

## HISTORY OF ONCOLOGY

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### The history of x-ray therapy

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#### Summary

*The aim of this article is to present briefly the accidental genesis of x-ray therapy that during its first application provoked great expectations and euphoria, soon followed by difficulties and disappointments due to the abuse of ra-*

*diation and to the inexperience of the first radiotherapists. Nowadays, the use of radiotherapy is restricted to certain types of cancer with excellent treatment results and with less adverse effects.*

**Key words:** cancer, radiotherapy, x-ray martyrs

At the beginning the first radiologists had, after repeated exposures to Roentgen radiation, the unpleasant surprise to notice personally the appearance of painful cutaneous necrotic lesions (radiodermatitis). Indeed, Leopold Freund [1] and Edouard Schiff [2] of Vienna were the first to describe in 1896 the depilatory effect produced by Roentgen rays, which they used to treat dermatitides. In 1898, Paul Oudin, Toussaint Barthélemy and Jean Darier reported on cutaneous and visceral accidents following the use of x-rays [3].

From 1897, several doctors had the idea to provoke this reaction in order to treat the ringworm infection, lupus and cancer. Radiotherapy that does not present any common point with the traditional art of healing (serums, vaccines, surgery, medicines), gives rise to great hopes. Conversely to surgery, these invisible and painless rays do not frighten. Patients that refuse surgical intervention for a breast or uterine cancer submit to radiotherapy in good grace. And the tumors “are melting” as if by magic.

In Germany, Hermann Gocht obtained a few improvements in inoperable breast cancers [4]. Then in 1900, Thor Stenbeck and Tage-Anton-Ultime Sjögren of Sweden published an account on the cure of skin cancers [5]. In 1901, Carl Beck [6] of the United States, reported the disappearance of a melanoma, and Francis Williams of Boston described two cases of the lip that were cured by roentgen therapy.

In 1900, Wallace Johnson and Walter Merrill [7] wrote the first article in English detailing the favor-

able results of radiation therapy for cancer of the skin. However, the earliest therapeutic use of radiation was to treat benign rather than malignant conditions.

According to the Brechers [8], there were 3 major pathways to the development of radiation for therapeutic purposes. The first was “simple, empirical curiosity. Let’s try it out and see what happens”. A number of investigators decided to experiment with these new rays to see whether they might have some positive effect on patients with inoperable tumors. Indeed, as early as 7 months after Roentgen’s discovery of x-rays, a report in the *Medical Record* described the work of V. Despeignes of Lyons [9], who had described “a case of gastric carcinoma which had appeared to be greatly benefited by the transmission of the rays through the seat of disease”. Improvement was transient and the patient died afterwards.

A second pathway toward the development of radiation therapy was the report by John Daniel in April 1896 [10] that an excessive dose of x-rays caused human hair to fall out. Before the end of the year, several investigators in Europe and the United States were actively using x-rays for the treatment of hypertrichosis, especially on the faces of women. By serendipity, this work led to the discovery of other uses. An eminent Chicago dermatologist, William Allen Pusey [11], noted that a woman he was treating for excess hair had “on the chin and around the mouth... an acne simplex of moderate severity”. To his surprise, after the use of x-rays the acne disappeared and did not recur. Similar accidental discov-

eries probably occurred in Europe, where reports before 1900 included the successful use of x-rays to treat tinea capitis (ringworm of the scalp), favus (a parasitic skin infection), sycosis (inflammation of the hair follicles), and chronic eczema.

The third pathway toward the discovery of the therapeutic usefulness of x-rays was the successful treatment of several skin conditions using ultraviolet light therapy reported by Niels Finsen of Copenhagen in 1900. To obtain a good result with the Finsen lamp, it was necessary to produce a “reaction which might vary in degree from an erythema to a vesicular or bullous dermatitis” [12]. Because x-rays produced a reddening of the skin much like sunburn and were considered by some at that time to be merely a variation of ultraviolet light, it probably occurred to many clinicians that x-rays might have similar therapeutic effects.

In 1899 Philip Mills Jones of San Francisco reported a case of a 55-year-old patient who had in his right forehead 3 ulcerating lesions and one large, hard nodule which had not yet broken down. He had undergone a variety of treatments, including cautery, curetting, creosote, silver nitrate, and hydrogen dioxide. Jones selected a “soft” tube and began x-ray exposures of the patient’s right forehead. A sheet of lead was arranged so as to protect the whole of the head; a hole cut in the lead sheet allowed the x-rays to reach all the diseased areas, with the exception of one of the ulcerating lesions. This one small lesion was protected as a sort of control upon the treatment... At the end of 4 weeks, the whole area, with the exception of the one ulcer protected, was healed and the nodule had disappeared” [2].

The protected ulceration had meanwhile increased in size. “I then exposed the ulcerated area that had been previously protected by the lead plate. In 3 weeks this quite healed”.

The discovery that x-rays were effective against skin cancer soon followed reports that they were valuable in treating tuberculosis of the skin. Credit for initiating x-ray treatment of skin cancer is often given to two Swedes, Thor Stenbeck and Tage Sjögren, each of whom independently demonstrated a case of epithelioma treated with x-rays at a meeting of the Swedish Medical Society in December 1899. Johnson and Merrill reported a series of favourable results in 5 patients. These findings were confirmed by the noted Boston radiologist, Francis H. Williams [13], who presented his therapeutic work in his classic 1901 textbook. Soon after there were many detailed and convincing reports of successful x-ray treatments, generally illustrated by astonishing “before-and-after” photographs.

Perhaps the first report of a deep-lying internal

cancer cured by x-rays was the celebrated case of Clarence E. Skinner. The patient was suffering from a rapidly growing malignant fibrosarcoma of the abdomen. Her case was considered entirely hopeless. After almost 80 x-ray treatments, the tumor had shrunk in volume by about 20%, making it necessary for her “to shorten her waistbands and the fronts of her skirts to keep them from dragging on the ground”. A year and a half later, after a total of 136 applications of the x-ray, Skinner could proudly report to the referring physician that his “entirely hopeless” patient was feeling well and again teaching in school. Ironically, 5 years later she subsequently developed a radiation-induced cancer of the skin [14].

The word “rays”, that is not yet full with its tragic connotation, becomes a synonymous of miracle and, in 1903, Debaut Manoir writes in *La Gazette Médicale de Paris*: “But today we talk about treating breast cancer subcutaneously, by x-rays, without provoking skin lesions... these rays may act in a given point. We can localize their action in a square centimeter, for example the head of pancreas: through the skin of the abdomen and intestines ... This invention will give a good blow to cancer surgery. All surgeons are interested to be equipped, in order to treat by x-rays instead of surgical knife” [15].

Enthusiastic reports initially appeared extolling the virtues of radiation therapy for a whole host of benign and malignant conditions. In 1904, Pusey’s treatise [11] reported the author’s own experience with x-ray therapy in 52 different diseases. Two years previously, Heber Robarts (1902) had estimated that “there are about 100 named diseases that yield favourably to x-ray treatment”.

One reason for the excessive enthusiasm of many early reports may have been the favourable psychological effect of the x-ray treatment on patients.

X-rays were reported to have impressive success in suppressing pain. As Seabury W. Allen noted “Not infrequently patients whom I have subjected to x-rays for one cause or another have spoken of the relief of the pain or discomfort which previously existed in the part exposed”.

A strange early use of radiation therapy was the relief of blindness. It was suggested that exposure to x-rays might have a beneficial effect on certain types of blindness, especially those from cataracts. Edison [16] reported “favourable” results. Francis de Astudillo [17], reported improvement in 11 cases of blindness after treatment with x-rays. However, careful analysis of these and subsequent optimistic articles clearly indicated the futility of radiation therapy to alleviate blindness, and such treatment was soon abandoned.

## From the miracle to nightmare

The time for disillusion came. After a short remission period, the relapses were numerous, making new sessions necessary. In some cases the tumors seemed to have received a true “whipping”. Finally, it was necessary to admit that radiotherapy could be useful only as a surgical adjuvant, to delay or to restrain the relapses. Apparent cures, remissions for some weeks, even some days, are sources of disillusion all the more cruel since the new sessions sanction the evil renaissance. Several observations finish by the mention “the patient did not return”. Elsewhere they admit the failure: “We continue the sessions, but without a hope to treat” [18]; “We maintain them to inspire the patient’s confidence”; “We may restart the treatment, but only for moral purpose” [19].

These discouraging experiences should not be surprising, for in the absence of specialized training programs, virtually all the early practitioners in x-ray therapy were dermatologists and surgeons who had no understanding of the physical nature or biological effects of the new and mysterious agents with which they worked.

In daily practice, the radiologists and radiotherapists work in the dark. There are no reliable methods for measuring the amount of x-ray therapy given or even a generally agreed unit of dose. Radiographic devices do not exist. A simple Crookes vial, a fluorescent screen and some sensitive plates constitute their unique equipment. When the office is out of electric current, it is necessary to load the dynamo to crank. Often, the radiographic vial is also used for radiotherapy. The practitioners use it up to the limit, so it is not rare that it shatters to the patient’s nose. After that, they could obtain surprisingly different results depending if the patient was under a new vial or to a vial in the agony. By the time, tubes that run satisfactory could provoke the sudden appearance of radiodermatitis (Photo 1) or hair loss. As a vial expires, a new one, more powerful and of another workmanship provokes severe burns.

The early radiotherapists initially adopted treatment techniques involving massive exposures, aimed at the eradication of tumors in a single treatment, comparable with the extirpation of tumors by surgery. Therefore, it was to be expected that the primary morbidity, and even the acute mortality, of such massive-dose treatment was often comparable with major surgery at that time. Patients who survived the immediate post-irradiation period often experienced impressive partial or complete regression of their tumors, but these initial responses were all too often followed by major complications, as well as a high rate of tumor recurrence [20].



**Photo 1.** X-ray dermatitis (1897).

The exposure time varies. Patients are submitted to 150 or 200 hours of radiation, 5 or 6 hours per session, depending on the technician. Some of them place the tube very close to the treating surface or to x-ray, others move it excessively away.

A patient is submitted, in a 15 days interval, to 3 x-rays sessions, each lasting an hour or more, under uncomfortable conditions, lying on the wooden floor of the medical office and prop up on books. “Irritation, redness, vesicles, skin loss and bedsores” appear soon at the hip level. She registers a complaint. The Civil Court of Paris condemns the radiologist to pay to his patient 5000 French francs for injuries [21].

Another patient, suffering from facial neuralgia, is presented to a radiotherapist that he promised to heal him after 10 sessions of x-rays, payable in advance. The treatment provokes hair loss and an attack of conjunctivitis without relief the headaches. The practitioner is condemned to pay 3000 French francs for injuries [22].

On the other hand, the case of a patient who claimed the sum of 40000 French francs to his radiologist, maintaining that a x-ray treatment performed 2 years ago at her foot caused gastric disease and pulmonary congestion, simply did not suite to her pretensions. She was ordered to pay costs [23].

The empiricism is the rule and radiology, as radiotherapy, will be approximate techniques until the widespread use, after 1905, of the first measurement devices (spintrometer, radiochronometer) [24].

In 1906, A.R. Robinson [25] stated that roentgen-ray devices had been too widely used, even to the extent that they warranted the designation of “race suicide machines”. Attempts were even made to introduce legislation that would outlaw the use of roentgen rays. Nevertheless, the advantages of radiation therapy were recognized, and it was clear that some tumors



responded unexpectedly well, while others became operable despite initial inoperability.

The general consensus was well stated by W.B. Coley [26], who concluded that “the amount of success that has been obtained, while less than we had hoped, is sufficient to make it strongly advisable to continue the work in selected cases”.

Radiologists and radiotherapists at the experimentation era pay an even heavier tribute. The first operators are rapidly victims of more or less severe burns, ulcerations, skin atrophies. Several complain about headaches and hair loss. Their nails start to fall. Those that push back are hard and easily broken.

In 1905, Tilden Brown presents to the Academy of Medicine of New York a report relating the x-ray effects with the sexual functions. He noticed an absolute azoospermia among 10 persons that, during the 3 last years, worked to radiographic or radiotherapeutic jobs. Even if the phenomenon does not induce a decrease of virility, even if sterility ends up by disappearing after some months when all exposure to radiation ceases, the report is not less alarming [27].

There are more serious facts. On old radiodermatitis may appear rapidly progressive cancer necessitating often limb amputation (Photo 2). It is from America that come the most distressing news. Porter and White [28] publish 12 cases of non equivocal cancers provoked by a lethal dose of radiation; the number increases to 38, two years later. Thus, as Jayle underlines: “It is horrible to think that those that handle the x-rays can stop and even heal certain developed epitheliomas on others but they are not able to stop on themselves the evolution of the same disease and die of this cancer that they fight and they would never have had it if they did not work in radiotherapy” (Photo 3).

More exposed than doctors, the first manufacturers of cathodic tubes, that used to test the vials on their own hand, are affected in frightful proportions and, in the best cases, they had to be amputated before the metastases start their deadly work. It is necessary to wait till 1920 until the widespread use of protection techniques decreases the number of accidents.

But at that period and even a long time later, numerous were the pioneers of x-radiation, conscious

or unconscious victims, known or ignored, that died, victims of its distant consequences.

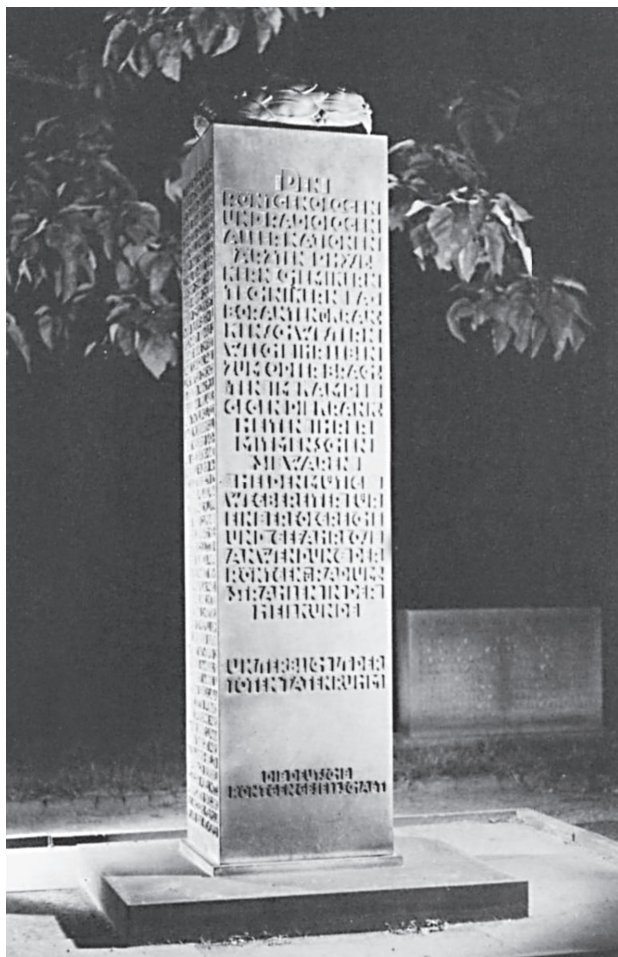
### The role of Emil Grubbé on the early days of x-ray therapy

A discussion of the early days of radiation therapy would be incomplete without mentioning Emil Grubbé (Photo 4) [29]. After several months of testing the vacuum of his tube by placing his left hand between the tube and fluorescent substance, Grubbé developed a severe dermatitis on the back of his left hand and allegedly, as he wrote, “I happened to be the first person detrimentally affected by these new rays”.

Grubbé reported that he was soon sent two patients, one with carcinoma of the breast and the other with lupus vulgaris, to treat with x-rays (Photo 5). “For the first time in history, x-rays had been used for treatment, not diagnostic purposes”. Neither patient seems to have responded favourably. Grubbé frankly admitted



**Photo 2.** Carcinoma developing after an x-ray burn (1904).



**Photo 3.** Monument to x-ray and radium martyrs in Hamburg, Germany.

that “No dramatic results were obtained. Neither case was reported clinically by the physicians who sent them to me because both patients died within a month after commencing x-ray treatment, and before sufficient cumulative effects had been obtained in either case to warrant any conclusions as to the value of the new therapeutic agent. . . . This, briefly, is the story of the origin and birth of the treatment of diseases with x-rays”.

Grubbé again stressed his role in the conclusion of his autobiography: “I have lived long enough to see the child that I fathered develop into a sturdy, mature, and worthwhile product; and I hope, as I approach the evening of my day, to see even more uses for x-ray therapy in the alleviation of the ills of mankind”.

In the absence of any record in a scientific publi-

cation, was Grubbé’s story true? Undoubtedly, Grubbé had worked with x-rays and he underwent multiple surgical procedures for radiation-induced injury. But did he really play a major role in the development of radiation therapy? [30].

This curious story took an ironic final twist. A prominent radiologist, Paul C. Hodges (Photo 6) [31], was commissioned to write a definitive biography of Emil Grubbé. After research, Hodges unequivocally established that Grubbé was a publicity seeker who was “vain, boastful, incompletely truthful” and an unreliable witness concerning his own accomplishments. Not only was there no contemporary support for Grubbé story, but all the circumstantial evidence appeared to argue against acceptance of his claims. As the Brechers [32] concluded “Grubbé’s story is so implausible, so lacking in contemporary corroboration, and in such irreconcilable conflict with readily provable facts, and Grubbé’s untruthfulness in other respects is so readily demonstrable, as to warrant the inclusion of his claims in this postscript rather than in the body of a history of American radiology”.

## Epilogue

Today, the use of radiotherapy for treating benign diseases is considered quackery and is rigorously avoided. It is worth remembering, however, that years ago, before the introduction of antibiotics, chemotherapeutic



**Photo 4.** Emil Grubbé (1875-1960).



**Photo 5.** X-ray treatment of lupus of the face (1898). Left, before and right, after 17 treatments of 15 min each over 2 months.



**Photo 6.** Paul Hodges.

agents, and steroids, there were a host of chronic inflammatory and non-specific lesions that were unsightly disabling, and even dangerous to life that could be relieved by small, safe, almost homeopathic doses of radiation.

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