

# THE ROLE OF ROENTGEN THERAPY IN THE TREATMENT OF BRONCHIOGENIC CARCINOMA

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Bronchiogenic carcinomas are being treated by surgery, radium, roentgen therapy, and combinations of these procedures.

Attempts have been made to implant radon seeds or radium needles interstitially or to place other types of radium containers in apposition with the malignant tissue through bronchoscopes. Although apparently most carcinomas of the lung begin in major bronchi and near the hilum, radium treatment can be employed only in a few selected cases where the disease is so located that it is accessible through bronchoscopes or by some other equally simple surgical approach which facilitates the application of the radium containers. However, the sphere of therapeutic effectiveness of the radium radiation is only a few centimeters from its source; therefore, radium therapy has quite limited usefulness because in the majority of cases the carcinoma will have extended beyond its destructive influences. Also, it would seem that surgical excision would give better prospect of cure in the same types of localized growths for which radium treatment might be considered because of the accessibility of the tumor.

Undoubtedly, more patients with bronchiogenic carcinomas have been treated by roentgen therapy than by any other procedure. During the past ten years, a diagnosis of primary cancer of the lung has been made in sixty-three cases at the Cleveland Clinic. Of these, we have given roentgen therapy to thirty, most of the others having been too far advanced to justify treatment. Many of the patients were benefited; cough, pain, and hemoptysis were diminished but I cannot state that survival in any proved case was longer as a result of the treatment than the average life expectancy of about one year from the time the diagnosis was made.

The benefits and limitations of roentgen therapy for bronchiogenic carcinoma must be interpreted on the basis of our knowledge about the origin, development, and clinical course of the disease and also according to the physical and biological effects of the radiation.

Pathologists disagree about the classification of cancers of the lung on the basis of histogenesis and morphology. However, their controversies do not concern clinicians. It is certain that all bronchiogenic carcinomas originate in or from epithelial cells of the mucosa lining the bronchial system. Very few of these cancers are of pure unicellular morphology. They are pliomorphic. The degree of differentiation varies considerably in different growths and also in different areas of a single growth whether the predominate cellular structure is the squamous cell type with flattened cuboidal or cylindrical epithelial cells having

different shapes of nuclei and variations in stroma, or has the glandular arrangement of adenocarcinoma.

We know that the embryonic, less differentiated types of cells are the most radiosensitive while those of higher degree of differentiation are comparatively resistant. Epitheliomas, as a class, are well differentiated and therefore most of them are resistant. Since cancers of the lung are epitheliomas, they likewise are radioresistant even though some may be composed of a considerable proportion of comparatively undifferentiated types of neoplastic epithelial cells. Therefore, we cannot expect cancers of the lung or their metastases to be destroyed by any less intensity of irradiation than similar epitheliomatous neoplasms in other locations. It has been found that most squamous cell carcinomas or adenocarcinomas cannot be destroyed completely with an intensity of homogeneous radiation less than the equivalent of from 5,000 to 10,000 roentgens or more. Cancers of the lung which have similar origin, structure and growth characteristics must require as much as this to eliminate them. We cannot administer such great intensities into the chest safely by any technic now in use although we more nearly approach it by prolonged irradiation. We probably do not administer quite as much radiation into cancers of the lung as we estimate. It has been shown that the aerated lung is not nearly as good a scattering medium as solid structures. The secondary radiation may be nearly the same in the consolidated area of the cancer as in other dense tissues, yet that from the surrounding aerated lung is less; consequently, the total dose in the disease area is reduced to some extent and not as great as may be calculated from standard absorption charts.

In addition to the technical difficulties which confront roentgen therapists in destroying primary cancers of the lung, they have the same biological problems to deal with as surgeons. By the time the diagnosis of the disease is made, the mediastinal structures, including the lymph glands, usually are involved or metastases have developed in distant regions in the majority of cases. It has been proved that when carcinomas have metastasized to lymph nodes, the intensity of radiation that may destroy the primary growth completely may not be sufficient to eliminate the disease from lymph glands, although neoplastic cells in them may subsequently lie dormant for some time. Therefore, since cancers of the lung are almost always inherently radioresistant epithelial neoplasms that have usually metastasized to lymph glands before treatment is instituted, and since these metastases are equally resistant or more resistant than the primary growth, we cannot be optimistic about the possibility of curing the disease by methods of administering roentgen therapy that are in use today.

Unfortunately, some clinicians, especially surgeons, are prone to estimate the benefits of therapeutic procedures for malignant diseases only

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from statistical proof that the percentage of survivals for a specified time is increased in comparison with other methods. They often consider as ineffectual or useless those methods, the benefits of which cannot be computed on some arithmetical basis. They may entirely disregard palliative effects or prolongation of economic usefulness of patients that may result from treatment, but which cannot be calculated by mathematics.

Although few cancers of the lung may be curable by roentgen therapy and although there still is no satisfactory statistical proof that lives have been definitely prolonged, we have reason to believe from clinical evidence that most patients treated are relieved of distress and that there are no other therapeutic methods so effectual.

Since bronchiogenic carcinomas are histologically pliomorphic, some of the less differentiated cells may be more radiosensitive than others. Therefore, irradiation may destroy the radiosensitive cells, thus reducing the bulk of the tumor and its rate of growth, but the radioresistant cells will not be affected and will continue to reproduce.

Probably the most important benefit derived from irradiation is brought about by the effect on the inflammatory infiltrations that are present in and around the lesion. Absorption of these inflammatory exudates which takes place following treatment may increase the air volume of the lung to some extent and also relieve cough, dyspnea, and pressure pain and at the same time diminish the density and size of the lesion seen radiographically. But this apparent improvement shown radiographically sometimes may be misleading. No doubt the reduction in size and density of the shadows often is due to the absorption of inflammatory exudates which gives the impression that the growth has been influenced to a greater extent than actually takes place. Cough may be caused by pressure of lymph nodes enlarged by inflammation or metastases and these may be reduced in size by treatment, thereby giving relief. Ulcerations and granulations which bleed may be affected when capillaries are contracted and obstructed so that hemoptysis is diminished or stopped temporarily. Since roentgen therapy probably will reduce the inflammation about a bronchiogenic carcinoma, it may be advisable in some cases to give preoperative treatment, thus facilitating the operative procedure.

It is not advisable to give roentgen therapy to every patient with bronchiogenic carcinoma and not infrequently intensive prolonged treatment is unwise. It is useless to treat patients in advanced stages of disease when a large proportion of the lung already is destroyed or when they have severe dyspnea or are cachectic and anemic. The reaction often increases their discomfort and they do not respond satisfactorily. Others in better general physical condition probably had better be treated by moderate intensity only in the hope of giving symptomatic

relief. Those in good physical condition and in stages of disease too advanced for operations may be given intensive prolonged irradiation. Roentgen therapy sometimes is indicated following operation because there is no way of ascertaining whether all the malignant tissues have been excised and if any remains, roentgen therapy may delay its growth. When intensive prolonged irradiation is to be given, it should be remembered that a considerable blood volume passes through the lung during the exposure time and that white blood cells will be destroyed. In addition, a fairly large proportion of the red marrow of the ribs, sternum, and vertebrae is affected so that the production of erythrocytes may be restricted. I have seen a patient whose leukocytes have been reduced to less than one thousand and erythrocytes reduced to two million by prolonged irradiation of the chest. Counts of the blood cells should be made during the course of prolonged irradiation and treatment stopped or modified when there are indications of serious damage. Supportive measures, often including transfusions, should be employed. The possibility of producing pulmonary fibrosis need not give concern.

#### CONCLUSIONS

1. The results which may be expected from the treatment of bronchiogenic carcinoma depend primarily upon the extent of disease.
2. If the disease is well localized in the lung, operation is indicated.
3. When the disease is too extensive to be completely removable, roentgen therapy is indicated for palliation if the general condition of the patient is such that irradiation therapy can be tolerated.