

## Radiation Therapy Alone for Early Stage Non-small Cell Carcinoma of the Lung

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**Purpose** : To evaluate the outcome of early stage non-small cell lung cancer patients who were treated with radiation therapy alone and define the optimal radiotherapeutic regimen for these patients.

**Materials and Methods** : A retrospective review was performed on patients with stage I or II non-small cell carcinoma of the lung that were treated at our institution between June, 1987 and May, 2000. A total of 21 patients treated definitively with radiation therapy alone were included in this study. The age of the patients ranged from 53 to 81 years with a median of 66 years. All the patients were male. The medical reasons for inoperability were lack of pulmonary reserve, cardiovascular disease, poor performance status, old age, and patient refusal in the decreasing order. Pathological evidence was not adequate to characterize the non-small cell subtype in two patients. Of the remaining 19 patients, 16 had squamous cell carcinoma and 3 had adenocarcinoma. Treatment was given with conventional fractionation, once a day, five times a week. The doses to the primary site ranged from 56 Gy to 69 Gy. No patients were lost to follow-up.

**Results** : The overall survival rates for the entire group at 2, 3 and 5 years were 41, 30 and 21%, respectively. The cause specific survivals at 2, 3 and 5 years were 55, 36 and 25%, respectively. An intercurrent disease was the cause of death in two patients. The cumulative local failure rate at 5 years was 43%. Nine of the 21 patients had treatment failures after the curative radiotherapy was attempted. Local recurrences as the first site of failure were documented in 7 patients. Therefore, local failure alone represented 78% of the total failures. Those patients whose tumor sizes were less than 4 cm had a significantly better 5 year disease free survival than those with tumors greater than 4 cm (0% vs 36%). Those patients with a Karnofsky performance status less than 70 did not differ significantly with respect to actuarial survival when compared to those with a status greater than 70 (25% vs 26%,  $p > 0.05$ ).

**Conclusion** : Radiation therapy alone is an effective and safe treatment for early stage non-small cell lung cancer patients who are medically inoperable or refuse surgery. Also we believe that a higher radiation dose to the primary site could improve the local control rate, and ultimately the overall survival rate.

**Key Words** : Non-small cell lung cancer, Early stage, Radiation therapy

### Introduction

The general consensus among the oncologists is that surgical resection offers the optimum chance for cure in patients with early stage non-small cell carcinoma of the lung.<sup>1)</sup> The role of radiation therapy is typically confined to the patients with un-

resectable lesions and to the small group of patients with resectable disease either who are medically inoperable or who refuse surgery. In some instances, patients choose radiation therapy that has less potential of immediate treatment related risks than surgery, even though it may be less effective in achieving cure.<sup>2)</sup> Several reports have documented the outcome with radiotherapy alone for patients with potentially resectable non-small cell lung cancer.<sup>3-8)</sup>

This study retrospectively analyzed the records of the patients with early stage non-small cell lung cancer who were treated with radiotherapy alone in our institution.

We tried to investigate the results of radiation treatment and

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optimal radiotherapeutic regimen in these patients.

## Materials and Methods

A retrospective review was performed on patients with stage I or II non-small cell carcinoma of the lung who were treated at Department of Therapeutic Radiology, Hanyang University Hospital between June, 1987 and May, 2000. Total of 21 patients treated definitively with radiation therapy alone were included in this study. Patients who had any attempt of surgical resection after the radiotherapy or administration of chemotherapy were excluded from the study. The age of the patients ranged from 53 to 81 years with median age of 66 years. All of the patients were male. The medical reasons for inoperability were lack of pulmonary reserve, cardiovascular disease, poor performance status, old age and patient refusal in the decreasing order.

Diagnostic work up and staging procedures included history taking and physical examination, chest PA, bronchoscopy, sputum cytology, chest CT, whole body bone scan and brain CT. Histologic confirmation was obtained in all of 21 patients. However, pathologic evidence was not adequate to characterize the non-small cell subtype in two patients. Of the remaining 19 patients, 16 had squamous cell carcinoma and 3 had adenocarcinoma. The tumor size was recorded in all cases and measured as the largest transverse diameter in pretreatment chest radiographs or CT scan. Patients were only clinically staged and none of the patients underwent mediastinoscopy. The patients characteristics according to age, T and N stage, AJCC stage, histology, performance status and tumor size are shown in Table 1.

All of the patients were treated with megavoltage linear accelerator producing maximum of 10 MeV photons. Anterior-posterior parallel opposed portals were used to encompass the primary site and the regional mediastinum in majority of patients. Only primary site was treated in six patients. Cone down boost field was used to treat the primary site with adequate margin following the large field irradiation. Treatment was given with conventional fractionation, once a day, five times a week. Delivered daily dose was 180 or 200 cGy. Distribution of patients according to total radiation dose is shown in Table 2. Mediastinal dose ranged from 34 Gy to 46 Gy. The dose to the primary site ranged from 56 Gy to 69 Gy.

Radiation therapy and hospital records were reviewed and the referring physicians were contacted when necessary to obtain the follow-up information. No patients were lost to follow-up. Survival was calculated from the day one of the radiation therapy. Local progression was defined as the radiographic evidence of tumor progression. Statistical comparison was made by Chi square test.

## Results

The overall survival rate for entire group of patients was 41% at 2 years, 30% at 3 years and 21% at 5 years, with median survival of 23 months as shown in Fig. 1. The cause specific survival rate was 55% at 2 years, 36% at 3 years and

Table 1. Patients' Characteristics

	53~81 (median 66)
Age	53~81 (median 66)
T stage	
T1	4
T2	15
T3	2
N stage	
N0	19
N1	2
AJCC stage	
Ia	4
Ib	13
IIa	1
IIb	3
Performance status*	
<70	5
>70	16
Histology	
Squamous cell carcinoma	16
Adenocarcinoma	3
Non specified	2
Tumor size	
<4 cm	15
>4 cm	6

\*Karnofsky performance status

Table 2. Distribution of Patients according to Delivered Dose

Dose	No. of patients
56~60 Gy	2
60~64 Gy	14
64~68 Gy	4
>69 Gy	1
Total	21

25% at 5 years, respectively. Intercurrent disease was the cause of death in two patients.

The cumulative local failure rate at 5 years was 43% as shown in Fig. 2. Nine patients out of 21 patients had treatment failures after the attempt of curative radiotherapy. The major pattern of failure was local recurrence. Local recurrences as the first site of failure were documented in seven patients. Therefore, local failure alone represented 78% of the total failure. Distant failure alone was noted in only one patient in this study.

Those patients whose tumor sizes were less than 4 cm showed a significantly better 5 year disease free survival rate than those whose tumors were greater than 4 cm (32% vs 0%). None of the four patients whose tumor sizes were larger than 4 cm survived for 5 years. Those patients with a Karnofsky performance status less than 70 did not differ significantly with respect to actuarial survival rate when compared to those whose status was greater than 70 (25% vs 26%,  $p>0.05$ ). There were

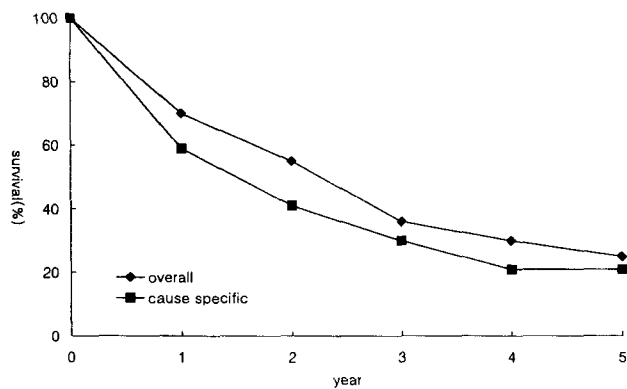


Fig. 1. Overall and cause specific survival for entire group of patients.

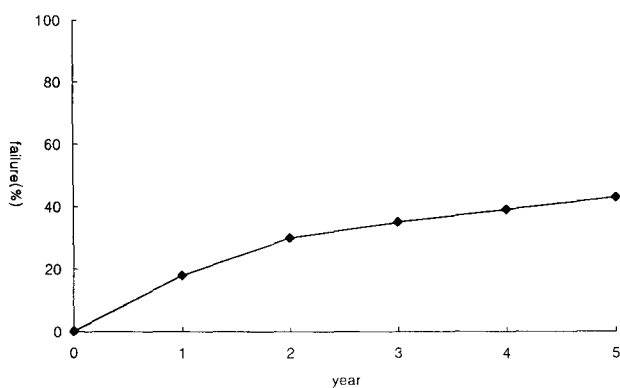


Fig. 2. Cumulative local failure rate.

no documented severe acute or chronic complications during or after the treatment. None of the patients had to cease the treatment because of the acute toxicities. Acute esophagitis was documented in 60% of patients and one patient was noted to have acute pericarditis.

## Discussion

Surgery is the preferred form of treatment for early stage non-small cell lung cancer. However, there are subsets of patients who either refuse surgery or are medically inoperable. These patients are often treated with radical radiation therapy alone. Hilton reported a 22.5% five year overall survival in prospective study on 38 patients with early stage lung cancer in 1960.<sup>4</sup> This result was not significantly less than the five year survival achieved with curative surgery. Five year survival rate of approximately 30% level could have been achieved by curative surgery at that time on the patients with early stage non-small cell lung cancer.<sup>7</sup> Since the operative mortality for elderly patients was approximately 10%,<sup>9, 10</sup> radiation therapy was considered as an alternative modality in all Stage I patients.

However, the study reported by other investigators showed lower long term survival rate in radiation alone group,<sup>5</sup> compared with patients treated with radical surgery (7% vs 23% at 4 years). Based upon this dismissing result, further investigation has not been readdressed for the following twenty years. Cooper compared a group of operable lung cancer patients treated with radiation therapy alone to a similarly staged group of resected patients over the age of 70.<sup>11</sup> He reported improved survival in the resected group (45% vs 10% at 3 years). However, his review was criticized in terms of delivered radiation dose and patient selection.

Haffty and Zhang documented encouraging 5-year survival rates of 21% and 32% for patients treated with curative radiation therapy.<sup>3, 8</sup> Also Sandler reported 11% 5-year survival rate in these patients.<sup>12</sup> Overall survival rate obtained in the present study is somewhat similar to those in other studies although patients selection might be different in each study. The patients in Hilton's report were young with a median age of 57 years and in good performance status.<sup>4</sup> Although we were not able to show significant difference in survival according to performance status, health status seemed to affect survival rates.

In our study, local control rate was not as good as one could expect. More than 50% of patients showed local failures in our study. However, stage I non-small cell lung cancer patients treated with radical surgery were noted to have 10~15% local failure rates.<sup>3)</sup> When considering radiation therapy as an alternative to surgery, it should be considered that local failure may have an influence on survival. Thus, improved local control rate is necessary to achieve better survival rate in the management of early stage non-small cell lung cancer.

Local control rate was noted to be dose dependent in RTOG studies.<sup>13)</sup> Intrathoracic failure rates for patients treated with 60 Gy, 50 Gy and 40 Gy were 27%, 38% and 48%, respectively. Also Sherman found a 50% failure rate for doses of less than 50 Gy and a 5% failure rate for doses of 60 Gy or more.<sup>14)</sup> This represents higher dose seemed to have an impact on improved survival. In our study, patients treated with higher radiation dose showed better survival than those treated with lower dose, although each group had limited number of patients.

The major pattern of failure in our study was local failure especially in primary tumor site. It is controversial whether regional lymphatic chains should be encompassed in the radiation field. The value of treating lymph nodes remains equivocal if the local tumor is not controlled adequately. Because majority of patients are old or have poor pulmonary function, it is recommended radiation field be reduced as much as possible to encompass the primary site and the surrounding normal tissue. Reducing the target volume to include primary site and first echelon of lymphatic chain may allow us to increase the radiation dose delivered to the target while minimizing the dose to the surrounding normal tissues.

Based on our results, we conclude that radiation therapy alone is an effective and safe treatment for early stage non-small cell lung cancer patients who are medically inoperable or refuse surgery. Also we might believe that higher radiation dose to the primary site could improve local control rate, and ultimately overall survival rate.

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## 초기 비소세포폐암의 방사선 단독치료

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**목적:** 초기 비소세포폐암 환자에서 방사선 단독치료의 결과를 분석하고 최적의 방사선 요법을 알아보고자 함이 본 연구의 목적이다.

**재료 및 방법:** 1987년 6월부터 200년 5월까지 본원에서 방사선치료를 받은 제1 및 제2병기 비소세포폐암 환자를 후향적으로 분석하였다. 근치적 목적으로 방사선 단독요법으로 치료 받은 21명의 환자를 대상으로 하였다. 환자의 나이는 53세부터 81세이었으며 중앙값은 66세이었다. 모든 환자는 남성이었다. 수술이 불가능하였던 이유는 폐기능의 손상, 심혈관계 질환, 열악한 전신상태, 고연령, 수술 거부 등이었다. 16명은 편평상피암, 3명은 선세포암이었고 2명은 불분명하였다. 전통적 방법으로 하루에 한번 일주일에 5회씩 치료하였으며, 원발부위의 조사량은 56 내지 69 Gy이었다. 모든 환자에서 추적이 가능하였다.

**결과:** 모든 환자에서 2년, 3년, 5년 생존율은 각각 41%, 30%, 21%이었으며 중앙값은 23개월이었다. 2년, 3년, 5년의 질환관련 생존율은 각각 55%, 36%, 25%이었다. 2명의 환자는 기타 질환으로 사망하였다. 5년 국소재발율은 43%이었으며 21명중 9명이 치료 실패를 경험하였다. 국소재발은 7명에서 나타났으며 따라서 국소재발이 치료실패의 78%를 차지하였다. 종양 크기가 4 cm 이하인 환자에서 5년 무병생존율이 4 cm 이상인 환자보다 높게 나타났다. 종양 크기가 4 cm 이상인 환자 모두는 사망하였다. 카르노프스키 전신상태는 생존율에 영향을 미치지 못하였다.

**결론:** 수술이 불가능한 초기 비소세포폐암 환자에서 방사선 단독치료는 안전하고 효과적인 치료방법이었으며 본 연구의 결과로 비추어 볼 때 원발부위의 방사선 조사량을 높이는 것이 국소관해율을 증가시키고 나아가 생존율도 증가시키리라 사료된다.

**핵심용어:** 비소세포폐암, 초기 병변, 방사선치료