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Responsible Investigators: Bertram V. A. Low-Beer; Frank W. Allen; Kendrick C. Smith; Anne G. Low-Beer.

University Departments: Radiology & Biochemistry

Financial Support 1954-55: UC $ 8,924.00 UC Cancer Research Coordinating Committee; $ 1,386.00 Christine L. Webster Research Fund.

Title of Project: Determination of Nucleotide Levels in the Blood and Tissue of Animals and in the Blood and Tissue of Patients with Cancer Before and After Therapeutic Radiation with X-rays and Isotopes.

The aim of this study is to determine whether or not, following therapeutic irradiation with X-rays and radio-isotopes, there is a change in nucleotides qualitatively and quantitatively in the irradiated tissues and in blood. It is assumed that the presence or absence of such changes may be prognostically significant as far as the response of tumors to radiation therapy is concerned.

This work was started on a voluntary basis without financial support in 1953. The first three months since July 1, 1954 were spent in establishing the laboratory on the San Francisco Campus. The laboratory facilities are located partly in the Radioactivity Center and partly in Experimental Surgery. Equipment and supplies were procured and an electrophoretic unit was built by Dr. Kendrick C.

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Smith. The electrophoresis apparatus permits us to study a number of enzymes which are known to be concerned in the metabolism of nucleic acids of tissues. Of immediate interest are the deaminases, phosphorylases, specific phosphatases, and specific nucleases, including ribonuclease.

In contrast to heretofore published methods, this technique, which was developed on the Berkeley campus in the Department of Biochemistry, permits the determination and characterization of specific intermediary products as well as end products.

As a start, rat pancreas tissue was selected for the study, since it is readily available and since we have a rat pancreatic tumor available for correlative studies, and particularly since simular pancreatic studies on beef pancreas are being carried out in the laboratory of Dr. Frank W. Allen.

The chromatographic equipment has not been ordered because of the pending decision of the Health Safety Division concerning the type of equipment and location for chromatographic work on the San Francisco Campus. A decision concerning this problem is urgently needed.

Publications To Date: None.

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Responsible Investigators: B. V. A. Low-Beer and H. Glenn Bell

University Departments: Radiology and Surgery

Financial Support 1954-55: W. H. Crocker Trust Donation- $ 1,800.00.

Title of Project: Treatment of Cancer of the Breast by Surgery Combined with External and Internal Irradiation: A New Concept.

The aim of this clinical study is to investigate and determine whether or not the survival rate of patients with breast cancer can be improved by:

a. Combining surgery and radiation therapy in such a way that the radiation treatment is started at the time of surgery, using an internally applied radioactive agent.

b. Using more intensive irradiation in addition to the former treatment to the primary area of tumor spread.

The concept of breast cancer treatment in the past six decades has been the surgical removal of the primary and some of the regional lymph nodes with or without pre- or post-operative irradiation. Experience has shown that the most extensive surgical procedure, even in patients who had their tumor apparently localized to the breast (Stage I), result in a five-year survival rate of only 80%, and a ten-year survival rate of 55 - 60%. It is also known that some patients with Stage I lesions returned even after 15 - 20

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years with metastases, usually distant from the area of primary site. For these and other reasons, we have felt for a number of years that the treatment of breast cancer should be directed to the whole body at the time diagnosis is made, and this treatment should be a combined local surgical and radiological procedure.

Radioactive phosphorus is known to concentrate in most types of breast cancer. (We developed a diagnostic method for differentiation of benign from malignant breast tumors, based on this selective concentration, in 1944). We treated experimentally a small number (8) of patients with Stage II or III breast cancer in the period between 1945 and 1947. Subsequently we observed these patients for recurrences and possible late hematological effects. In 1951, when no untoward hematological effects were found in these patients, and five out of eight were alive, it was decided to resume this type of treatment.

In 1952 it was decided to treat Stage I, II, and III cancer patients by a combination of internal administration of P^{32}, started on the day of surgery, and intensive irradiation of the areas of first lymph node spread (axilla, supraclavicular area, and mediastinum).

So far, 96 patients have been treated by this method. Evaluation concerning survival cannot be made because of the short-time that has passed. The patients are being studied for hematological effects of radiation, and any

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other possible untoward effects of this treatment. Except for temporary depression of hematopoiesis (mainly a drop of the white blood cell count and platelet count which recovers entirely within four to eight weeks following conclusion of treatment without any specific medication), there have been found no untoward effects.

Parallel to these clinical studies, experimental studies are being carried out in animals concerning the effect of P^{32} on tumors.

Publications:

Bell, H. Glenn and Low-Beer, B. V. A. Cancer of the Breast - A Curable Disease (in press).

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