The beginning of using X-rays and the evolution of equipment for the treatment of ocular cancer

Konstantinos Laios MD PhD[1], Maria Zozolou Md[2], George Generalis MD, PhD[2], Maria Lymperi PhD[3], Chryssanthy Koutsandrea MD, PhD[1], Marilita M. Moschos MD, PhD[1,4]

1. 1st Ophthalmological Department, Medical School, National and Kapodistrian University of Athens
2. Medical School, National and Kapodistrian University of Athens
3. 1st Propaedeutic Department of Surgery, Medical School,National and Kapodistrian Uiversity of Athens, Hippocration Hospital, Athens, Greece
4. Biomedical Research Foundation, Academy of Athens

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Corresponding author:
Konstantinos Laios MD, PhD
Athinodorou 1, Kato Petralona, 118 53, Athens, Attiki, Greece.
Tel.: 00306947091434, Fax: 00302103474338.
konstlaios@gmail.com

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Abstract
Until the early 20th century enucleation of the eyeball or its partial excision were the basic treatments for ocular cancer. The discovery of X-rays by Wilhelm Conrad Röntgen (1845-1923) offered new possibilities to the treatment of ocular cancer either as mono or as adjuvant therapy. Nowdays this treatment is more sophisticated.

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Introduction

Ancient Greek physicians as Demosthenes Philalethes (1st century AD) and Rufus of Ephesus (between 1st and 2nd century AD) were the first to describe ocular cancer. They believed that this disease derived from the plethora of black bile in the eye and it was described as a tumor on the eyeball or of the nearby anatomical structures with or without ulcers. Ulcers in the ocular region when difficult to be treated were also considered as malignant [1]. This ancient Greek concept remained valid till the 19th century, when histopathology grew and described many types of ocular cancer such as carcinoma, epithelioma, melanoma, sarcoma and retinoblastoma later called glioma [2]. At the beginning of the 20th century enucleation or partial excision of the eyeball in the early stages were the basic treatments for ocular cancer [3]. In 1895, W. C. Röntgen (1845-1923) discovered X-rays [4] and only a year later, in 1896 V. Despeignes (1866-1937) [5] used X-rays for the first time as an adjuvant treatment in a patient who also had gastric cancer, with initially spectacular results, even if after a few months this patient died [6].

The first application of X-rays in ocular cancer

H. L. Hilgartner (1868-1937) an ophthalmologist from Austin, Texas (Figure1), was the first who applied X-rays against ocular retinoblastoma or glioma in 1903. A little girl of three and a half years old was diagnosed with double ocular gliomas. Her parents in order to avoid double enucleation, which was suggested by other ophthalmologists, visited Dr. H. L Hilgartner's office, who suggested to apply X-rays in both girl's gliomas. This girl suffered a great pain and became blind because cancer had reached the pupil filling the vitreous. She was also cachectic and its life was in great danger [7]. Dr. H. L. Hilgartner used perforated lead plates in order to protect the head and the face of the patient from the radiation. Treatment with X-rays was scheduled in sessions of 15 minutes duration for 24 days without intervals. An interval for two weeks followed and X-rays treatment as above was repeated for a period of three weeks with equal intervals. The whole treatment lasted eight months. After the second session the pain subsided and after eight months the girl had gained weight, her left eye was free from malignancy and the right one was shrunken by two thirds of its normal size because of inflammation due to X-rays [7]. The final results of this treatment were never published. After this first publication ophthalmologists in USA and Europe suggested and used X-rays treatment not only for ocular glioma [8] but also for other types of ocular cancer [9].

Figure 1. Henry Louis Hilgartner (1868-1937). The first who applied X-rays against ocular cancer in 1903.

Further applications with better equipment

On early 20th century it was obvious that X-rays were particularly effective against ocular glioma (retinoblastoma), epitheliomas and other malignant diseases such as Rodent or Jacobs ulcers [10]. At that time it was considered that X-rays in ocular diseases could destroy only the surface and depth of cancers but also the surrounding tissues [10].

X-rays were considered either as an adjuvant treatment for ocular cancer [11] or as a complete treatment especially in malignant ulcers and eyelid cancer. For complete treatment, three or four sessions of treatment per week were applied while the radiation source was positioned 30-50cm from the patient. Physicians were well aware that this treatment could present serious side effects, since apart from the loss of eyebrows and eyelids there was a risk of conjunctival burns and inflammation on the cornea and iris [10].

Regarding the X-rays equipment (Figure 2) for radiotherapy that were used at the early 20th century for the treatment of ocular cancer, the first generation of the equipment used a cold cathode or Crookes X-ray tubes. Crookes tubes generated the electrons needed to produce X-rays by ionization of the residual air in the tube, instead of a heated filament, so they were partially evacuated. They used a glass bulb with around 10^{-6} to $5X10^{-8}$ atmospheric pressure of air (0.1 to 0.005 Pa). An aluminum cathode plate at one end of the tube created a beam of electrons, which struck a platinum anode target at the center generating the X-rays. The anode surface was angled so that the X-rays would radiate through the side of the tube. The cathode was concave so that the electrons were focused on a small (~1 mm) spot on the anode, approximating a point source of X-rays [12].

An improvement of this tube was introduced by W. Coolidge (1873-1975) in 1913 who introduced the "Coolidge tube", also called "hot cathode tube". In this tube the electrons were produced by the thermionic effect from a tungsten filament heated by an electric current. The filament was the cathode of the tube. The high voltage potential was between the cathode and the anode, the electrons were thus accelerated, and then directed to hit the anode. There were two specific designs of this tube: the so called end-window tubes and the side-window tubes. End window tubes usually had a transmission target thin enough to allow X-rays and electrons to pass through following the same directions. A common type of the end-window tube has the filament around the anode and the electrons have a curved path [13].

What is special about side-window tubes was electrostatic lens used to focus the beam onto a very small spot on the anode which was precisely angled to allow the escape of some of the X-ray photons which are emitted perpendicular to the direction of the electron current. The anode was usually made out of tungsten or molybdenum. The tube had a window designed for escape of the generated X-ray photons through a window [13].

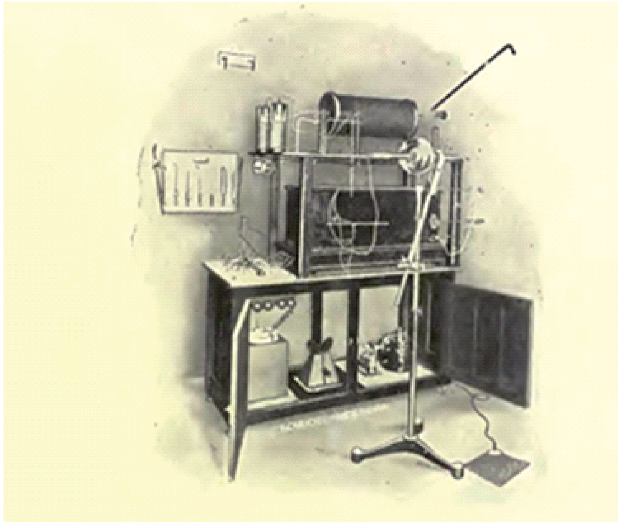

Figure 2. X-rays equipment used for the treatment of ocular cancer at early 20th century.

The control panel of the X-rays emitting equipment used for the treatment of ocular cancer had devices to estimate the kilovoltage, to adjust the voltage to the primary coil and to measure the current of the equipment [12].

In the following years, X-rays therapy was focused on the dosimetry of the irradiation, which was now higher in cases of ocular melanoma.

From the second half of 20th century new types of irradiation sources and equipment were introduced, such as radioactive plaques, betatron and linear accelerator [14]. More effective treatments against ocular cancer are used today, like stereotactic radiosurgery and conformal proton beam radiation therapy, in which proton beams deliver more energy specifically on cancer cell less harming surrounding tissues [15].

In conclusion: Treatment by X-rays soon overshadowed that of radium salts [16] because it was cheaper, easier, friendlier to the environment and more effective for the treatment of ocular cancer. This new treatment began at early 20th century. From the second half of 20th century new types of irradiation sources and equipment were introduced, such as radioactive plaques, betatron and linear accelerators. Furthermore, stereotactic radiosurgery and conformal proton beam radiation are now applied [17].

The authors declare that they have no conflicts of interest

Bibliography

1. Karaberopoulos D. (Registr. - Reapp.). *Aristotle Kouzis, Cancer in ancient greek doctors* 1902. Athens, Ed. Stamouli, 2004.
2. Ginsberg S. *Grundriss der pathologischen Histologie des Auges*. Berlin, Karger, 1903.
3. Wood CA. A *System of Ophthalmic Operations*. Vol. I-II. Chicago, IL, Cleveland Press, 1911.
4. Glasser O. *Wilhelm Conrad Röntgen und die Geschichte der Röntgenstrahlen*. Berlin, Springer, 1959.
5. Despeignes V. Observation concemant un cas de cancer de l'estomac traite par les rayons Roentgen. Lyon Medical 26 juillet 1896, 428-30.
6. Sgantzos M, Tsoucalas G, Laios K et al. The physician who first applied radiotherapy, Victor Despeignes, on 1896. *Hell J Nucl Med* 2014 Jan-Apr; 17(1), 45-6.
7. Hilgartner 1903: Hilgartner HL. 'Report of case of double glioma treated with x-ray'. T*ex Med J* 1903; 18: 322-3.
8. Balmer A, Munier F, Zografos L. '100e Anniversaire du premier traitement d'un rétinoblastome par irradiation (Hilgartner, 1903)'. J *Fr Ophtalmol* 2003 Dec;26(10): 1089-96.
9. Zografos L. Radiothérapie: Introduction et survol historique, in Zografos L. (Ed). *Tumeurs intraoculaires*. Paris: Societe francaise d'ophtalmologie et Maison, 2002: 27-41.
10. Wood CA. *A system of ophthalmic therapeutics; being a complete work on the non-operative treatment, including the prophylaxis, of diseases of the eye*. Chicago, IL, Cleveland Press, 1909.
11. Mayou MS. *The uses of x rays in ophthalmic surgery*. London, Rebman, Limited, 1903.
12. Eisenberg RL. *Radiology: an illustrated history*. St. Louis, MO, Mosby Year Book, 1992.
13. Wolff MF. 'William D. Coolidge: Shirt-sleeves manager: Famous for two wide-ranging inventions, this engineer proved himself an innovative manager as he guided the renowned GE Research Laboratory through some of its most turbulent years'. *IEEE Spectrum* 1984; 21 (5): 81-5.
14. Sagerman RH, Alberti W, Abramason DH. *Radiotherapy of intraocular and orbital tumors*. Berlin, New York, Springer, 2003.
15. Damato B. *Ocular tumours: diagnosis and treatment*. Boston, Butterworth-Heinemann, 2000.
16. Beclere A. *Radiologie et radiumtheapie*. Paris, Maloine, 1921.
17. Grossinklaus HE. *Pocket guide to ocular oncology and pathology*. New York, Springer, 2013.