

## **The role of radiotherapy in lung cancer treatment. Report from Slovenia**

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**Background.** *In order to evaluate the role of radiotherapy in lung cancer treatment in Slovenia, 276 pts treated in 1988 at the Institute of Oncology in Ljubljana were investigated.*

**Patients and methods.** *There were 253 males and 23 females, aged 31–83 yrs (median 59); 6 pts had clinical St.I, 19 St.II, 78 St.IIIa, 65 St.IIIb and 108 pts had St.IV lung cancer. Distant metastatic sites were as follows: generalised in 29 pts, bone in 32, brain in 21, liver in 9 and other organs in 14 pts. Of 267 histologically confirmed lung cancers, 126 were squamous, 62 small-cell, 44 large-cell, 23 adenocarcinomas, and 12 others (mixed, unspecified). Performance status (Karnofsky) was assessed as > 70 in 199, 50–70 in 57 and < 50 in 20 pts. Primary therapy was: RT in 189, RT + ChT in 44, OP + postop. RT in 20, OP + ChT in 2, ChT in 14, and solely symptomatic in 7 pts. In 253 pts treated by RT, tumor dose was > 5.000 cGy (= radical) in 88, palliative in 156, and only initial in 9 pts. RT as the only method of treatment was applied loco-regionally (& supraclavicular) in 135, to local + distant metastases in 8, only metastases in 43, whereas in 3 pts first to distant metastases and later on to the lung.*

**Results.** *By the end of 1993, 7/276 (2.5%) pts were still alive. One-year survival of all treated pts was 25%, and two-year 9%. Of 75 pts irradiated loco-regionally with radical doses, 49% survived one year, 17% two years, and 3% 5 years. There was a significant difference in the survival according to tumour dose ( $p < 0.001$ ) and performance status ( $p < 0.001$ ), but none with reference to clinical stage I–IIIb ( $p < 0.1$ ) and histology ( $p < 0.1$ ). Treatment response was assessed after loco-regional radiation in 79%, and after radiation of metastases in 70% of cases.*

**Conclusions.** *Radiotherapy has proved beneficial for the majority of our patients in terms of life quality and short term survival.*

**Key words:** lung neoplasms-radiotherapy, lung cancer, radiotherapy; survival analysis; indications, life quality

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### **Introduction**

Radiotherapy is the most common specific met-

hod of lung cancer therapy. Unfortunately, not so much owing to its success, but rather due to the lack of more suitable treatment methods. Radiotherapy could be performed in cases of inoperable non-small and small-cell cancer with or without, chemotherapy. The aim of radiotherapy is to diminish the disease-related problems caused by a lung tumour and/or its regional and

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UDC: 616.24-006.6:615.849.114

distant metastases, and to prolong the duration of survival, sometimes also to cure. Another important reason is that such specific treatment maintains the patient's hope that not everything has been lost yet, since the patient is not treated only symptomatically.

In the selection of patients, we had to consider the actual possibilities for radiation: the capacities of radiation machines and hospitalization possibilities for in-patients.

This paper is aimed to present a review of one-year turnover of patients admitted to the Institute of Oncology Ljubljana in 1988: the types of patients managed, the primary treatment approaches used and the results obtained.

### Patients and method

In 1988, 795 new cases of lung cancer were registered by the Cancer Registry of Slovenia. The incidence per 100,000 population was 68.4 for males and 12.7 for females.

Thoracic surgery was performed at the Department for Thoracic Surgery, Univ. Medical Centre Ljubljana, and at the Thoracic Surgery of the General Hospital of the second greatest Slovenian town, Maribor.

All radiotherapy is concentrated at the Institute of Oncology Ljubljana. The radiation facilities comprise 2 linear accelerators, 2 cobalt unites, 1 conventional x-ray machine and 2 superficial x-ray machines.

Chemotherapy was performed at the Institute of Oncology Ljubljana, and at the Institute for Respiratory Diseases Golnik.

There were 369 new patients with lung cancer treated at the Institute of Oncology Ljubljana in 1988, but only 276 of them were evaluable. This represents 35% of the registered and 75% of those treated in the year under study. There were 253 males and only 23 females, aged 31–83 years, median 59 years; 220 of these patients were in the age of 50–70 years.

Of 267 histologically confirmed lung cancers, 126 were squamous, 62 small-cell, 44 large-cell, 23 adenocarcinomas and 12 others (mixed, unspecified), whereas 9 were microscopically not confirmed.

Clinical stage was established on the basis of clinical examination, chest x-ray, bronchoscopy and abdominal ultrasonography. Other procedures such as chest CT, bone scan and other x-ray examinations were performed only in the case of suspicious symptoms or doubtful operability. Six patients had stage I, 19 stage II, 78 stage IIIa, 65 stage IIIb and 108 stage IV lung cancer. Distant metastatic sites were as follows: generalized in 29 patients, bone in 32, brain in 21, liver in 9 and other organs in 14 patients.

Performance status (Karnofsky) was assessed as >70 in 199, 50–70 in 57 and <50 in 20 patients.

Reliable data on the duration of symptoms were available for 224 patients: <3 months in 146, 3–6 months in 37, 6–12 months in 23 and >12 months in 18 patients.

The leading symptoms at the beginning of treatment were due to primary tumour in 161, regional metastases in 12, both in 11, and distant metastases in 72; 7 patients presented with general symptoms while 13 were asymptomatic.

Most patients, 222 (80%), were referred to the Institute after previous team consultation, 43 (16%) patients on the basis of phone agreement and 11 (4%) without previous agreement.

The primary treatment was as follows in Table 1.

**Table 1.** The primary treatment of lung cancer patients.

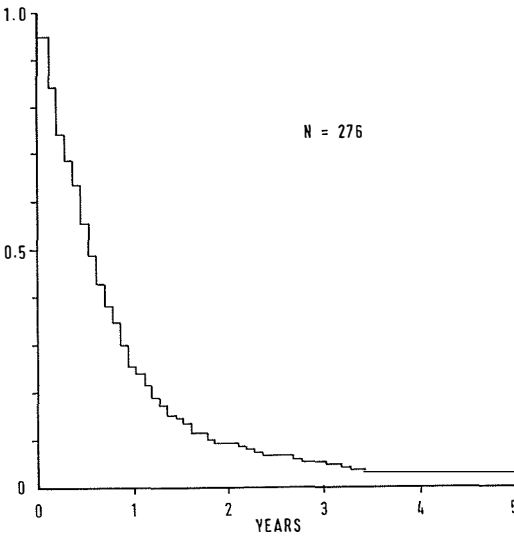
Treatment method	No. of pts.	Percent
radiotherapy	189	68 %
radiotherapy + chemotherapy	44	16 %
surgery + radiotherapy	20	7 %
surgery + chemotherapy	2	1 %
chemotherapy	14	5 %
symptomatic only	7	3 %
Total	276	100 %

Radiotherapy was applied in 253/276 (92%) patients. Of these, 88 patients received a "radical" tumour dose, i.e. equivalent dose > 5,000 cGy in 5 weeks, whereas 156 had a lower palliative dose. In 9 patients radiation was started and finished before an expected pallia-

tive tumour dose could be achieved. In 7 patients radiation was planned but was cancelled before even started because of complications. Daily doses were 250–400 cGy, radical radiation was delivered according to split-course regimen.

**Results**

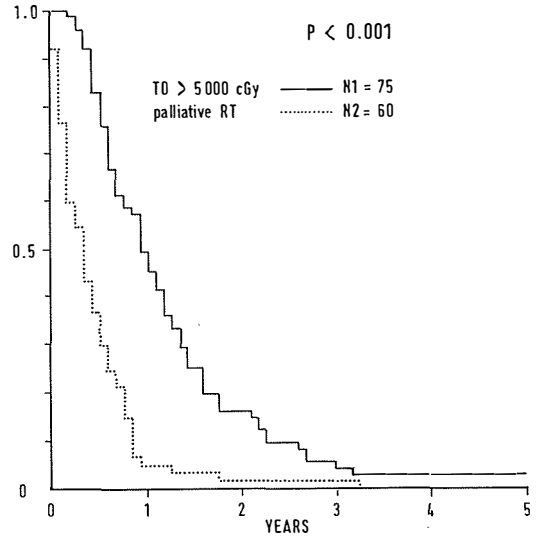
By the end of 1993, 7 of 276 (2.5%) treated patients were still alive. One-year survival was 25% and two-year 9% (Figure 1). The value



**Figure 1.** Patients with lung cancer treated in 1988 at The Institute of Oncology of Ljubljana.

of radiation could be estimated in patients treated by radiation alone, without chemotherapy or previous surgery, either of primary lung tumour and regional metastases or distant metastases. Radiotherapy as the only method of treatment was applied loco-regionally in 135, to lung and distant metastases in 8, only metastases in 43, whereas in 3 patients was radiotherapy applied first to metastases and later on the lung.

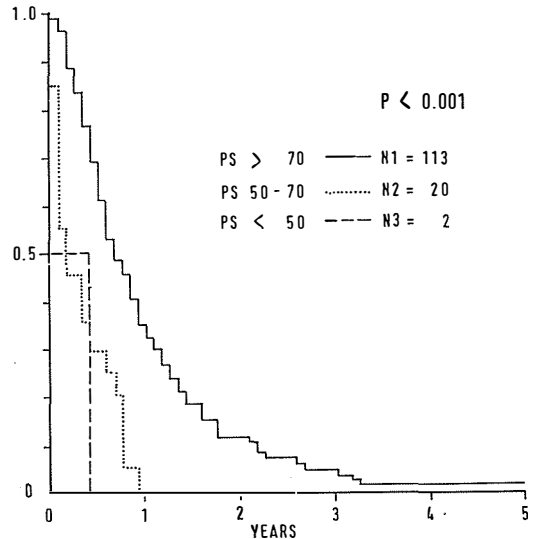
The survival of radically loco-regionally irradiated patients is significantly better ( $p < 0.001$ ) than that of palliatively irradiated ones (Figure 2). After radical irradiation one- and two-year



**Figure 2.** Survival after loco-regional radiation therapy by tumour dose.

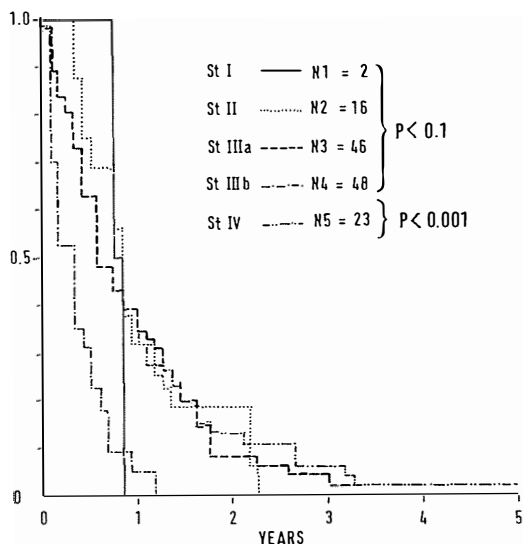
survival was 49% and 17% respectively, but five-year survival was only 3%. In palliatively irradiated patients one-year survival hardly reached 19%; all the patients died in 3.5 years.

Survival by performance status was significantly different ( $p < 0.001$ ) (Figure 3). Survival in



**Figure 3.** Survival after loco-regional radiation therapy by performance status.

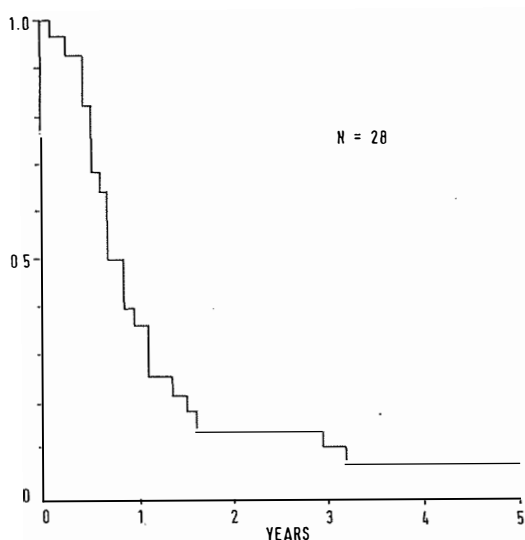
stage I–IIIb was not statistically different ( $p < 0.1$ ), but there was difference in stage IV ( $p < 0.001$ ) (Figure 4). Histology of nonsmall cell



**Figure 4.** Survival after loco-regional radiation therapy by stage.

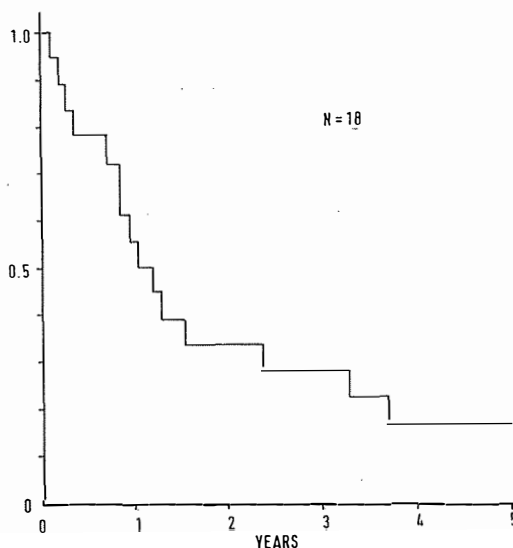
cancer irradiated loco-regionally has not influenced survival ( $p < 0.1$ ).

Survival of 28 patients with small-cell carcinoma treated by chemotherapy and loco-regional radiotherapy is evident from Figure 5. There

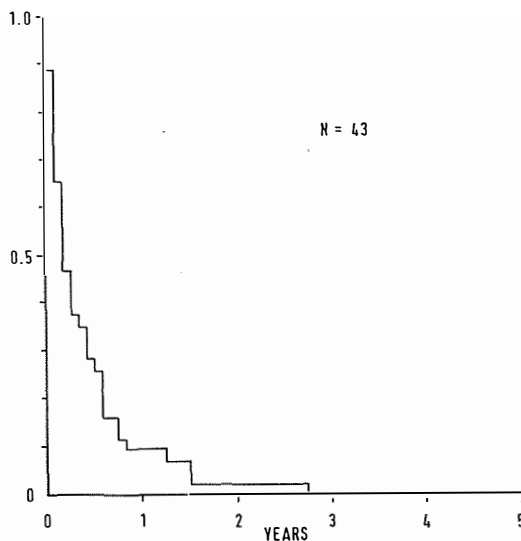


**Figure 5.** Survival after chemotherapy and loco-regional radiation therapy.

are also patients treated by chemotherapy before admission to the Institute for radiotherapy and therefore their survival is not a reliable indicator of such treatment. It refers only to the survival after admission to our Institute. Similar situation is associated with the survival of patients irradiated after surgery (Figure 6):



**Figure 6.** Survival after surgery and postoperative loco-regional radiation therapy.



**Figure 7.** Survival after radiation therapy for metastases.

besides the patients irradiated postoperatively, the group also comprises those with bronchial or mediastinal recurrence.

The survival after radiation of metastases was considerably shorter: Only 9% of patients survived one year, and all of them died within 3 years from the beginning of therapy (Figure 7).

Effectiveness of radiation could be estimated not only by survival but also by objective and subjective response reflected in the presence or absence of patient's disease-related problems. Adequate data were available for 211 of 253 patients (Table 2).

**Table 2.** Effectiveness of radiation of lung cancer patients.

Radiation results	No. of pts	Percent
obj. + subj. response	107	51 %
subj. response	31	15 %
obj. response	15	7 %
st. idem	43	20 %
progression	15	7 %
Total	211	100 %

Radiation response was estimated in 153 of 211 (73%) patients; In 112 of 135 loco-regionally irradiated patients the results were as follows in Table 3.

**Table 3.** Results of loco-regionally irradiated patients with lung cancer.

Radiation results	No. of pts	Percent
obj. + subj. response	58	52 %
subj. response	18	16 %
obj. response	12	11 %
st. idem	20	18 %
progression	4	3 %
Total	112	100 %

Radiation response was obtained in 88 of 112 (79%) patients.

In patients irradiated of distant metastases, the results were available for 27 of 43 patients (Table 4).

**Table 4.** Patients irradiated for distant metastases.

Radiation results	No. of pts	Percent
obj. + subj. response	13	48 %
subj. response	6	22 %
obj. response	0	0 %
st. idem	6	22 %
progression	2	8 %
Total	27	100 %

Radiation response was obtained in 19 of 27 (70%) patients.

The duration of response in patients irradiated loco-regionally was reliably assessed in 67 patients only (Table 5).

**Table 5.** The duration of response in patients irradiated loco-regionally.

Duration of response	No. of pts.
< 2 mos	10
2-6 mos	18
6-12 mos	19
> 12 mos	20

## Discussion

The patients treated at the Institute of Oncology were mostly in progressed stage of disease, aged from 50 to 70 years, with good performance status, and a few-month history of chest symptoms. Among those treated only by radiation there were no operable cases. Four fifths of patients were discussed at team consultation with thoracic surgeon who suggested additional examinations such as CT, mediastinoscopy, parasternal mediastinotomy, thoracoscopy or exploratory thoracotomy.

The report includes routines cases and therefore examinations performed before treatment were extremely rational and in agreement with the principles of lung cancer management accepted in last year.<sup>1</sup> Probably, the actual tumour stages were higher than stated in the report because of the unavailability of CT and radionuclide examinations.

The patients were referred to the Institute soon upon the completion of diagnostic proce-

dures so that the therapy could be started without delay. Radiotherapy was a primary treatment in 92 % of patients. Despite the planned radiation treatment, 7 patients received only symptomatic therapy because of rapidly deteriorating condition. In 9 patients radiation was started, but the intended palliative dose could not be achieved. In order to diminish the number of fractions and to shorten hospitalization time, the daily doses used most frequently were 250, 300 and 400 cGy. Split-course regimen is very suitable for lung tumours in order to alleviate esophagitis; on the onset of this symptom, a 3–4 week break is made. Sometimes after the break new disease symptoms may appear which render further radiation unreasonable.

Equivalent tumour dose  $> 5.000$  cGy/5 weeks calculated by Kirk and coworkers<sup>2</sup> is considered as radical. However, this dose was not found to be curative. Generally, it is very difficult to speak about curative radiotherapy with such a low five-year survival rate. This depends on the selection of patients rather than on the kind of radiotherapy and support therapy. Most articles report results by Smart and Hilton in 1966:<sup>3</sup> in 40 selected irradiated patients with lung cancer five-year survival was achieved in 22.5 %. The 32 % five-year survival was reported by Zhang and co-workers 1989<sup>4</sup> in 44 patients with operable non-small cell lung cancer who have refused surgery. In most unselected patients the survival was essentially lower and did not exceed 5 %.

Better survival of radically irradiated patients and patients with higher performance status has confirmed our criteria for the selection of treatment method: unrestricted use of high-dose radiation therapy in patients with lower performance status and/or progressed tumour does neither improve the survival nor alleviates the symptoms. Therefore, patients in worse general condition were irradiated with palliative doses and the resulting survival rates were lower.

The survival of patients with small cell cancer after combined chemotherapy and radiation of lung tumour and regional lymph nodes was reported to be somewhat better than that ob-

tained by chemotherapy alone, but above all, there were less loco-regional recurrences.<sup>5</sup> Repeated bronchoscopy after complete regression evident on x-ray often confirms a tumour of bronchial mucosa. Therefore, we consider irradiation of chest in limited stage small cell lung cancer despite possible loco-regional regression after chemotherapy indicated for safety reasons.

We did not perform routines prophylactic cranial irradiation. The exception were some patients included in the study in whom prophylactic cranial irradiation was ordered in protocol.

The preoperative radiotherapy was not performed. The postoperative radiation therapy was performed in the cases of nonradical surgery, metastases in mediastinal lymph nodes and recurrence. Five-year survival of those patients was 17 %.

### Conclusion

Radiotherapy as a primary treatment modality for lung cancer was performed in 92 % of our patients.

Suitable for radiation were patients with inoperable or nonradical operated lung cancer, mostly with progressed disease and good performance status, with symptoms of primary tumour, regional and/or distant metastases.

Treatment response was obtained after loco-regional radiation in 79 % and after radiation of metastases in 70 % of patients. We believe that the improved quality of life may result in better short term survival.

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