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Critical Review

Preserving the legacy of reirradiation: A narrative review of historical publications

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Abstract

Purpose: The purpose of this study is to illustrate the historical development of reirradiation during several decades of the 20th century, in particular between 1920 and 1960.

Methods and materials: We chose the format of a narrative review because the historical articles are heterogeneous. No systematic extraction of baseline data, treatment details, or follow-up care was possible in many cases.

Results: Both hematological malignancies and solid tumors were treated with a second course of radiation therapy, and indications included local relapse, regional nodal recurrence, and second primary tumors developing in a previously treated region. The literature consists of retrospective single-institution analyses describing treatment approaches that included external beam radiation therapy, brachytherapy, or combinations thereof. Data on toxicities and survival were often provided. Breast cancer and gynecological, head and neck, brain, and skin tumors are among the entities included in this review.

Conclusions: The leading pioneers in the field are fully aware of many of the challenges we continue to debate today. These include the process of late tissue changes and development of personalized treatment approaches and better ways to select patients who are likely to benefit from a second course of radiation therapy.

Conflicts of interest: None.

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Introduction

Recent reviews and book chapters on reirradiation have mostly focused on clinical and experimental data from the past 25 to 30 years.[1-9] This policy carries the risk of disremembering long-term developments and the lessons learned from previous experience. Considering that in the beginning of the 20th century, ionizing radiation was often used to treat benign skin conditions, asthma, and musculoskeletal disorders, which tend to recur, and that treatment was far from standardized, repeat courses of treatment were probably prescribed in the earliest years. Of course, the dosimetric and technical limitations of early equipment and regimens were also applied for the treatment of malignant conditions, a setting necessitating much higher radiation doses than benign diseases[10]; therefore, in-field and marginal relapse were common problems.[11,12] In the absence of effective alternatives, in particular a lack of systemically administered anticancer drugs and safe surgical salvage, reirradiation was sometimes prescribed for common hematological and solid primary tumors. For this overview, the methodology, outcomes, and side effects of reirradiation were extracted from historical publications between 1920 and 1960 to compare them with modern clinical practice. We chose the format of a narrative review because the historical articles were heterogeneous and differed in several aspects from today's rigorously reviewed scientific literature. No systematic extraction of baseline data, treatment details, or follow-up care was possible in many cases.

Methods

Historical articles were identified from PubMed; the electronic archives of the *British Journal of Radiology*, *British Medical Journal*, *Strahlentherapie*, *Journal of the American Medical Association*, and *California Medicine* and its predecessors; and by crosschecking the references from already included articles and textbooks. The key words "reirradiation," "re-irradiation," "repeat radiotherapy," "second radiotherapy," "radiation retreatment," and "recurrent AND radiation therapy" were entered. English and German language articles were included. Any information a study provided about dose is described in the Results section. Unfortunately, several of the included studies provided no information about median dose or exposure. Some included a detailed description only of exemplary cases that the authors found particularly instructive.

Results

Although the focus of this review was on solid tumors, Desjardins reported a case of reirradiation of mediastinal Hodgkin disease in the 1920s.[13] In the treatment of chronic myelogenous leukemia, irradiation increased the duration of "efficient life" (a rigorous definition of this endpoint was not provided) by 30% (0.8 years), based on 82 cases reported in 1931.[14] Most often, the spleen was treated, and sometimes the spleen plus long bones. Survival outcomes were comparable regardless of treated volumes. Repeated cycles of low doses of radiation produced remarkable symptomatic improvement. The effect lasted from a few months to a year.

In 1926, Lee and Tannenbaum reported their experience with more than 300 patients managed for recurrent inoperable breast cancer at Memorial Hospital, New York.[15] The term inoperable referred to vastly different scenarios, including but not limited to technically inoperable lymph node metastases and widespread distant metastases. Roentgen rays, radium, or a combination of both was used. Individualized or personalized oncology is not a new idea, as reflected in the sentence "each patient is a special problem to be handled in a special way."[15] Lee and Tannenbaum also cited references from different countries, all of which demonstrated that reirradiation could be prescribed (eg, after failure of what was called prophylactic irradiation [postoperative adjuvant radiation therapy]). There was controversy in the literature regarding the usefulness of this approach, because some authors regarded recurrent tumors as not sufficiently radiosensitive to warrant further treatment.[16] Lee and Tannenbaum did not provide separate results for reirradiated patients. According to their general conclusion, radiation therapy for recurrent breast cancer prolonged the life of their patients and may have controlled the disease for a considerable number of years. Irradiation was used during later decades as well,[17] but, unfortunately, detailed outcome data were not reported.

For cervical cancer, radiation therapy had become an accepted treatment well before the Second World War. In describing their approach at the Los Angeles Tumor Institute, California, from 1930, Soiland and Costolow mentioned that "the duration of the first application is twenty-eight hours and the second application twenty-four hours, the radium being applied against the cervix and intrauterine at the same time."[18] "Following this, no further radium should be given for from six to twelve months. The patient is observed at monthly intervals, and late recurrences, appearing a year or so after the original treatment, are often treated with small doses of radium applied locally, although great care is exercised. Often, suspicious thickened areas remain for several months and finally disappear." This policy emphasizes a crucial point in decision making, namely to confirm the presence of active tumor before prescribing further treatment.

According to Healy, of 1574 patients with cervical cancer treated between 1918 and 1931 at Memorial Hospital, New York, only 11% required further radiation therapy.[19] Only 2 of these patients survived more than 3