other. Both the patients are on conservative management and having no significant morbidity. One patient died from non-malignant cause.

## Discussion

An airway obstruction secondary to extensive primary or recurrent bronchial malignancy is a frequent finding in patients of carcinoma lung with devastating effects for many of them. Number of modalities like surgery, laser therapy, photo-dynamic therapy, external beam radiotherapy, chemotherapy, stenting and endobronchial brachytherapy are available for management of malignant airway obstruction [5].

External beam radiotherapy, though proven to be an effective therapy, has limitations of exposing a greater volume of normal tissue to radiation while delivering optimal dose to the tumour. Also, in recurrent disease, this modality falls out of favour in those treated previously due to higher incidence of side-effects [2,3,7,8].

Endo-bronchial brachytherapy provides prompt and effective relief in symptoms caused by obstruction of the airway [4,9,6]. As it is delivering the dose very locally, no or minimal dose goes out of the bronchus. Therefore, it can also be used in previously irradiated patients. It provides rapid palliation of symptoms resulting in significant improvement in quality of life of such patients [2,3,7,8].

There is lack of uniformity in fractionation schedules across studies [10,11]. Some investigators have doses of 10Gy in single fraction while others have used smaller doses of 5Gy per fraction for 2 to 6 fractions. Although some authors opine that lowering the dose per fraction might lower the side-effects,there is insufficient data to support the same [6]. Also,whether any alteration in dose with the histological type is required or not, remains unclear.

In our study three dose schedules were used, 10Gy in single fraction, 2 fractions of 7.5Gy each, 2 fractions of 6.5Gy each.

10Gy single fraction treatment was given to two patients presented with poor prognosis or grade 4 dyspnoea. Unfortunately, one of these two patients died after 5 days of treatment. The reason of adverse outcome in this patient was unclear.

Other patients responded well to the prescribed doses.Patients with squamous and small cell carcinoma received 6.5Gy per fraction for 2 fractions, and those with adenocarcinoma received 2 fractions of 7.5Gy each.

The response to endobronchial radiotherapy alone appears to be inferior to that when used along with external beam radiotherapy [12,13]. In our patients, external beam radiotherapy of 30Gy in 10 fractions were used in all patients, either before (arm B) or after (Arm A) endobronchial radiotherapy. 47% of the patients had received anterior chemotherapy with poor response to the same. All the enrolled patients were in locally advanced stage.

Duration of remission of symptoms varied widely according to the symptoms. While some investigators observed best symptomatic improvement for haemoptysis, in our study we found most sustained relief of dyspnoea [14,15]. Most of the patient had considerable alleviation of symptoms after the first fraction of brachytherapy and after 2 fractions, there was relief in hemoptysis, cough, and pneumonia. Reduction of occlusion symptoms had a significant impact on the quality of life of our patients. Not only this, it improved compliance and adherence to further therapy. Squamous cell carcinoma histology was common compared to other histologies, p value was significant.

Complication of the treatment includes hemoptysis, bronchitis, pneumonitis, odynophagia, bronchial stenosis, broncho-oesophageal or broncho-pleural fistula formation [15]. While bronchitis, odynophagia and fistula formation are considered acute side effects, stenosis is a late complication [16,17]. In our patients, haemoptysis was noted in 2% while 6% developed pneumonitis. incidence of bronchial stenosis was 4%. None of the patients developed fistula. The expertise of Bronchoscopist is very important factor in reducing major acute complication i.e. hemoptysis and fistula. The selection of the patient and time of delivering the endobronchial brachytherapy fraction is also very important. Bronchial tumour with 100% occlusion and exophytic component should be treated with external radiotherapy upfront followed by the brachytherapy fraction to avoid fatal hemoptysis [18].

## Caveats of our study

1) Small sample size
2) Hypo-fractionated external beam radiotherapy was used in all the patients. The poor performance status warranted protraction of treatment period. Also concurrent chemoradiation could not be prescribed for the same reason.

## Conclusion

HDR brachytherapy is an excellent modality for palliation of symptoms resulting from malignant airway obstruction. It can be performed on out-patient basis with proper patient selection [19]. This modality can be very well used in patients treated with curative intention. It should be used as a boost treatment in bronchial growth. With studies having larger cohorts and investigation designs, present unanswered questions regarding this modality of treatment might be resolved in the near future.

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