**An Observational Study To Evaluate The Response Of External Beam Radiotherapy With And Without High Dose Rate Brachytherapy By Different Radiation Dose Schedules In Patients Of Carcinoma Middle Third Esophagus- An Institutional Experience.**

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**Abstract:** Radiotherapy plays an important role in the treatment of carcinoma esophagus. Owing to the anatomy of the esophagus and the surrounding vital structures, e.g. Lungs, heart spinal cord etc, it is not possible to deliver higher dose of external radiotherapy. Brachytherapy can be quite useful to boost the local area in both curative and palliative settings after external radiation.  
60 Patients of Carcinoma middle third Esophagus, treated between 2011- 2013, were taken in this retrospective observational study. Patients were delivered curative or palliative treatment according to the disease status at the time of presentation. The patients were classified into three groups:

GROUP 1: External Radiotherapy, 60Gray/30 fractions with 2Gray/fraction  
GROUP 2: External radiotherapy 40Gray/20fractions with 2 Gray/fraction followed by two fractions of Intraluminal brachytherapy (7.5Gray each at 1 cm depth)  
GROUP 3: External beam radiotherapy 30Gray/10 fractions with 3Gray/fraction, two fractions of intraluminal brachytherapy (7.5Gray each at 1 cm depth).  

HDR-Brachytherapy provides good clinical response, disease free survival with acceptable complications and improvement in quality of life in both curative and palliative settings.

1. **Introduction**

The prognosis of esophageal carcinoma is poor, in spite of the advancements in treatment techniques because of high rate of local recurrences and distal metastasis. Radiotherapy plays an important role in the treatment of carcinoma esophagus especially in patients who cannot undergo surgery. Radical radiotherapy in the dose of 50-60 Gray has been tried, but only external radiotherapy was found to be insufficient. Owing to the anatomy of the esophagus and the surrounding vital structures, e.g. Lungs, heart spinal cord etc, it is not possible to increase the dose of external radiotherapy. Brachytherapy by HDR loading systems can be quite useful to boost the local area in curative settings and improvement of symptoms in palliative settings after external radiation.

Here we have used three treatment schedules with combination of external radiotherapy and brachytherapy and analyzed the patients for local control, acute and late reactions, symptomatic relief and disease free survival.

2. **Methods and Materials**

60 Patients of histopathologically proven, Carcinoma middle third Esophagus, treated between 2011-2013, with following features were taken in the study.  
1) Median age 53 years  
2) Pre-treatment dysphagia grade II/III  
3) No evidence of any distant spread  
4) Not fit for concurrent chemotherapy because of co-morbid conditions.

These patients were divided into three groups as per follows:

1) Group 1 and 2: Tumour size ≤ 5cm, KPS Score > 60 and weight > 40 Kg.  
2) Group 3: Tumour size > 5cm, KPS Score < 60, Weight < 40 kg

**Treatment received**

Group 1: Patients received External Radiotherapy, 60Gray/30fractions with 2Gray/fraction.  
Group 2: Patients received external radiotherapy 40Gray/20fractions with 2 Gray/fraction followed by assessment after two weeks, then two fractions of
ILBT (Intraluminal brachytherapy) (7.5Gray/fraction at 1 cm depth)

Group 3: Patients received EBRT 30Gray/10 fractions @3GY/#, followed by response evaluation at two- three weeks then two fractions of ILBT (7.5gy at 1cm depth).

Treatment procedures which were used to deliver treatment were as follows:

In group 1, all patients were simulated. Oral contrast with Barium was given to delineate the oesophagus and the disease. A margin of 5cm above and below the disease was taken and a radial margin of 2.5cm was given. All patients were treated up to 40 Gray using AP/PA parallel opposed fields. Radiotherapy was delivered with 6 megavoltage photon beams on a linear accelerator. A barium swallow was repeated after 40 Gray. Patients were further treated up to 60 Gray by three field technique, with one anterior and two posterior oblique fields to spare the spinal cord.

In group 2, patients were treated in a similar fashion up to 40 Gray. A barium swallow examination was repeated before planning the boost treatment by brachytherapy. After a gap of one week, ILRT (Intraluminal Radiotherapy) was planned. Injection Atropine 0.8 mg was given to the patients, half hour before applicator placement. A dummy source was used to note the position of the applicator on the simulator and its position was confirmed. Patient was simulated and orthogonal X-rays were taken. The length to be treated was noted. The target length was defined as pre - treatment length with one cm margin proximally and distally. Dose was prescribed at 1cm depth.

Two fractions of 7.5Gray each were administered at a gap of one week in between. Patients were treated on HDR- microselectron with Iridium-192. In group 3, patients were given 30Gray/10 fractions by external beam followed by two sittings of Intraluminal brachytherapy.

The grading of dysphagia, acute reactions and complications was done by CTCAE 4.03 (Common Terminology Criteria for Adverse Events version 4.03)

Follow up

Patients were followed up monthly for first three months. They were evaluated for relief of dysphagia and local control at 3rd, 6th, 9th and 12th month symptomatically, radiologically, and endoscopically.

3. Results

The results obtained are tabulated in Table 1.

1. The patients of group 1 and 2 were similar in all regards. Those patients who showed good symptomatic relief after 40Gray of EBRT, were administered ILBT boost in group 2.

2. Post treatment weight gain was (80%) 16/20 in group 2 and 13/20 (65%) in group 3 i.e. it was better in the combination arm rather than EBRT alone arm. Complete response at six months was also maximum in group 2 (65%).

3. p value was found to be significant for acute reactions during treatment and endoscopic dilatations required post treatment. The complete response at six months in the ILBT arms was 65% and 50% though the p value was not significant.

4. Median Disease free survival was found to be 9 months, 11 months and 8 months in arm 1, arm 2 and arm 3 respectively.

Table 1

<table>
<thead>
<tr>
<th>parameters</th>
<th>Arm 1</th>
<th>Arm 2</th>
<th>Arm 3</th>
<th>Pvalue</th>
</tr>
</thead>
<tbody>
<tr>
<td>No.of pts gaining weight post treatment</td>
<td>12/20 (60%)</td>
<td>16/20 (80%)</td>
<td>13/20 (65%)</td>
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</tr>
<tr>
<td>Acute reactions during treatment</td>
<td>16/20 (80%)</td>
<td>12/20 (60%)</td>
<td>7/20 (35%)</td>
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<tr>
<td>Clinical improvement at three months</td>
<td>8/20 (40%)</td>
<td>12/20 (60%)</td>
<td>13/20 (65%)</td>
<td>0.15</td>
</tr>
<tr>
<td>Biopsy negative at three months</td>
<td>6/20 (30%)</td>
<td>12/20 (60%)</td>
<td>9/20 (45%)</td>
<td>0.16</td>
</tr>
<tr>
<td>Complete response at 6 months</td>
<td>6/20 (30%)</td>
<td>13/20 (65%)</td>
<td>10/20 (50%)</td>
<td>0.05</td>
</tr>
<tr>
<td>Partial response at 6 months</td>
<td>14/20 (70%)</td>
<td>7/20 (35%)</td>
<td>10/20 (50%)</td>
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<tr>
<td>Endoscopic dilation required</td>
<td>0/20 (0%)</td>
<td>6/20 (30%)</td>
<td>8/20 (40%)</td>
<td>0.008</td>
</tr>
</tbody>
</table>

4. Discussion

External beam radiotherapy in combination with intraluminal brachytherapy appears to be a better treatment option than external radiotherapy alone.
The most common complication in this modality is strictures which requires endoscopic dilatation. By ILRT, high dose can be delivered to the tumour site without causing much radiation exposure to the surrounding structures.

**Brachytherapy in Curative settings**

In the curative setting, intraluminal brachytherapy has been used as a boost following external beam radiotherapy to deliver high dose to the tumour and restricting the dose to the surrounding critical structures at minimum.

The American Brachytherapy Society (ABS) has laid down guidelines for the selection of the patients for brachytherapy boost after external irradiation for curative intent of treatment, which are modified and summarized as below [4].

**Indications:**
1) Unifocal thoracic adenocarcinoma or squamous cancers
2) Maximum length 10 cm
3) No evidence of intra-abdominal or metastatic disease

**Contraindications**
4) Tracheal or bronchial involvement
5) Cervical esophagus location
6) Stenosis that cannot be bypassed

**Guiding principles:**
1) Applicator should have an external diameter of \( \geq 10 \text{ mm} \)
2) Avoid giving chemotherapy concurrently
3) Brachytherapy should follow external beam radiation therapy
4) Dose recommendations (3-4 weeks after 50-60 Gy EBRT)
5) HDR 10-12 Gray in two weekly fractions of 5-6 Gray each.

Dose escalation by brachytherapy has a significant potential of acute and late side effects. Concurrent chemotherapy should not be administered with the brachytherapy boost and the applicator diameter should be carefully selected[5].

**Brachytherapy in Palliative settings**

There is a lot of clinical data which supports the use of Intraluminal brachytherapy in patients of locally advanced incurable esophageal cancers, for symptomatic relief. The advantage of brachytherapy over external radiotherapy in this group of patients is, it provides more lasting symptom control in a shorter treatment time with spatially precise high radiation dose delivery, this reducing the unwanted side effects. It improves the quality of life of these patients and the overall complication rate is lesser as compared to stent placement for relief of dysphagia[6]. The American Brachytherapy Society has laid guidelines to select the patients who are candidates for palliative treatment by brachytherapy. They are as follows:

**Indications**
1) Unresectable local disease progression/recurrence after definitive radiation treatment
2) Adenocarcinoma or Squamous cancers of the thoracic esophagus with distant metastases
3) Stenosis
4) Dysphagia
5) Tumour haemorrhage
6) Alternative to stent placement

**Dose recommendation**
HDR 7-28 Gray in fractions of 5-7 Gray

**5. Conclusion**

With experienced hands, brachytherapy is an excellent way of delivering high dose of radiation to the tumour with minimal insult to the surrounding organs. It also has the potential of causing devastating adverse effects. So it needs great clinical expertise and support system to deal with the acute and late side effects. It calls for more clinical studies to define the dose schedules i.e. proportion of total dose to be delivered by external radiation and brachytherapy and adverse effects in both curative and palliative settings.

**6. Acknowledgements**

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**7. References**


