Radiotherapy in Thoracic Neoplasms*
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There is much material available for a statistical evaluation of the current status of radiotherapy in thoracic neoplasms; for primary carcinoma of the lung, six representative reports—three from this country by Leucutia (1958), Schulz (1957), and Leddy (1950), and three from England by Paterson (1950), Hilton (1955), and Brown (1952)—add up to a 2.4 per cent five-year survival rate in 1512 non-resectable cases, which may seem a hardly worthwhile reward from so much effort. But statistics of this kind, although they are the only objective measure we have, do not give a complete picture of the current status of radiotherapy in primary lung cancer; for they refer mostly to patients treated 10 or more years ago, and the last decade has been a period of rising standards and increasing knowledge in radiotherapy, comparable to (and reflecting and incorporating) those in thoracic surgery and general medicine. From another aspect, however, statistics of the results of treatment, whether by surgery or radiotherapy or chemotherapy or combined methods, give too favorable a picture, since the untreated patients are omitted and the size of this untreated fraction is not generally known. It was actually 45 per cent in the Joint Lung Cancer Clinic of the Brompton and Royal Marsden Hospitals in Landon (Bignall, 1958); in the years 1951-55 there were 1749 patients registered and 778 were not treated; of the 971 treated, 35 per cent had surgery, 59 per cent radiotherapy, 5 per cent had surgery followed by radiotherapy, and 1 per cent had pre-operative radiotherapy. Churchill (1958) reports that about 35 per cent of the pathologically-confirmed cases are currently resectable, and in this

FIGURE 1 (Case 1): August 1942—anaplastic carcinoma obstructing right lower lobe bronchus. FIGURE 2 (Case 1): August 1956—14 years after 4500 r T.D. Patient well and working.

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resected group the five-year survival rate is 28 per cent. Thus at the present time if there is no improvement in the results of treatment as given five or more years ago, out of 100 pathologically-confirmed and treated cases of primary lung cancer, there will be 10 five-year survivals from surgery and two five-year survivals from radiotherapy; it is my present opinion that this 12 per cent five-year survival rate could even now be doubled.

The various means available for improving the survival rate may be listed as follows:

1. In non-resectable cases, tumor-sterilizing doses of radiation can be safely given by well-planned radioactive implants at the time of thoracotomy, or by the use of supervoltage x-ray and telecobalt with proper dose-planning, or by a combination of the two. It would seem that knowledge of the existence of patients who have been cured of primary lung cancer by radiation alone is very unevenly distributed, so that patients with non-resectable but possibly radio-curable tumors are not given the opportunity of radiotherapeutic consultation or treatment.

2. In resected cases the survival rate of patients with proved metastases in the regional lymph-nodes is only one-third that of patients without lymph-node metastases. Post-operative irradiation of the regional lymph-nodes (or radioactive implants at operation) can improve the salvage rate in this group.

3. About 80 per cent of resected lung cancers show venous invasion, and preliminary studies suggest that many patients have free-floating cancer cells in the blood stream which disappear or decrease in number following irradiation of the primary tumor. The significance of, and the correlation (if any) between venous invasion and free-floating cancer cells in the blood with the incidence of distant metastases and survival rates are yet to be worked out, but it would seem a logical assumption that the use of pre-operative irradiation in selected cases would improve present results.

FIGURE 3

FIGURE 4

FIGURE 3 (Case 2): March 1, 1952—epidermoid carcinoma obstructing right main bronchus. FIGURE 4 (Case 2): Beginning aeration of right upper lobe during course of x-ray therapy.
4. Those lung cancers which give circumscribed shadows radiographically are much more likely to be resectable than the non-circumscribed ones, regardless of the particular cell-type. Since radiation therapy often produces tumor regression with the post-treatment radiograph showing better circumscription of the tumor, more use of pre-operative irradiation would again seem to be a logical step toward improving the survival-rate.

5. Although chemotherapy of lung cancer is not yet by itself a curative treatment, its use in combination with surgery and irradiation in both operable and inoperable cases may well add a further increment to the survival rate. The beneficial effect of the alkylating agents in oat-cell and other undifferentiated carcinomas is widely used, especially for mediastinal compression, and it is also possible that these agents can destroy free-floating cancer cells in the blood and perhaps even tumor emboli before these can become established metastases. The actinomycins have caused the radiographic disappearance of some types of pulmonary metastases and in some cases seem to potentiate the effects of irradiation, so that these agents may also prove useful in primary lung cancer.

Whether or not the wider adoption of these proposals resulted in a higher five-year survival rate, there would certainly be an improvement in the quality of palliation and the duration of symptom-free life, for in general the best palliation is the result of an attempt to cure which fails. The relief of symptoms such as cough, dyspnea, pain, hemoptysis and osteoarthropathy can be obtained by adequate radiation therapy in about 70 per cent of cases, and the disabling effects of metastases in brain or liver can likewise be relieved and so add several months of useful life to the patient.

The following case reports have been selected to illustrate the application of the above suggestions for improving the treatment of primary bronchogenic carcinoma.

Case 1: A 15-year cure by supervoltage x-ray therapy. A man aged 44 was referred to me in 1942 by Dr. Joseph Smart with atelectasis of the right lower lobe (Fig. 1); bronchoscopic biopsy was reported as anaplastic carcinoma, and the tumor was deemed inoperable because of the presence of enlarged hilar lymph nodes. A tumor dose of
4500 r was given in one month to the right chest and mediastinum through opposed large anterior and posterior fields with 1000 kv x-rays, and chest x-rays film in 1956 is reproduced in Fig. 2. He continues in excellent general condition and full work.

Incidentally this case also illustrates the scepticism concerning radiation cures of lung cancer, for the original pathologic slide was lost in 1943 when a land-mine destroyed part of the London Chest Hospital. Dr. Smart told me that when he showed the patient at a clinical meeting in 1954, no one would believe that the patient had indeed had a bronchogenic carcinoma, but fortunately the paraaffin block of the tissue biopsy was found in 1955, further sections confirmed the diagnosis of anaplastic carcinoma, and so even the most sceptical were finally convinced.

Case 2: A local cure by pre-operative supervoltage irradiation and pneumonectomy. A farmer aged 56 had increasing cough and dyspnea and 35 lb. weight loss over a six-month period, and pain in the back and blood-streaked sputum for one month. In the chest x-ray film (Fig. 3) the right thorax was opaque and the trachea shifted to the right; on bronchoscopy there was a tumor in the right main bronchus at the level of the main carina, and the biopsy was reported as epidermoid carcinoma. A tumor dose of 6250 r was given in one month with 1000 kv x-rays through opposed 10 x 10 cm anterior and posterior fields centered on the right main bronchus; the tumor regressed so that the upper lobe aerated (Fig. 4), then a plug of tumor an inch in size was coughed up (Fig. 5), followed by aeration of the middle and lower lobes (Fig. 6) and complete relief of the symptoms of cough, dyspnea and cachexia. At subsequent follow-up visits the patient remained symptom-free, but five months after treatment bronchoscopic biopsies showed persistent cancer in the bronchus intermedius and the main carina tumor-free. A right radical pneumonectomy was therefore performed; the 7 cm. tumor in the root of the right lower lobe had invaded the inferior pulmonary vein and adjacent pericardium, so this vein had to be transected at its junction with the left auricle, but all the hilar and mediastinal nodes were free from metastatic carcinoma. The patient remained well and working for two and one-half years, but then developed vertigo and staggering gait, clearly due to cerebellar metastasis. Since brain metastases are usually multiple, the whole brain was irradiated with 250 kv x-rays through opposed 11 x 20 cm. lateral fields to a tissue dose of 2950 r in five weeks, but without improvement in symptoms or signs. He died three months after this treatment, and at autopsy the only cancer found anywhere in the body was a solitary cerebellar metastasis of epidermoid carcinoma.

Case 3: Residual disease after simple pneumonectomy cured by postoperative supervoltage irradiation for 11 years. A woman aged 44 had a left simple pneumonectomy in 1942 for oat-cell carcinoma; the inferior pulmonary vein was both grossly and microscopically surrounded and invaded by the carcinoma, and was transected through tumor outside the pericardium. This region of known residual tumor was then given a tumor dose of 4200 r in 28 days with 1000 kv x-rays through opposed 8 x 8 cm. anterior and posterior fields. There have been neither symptoms nor signs of recurrent growth or metastases since, and in 1953—11 years after treatment—she reported that she was looking after her house and garden as usual and was in excellent health.

Case 4: Excellent palliation resulting from failed curative radiation therapy. In October 1956 a man aged 53 began to have generalized 'rheumatic' pains with inter-
mittent joint swellings; he felt increasing weakness and lost six pounds. When he noticed gross clubbing of his fingers and toes he went to a municipal chest clinic, where he was told that he had a small tumor of the lung. He came to consult me in February 1957 because some years previously I had treated his small daughter for recurrent malignant teratoma of the pelvis. His chest x-ray film (Fig. 7) showed a circumscribed shadow in the left upper lobe, and arrangements were made for bronchoscopy and admission to hospital for resection. He did not keep these arrangements or answer inquiries, but returned in September 1957 because of severe chest pain. The tumor (Fig. 8) was much larger than in February but still appeared operable; he again refused any procedures other than x-ray therapy; the sputum contained numerous cancer cells although the type could not be specified. A tumor dose of 6050 r was given in six weeks with 1000 kv x-rays; early in the course of treatment the severe chest pain and the painful polyarthritis were completely relieved, and the tumor regressed and in the chest x-ray film one year after treatment (Fig. 9) its shadow cannot be seen. In January 1958 he noticed increasing headache, nausea, vertigo and sub-occipital pain; he was admitted to hospital with the clinical diagnosis of multiple cerebellar metastases, (C.S.F. protein was 150 mg./100 cc.), and made complete recovery following irradiation of the whole brain with 250 kv x-rays, tumor dose 3120 r in three weeks. He continued in good health until July 1959—he even regained an excellent head of hair after the complete epilation caused by irradiation —when he had a return of the painful polyarthritis and clubbing of the fingers and toes. He had no cough and no cancer cells could be found in the sputum, but the chest x-ray film was suggestive of a hilar node metastasis just below the aortic knob. On this occasion telecobalt rotation therapy was used in order to avoid producing skin erythema in the previously irradiated area, and again there was early improvement in the osteoarthropathy. It is also interesting that on both occasions, during the treatment of the primary tumor and of the hilar metastasis 22 months later, as the polyarthritis subsided a generalized pruritus occurred, particularly over the shins, and persisted for some weeks. Figure 10 shows the chest x-ray film in February, 1960.

Primary bronchogenic cancer is of course the commonest thoracic neoplasm, but the principles of radiation therapy which have been illustrated in this paper are equally valid for other types of malignant disease, and the results are generally somewhat better. Examples were shown of a mediastinal lymphosarcoma well for 10 years; Hodgkin's disease of the mediastinal and cervical nodes well for seven years; Ewing's tumor of the rib and pleural cavity without local recurrence for six years and then fatal metastases in the opposite lung; a large neuroblastoma of the posterior mediastinum successfully removed after pre-operative radiation of the mediastinum; and various types of pulmonary metastases (liposarcoma, reticulum-cell sarcoma, osteogenic sarcoma, malignant synovia, malignant teratoma, neuroblastoma, Wilms' tu-

![Figure 9](image1.png)

**Figure 9** (Case 4): Sept. 23, 1958—no tumor shadow visible one year after 6050 r T.D.

**Figure 10** (Case 4): Feb. 2, 1960—patient symptom free.
mor) which disappeared following radiation therapy and did not recur for one or more years. Although in most cases the recurrence of hematogenous metastases is to be expected within a period of less than 12 months, the fact that there are even a few cases of prolonged control offers hope of improved treatment in the near future, since it is the radiation tolerance of the pulmonary alveoli which is the present limiting factor. If some reliable means of preventing or treating radiation pneumonitis and pulmonary fibrosis could be found, it would be possible to give pulmonary metastases a more effective tumor dose; or if a truly synergistic chemotherapeutic agent were available, the present permissible tumor dose of, say, 2000 r would be more effective.

SUMMARY

From an evaluation of the present status of radiotherapy in thoracic neoplasms, both primary and metastatic, five suggestions are made for the improvement of present results:
1. Better appreciation by the medical profession of what can even now be accomplished.
2. Provision of more supervoltage x-ray and telecobalt apparatus, and of more trained radiation therapists to use them.
3. More use of intelligent pre-operative and post-operative irradiation, and of radioactive implants at operation.
4. More hopeful treatment of hematogenous metastases,
   (a) of primary bronchogenic cancer to the brain or liver.
   (b) of pulmonary metastases from extrathoracic primary sites.
5. Investigations directed to the discovery of
   (a) a truly synergistic chemotherapeutic agent
   (b) the significance of free-floating cancer cells in the blood
   (c) a means of preventing or treating radiation damage to the lungs.

RESUMEN

Después de una valuación del estado actual de la radioterapia en las neoplasias torácicas tanto primarias como metastásicas, se hacen sugestiones para mejorar los resultados:
1. Mejor estimación por parte de los médicos de lo que puede obtenerse.
2. Provision de más supervoltaje en los aparatos de rayos X y de Cobalto, y más técnicos adiestrados para usarlos.
3. Mayor uso de la radiación pre y postoperatoria inteligentemente aplicada, así como de implantaciones de substancias radioactivas durante la operación.
4. Tratamiento más útil de las metástasis hematogénas:
   (a) de cáncer bronquiológico a cerebro o hígado.
   (b) de metástasis pulmonares de partida extratorácica.
5. Investigaciones dirigidas al descubrimiento de:
   (a) un agente terapéutico verdaderamente sinérgico.
   (b) la significación de las células libres flotantes en la sangre.
   (c) un medio para prevenir o tratar el daño de la radiación sobre los pulmones.

REFERENCES