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An Important Document for the History of Turkish Radiation Oncology: "The Principles of Radium Treatment"*

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Abstract

The aim of this study was to evaluate the information in the book about the usage of radium for treatment purposes in the light of current scientific knowledge by abbreviating and translating it into modern-day Turkish. With this study, Turkish Medical History will acquire a new source document. First, the book that was the subject of this work, was reviewed by the researchers. After the first evaluation, it was re-read by an academician, who is an expert in Turkish Language and Literature, and it was abbreviated in order to make it more articulate. Finally, after this process, the obtained information was interpreted in the light of current scientific knowledge. The book, which was written by a Turkish physician, covers utilization areas of radium, mechanism of effect and comparison with x-ray treatment. Written in the Young Turkish Republic about "modern medicine" practices, the book is considerably detailed and shows parallels with other practices of that period in the world. In addition to the brief theoretical information about the atom and radium, the application methods of radium treatment are covered by the book. Summarized information about the benefits and the risks of the treatment and warnings related to the practice can also be found in the book. The common feature of the medical books about x-ray and radium written almost a century ago is that they cover the theoretical information or the story of the discovery of x-ray and radium. On the other hand, "Radyumla Tedavi Esasları (The Principles of Radium Treatment)" was a unique pioneering work of its time covering the utilization methods of radium and x-ray, the advantages and disadvantages of these methods and the comparison of the two methods. It also discusses the administration methods of x-ray and radium, the pros and cons of these methods and the comparison of the two methods made it exclusive.

Keywords: Radium, Radium treatment, X-ray, Resit Sureyya, Medicine, Medicine History.

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Türk Radyasyon Onkolojisi Tarihi Adına Önemli Bir Belge: "Radyumla Tedavi Esasları"

Öz

Bu çalışmayla, Radyumla tedavi esasları adlı eserde yer alan radyumun tedavi amaçlı kullanımına ilişkin verilen bilgilerin günümüz Türkçesine çevrilip sadeleştirilerek güncel bilimsel bilgiler ışığında değerlendirilmesi amaçlanmıştır. Ayrıca bu çalışma ile Türk Tıp Tarihi yeni bir kaynak belge daha kazanmış olacaktır. Araştırmaya konu olan eser, öncelikle araştırmacılar tarafından gözden geçirilmiştir, yapılan ilk değerlendirmeden sonra Türk Dili ve Edebiyatı alanında uzman olan bir akademisyen ile tekrar okunarak kolay anlaşılmasını sağlamak için sadeleştirme işlemi yapılmıştır. Bu işlemin ardından elde edilen veriler güncel bilimsel bilgiler ışığında yorumlanmıştır. Bir Türk hekimi tarafından yazılan bu kitapta; radyumun kullanım alanları, etki mekanizması ve x ray tedavisi ile karşılaştırması yapılmaktadır. Genç Türkiye Cumhuriyetinde "modern tıp" uygulamaları hakkında yazılmış bu kitap oldukça ayrıntılıdır ve zamanındaki dünyadaki diğer uygulamalara paralellik göstermektedir. Kitapta atom ve radyum hakkında kısa teorik bilgilerin yanı sıra daha çok radyum tedavisinin uygulama yöntemlerinden söz edilmektedir. Ayrıca tedavinin yarar ve riskleri ile pratige yönelik olarak dikkat çekici uyarıları da içeren maddeler halinde verilmiş özet bilgiler yer almaktadır. Yaklaşık bir asır önce kaleme alınan röntgen ve radyum hakkında yazılan tıp kitaplarının ortak özelliği kuramsal bilgiden veya röntgen ve radyumun keşfinin hikâyesinden söz etmeleridir. Bu çalışmaya konu olan "Radyumla tedavi esasları" adlı kitap ise; radyum ve röntgenin uygulama yöntemleri, bu yöntemlerin olumlu/olumsuz yanları ve iki yöntemin birbirleri ile karşılaştırılması adına döneminde öncülük yapmış ayrıcalıklı bir eserdir.

Anahtar Kelimeler: Radyum, Radyumla tedavi, Röntgen, Reşit Süreyya, Tıp, Tıp Tarihi.

Introduction

The discovery of x-rays and radium led to the usage of these two methods for disease treatment and even pioneered the two main methods of radiotherapy. One of those two main methods is radiotherapy in which long-source-surface-distance is used. Later this was named external-beam radiotherapy. The other method is brachytherapy, which is based on short-source-surface-distance. Within those practices, radium was most commonly used, and between the years of 1900 – 1940, the usage of kilo voltage treatment (50 kV X-rays) was considered (Lederman, 1981; Kuter, 2002). In the later period between 1946-1996, studies

about megavoltage practices gained speed and tendencies towards radium applications rather than x-ray applications increased. After the invention of the computerized X-ray by Hounsfield in 1971, computed tomography was integrated into clinical applications and significant developments occurred in planning and simulating the radiation therapy, specifically around the 1980s (Lederman, 1981).

In the early 1900s, in addition to the x-rays used in diagnosis and treatment, radiumstarted to be used in treatment practices, such as the treatment of resistant organisms such as tuberculosis, cervix or rectum cancer or when a localized effect was desired (Simon, 1960).

During those years it was believed that low doses of radiation were harmless and the effects of high doses were temporary. Thus, radiation was often used to treat various kinds of diseases as a miracle method. The enthusiasm for radiation came to such a state that radium was mixed within drinking water, toothpaste, and facial creams, which was justified by its anti-bacterial effect (Picture 1). However, when studies showed the long-term effects of radium usage for treatment, opinions about radium changed. For example, in rectum treatments, which were the first utilization area of radiotherapy trials, radium covered plastic tubes and radium injections were used by placing them into the rectum for years and it was believed that this method was therapeutic. However, in 1930 it was claimed that this treatment did not prevent rectum cancer from spreading, but on the contrary, caused abscess, fistula, sepsis, and secondary malignancies and it was shown not to be a harmless practice (Geçim, 2010). The wide and uncontrolled usage of radium in medicine came to an end when it was realized that new cancers developed and side-effects were hard to overcome (Schmitz, 1924; Rowland, 1994).

Radium started to be used in the Ottoman Empire at the same time as in other countries and the concerns of radium and its advantages/disadvantages were the same (Ulman et al, 2005) During this period, the hazardous effects of x-rays and radium were not fully understood and protective measures were not adequately developed. Even the physicians performing these practices could not protect themselves from the hazardous effects. One physician was reported to have lost three fingers on his left hand (Başekim, 2015). In 1937 and 1939, the government introduced regulations to protect the health of patients and physicians and to standardize the practices (Radiyoloji, Radiyom ve Elektrikle Tedavi ve Diğer Fizyoterapi Müesseseleri Hakkında Kanun, 1937; Radyoloji, Radyum ve Elektrikle Tedavi Müesseleri Hakkında Nizamname, 1939).

During those years, when x-rays and radium were used commonly, the existence of written or translated books about x-rays and radium shows the importance given to this subject (Sülayman, 1905; Şemseddin, 1912; Lenk, 1924; Labord, 1927; Yusuf, 1927; Süreyya, 1927;

İsmail and Temel, 1928; Kazancıgil, 2005). The common feature of the medical books about x-ray and radium written almost a century ago (Table 1) is that they discuss the theoretical information or the discovery of x-ray or radium. However, *"Radyumla tedavi esasları"* reported the administration methods of x-ray and radium, the pros and cons of these methods and the comparison of the two methods, which makes it exclusive.

In the light of all these justifications, it is highly important that the book "*Radyumla tedavi* esasları", which was written in the first years of the Republic and prepared the base for the current field of Radiation Oncology, is discussed with regards to medical history. The aim of this study was to evaluate the information in the book about the usage of radium for treatment purposes in the light of current scientific knowledge by abbreviating and translating it into modern-day Turkish. Therefore, through this study, Turkish Medical History will acquire a new source document.

Method

The method which was used in this study is content analysis. Firstly, the book was reviewed and translated into modern Turkish by the researchers. After the first evaluation, it was read by an academician, who is an expert in Turkish Language and Literature, and it was abbreviated to make it more comprehensible. In the light of acquired knowledge, examples from the preface, content and pictures in the book were shared with the audience as a part of the article. Finally, this information was compared to the current literature and interpreted by two researchers, who are Radiology and Medical Oncology specialists.

Findings

The book "Radyumla Tedavi Esasları", which was written by Reşit Süreyya (1889-1962) in 1927, is a valuable document for the early history of radiation oncology in Turkey. The book was published by Kader Printing House, one of the most famous printing houses of the time, and it was 20x13 cm in size and consisted of 69 pages (Picture 2). The examined copy has an external cloth cover. The names of the author and the book and also the name of Doctor Burhan Fehmi, who ensured the publication of the book, are written on the inner cover. There are 52 pictures and 5 tables in the books. Some of them were hand drawn. It is seen that the images of the needles, the forceps and hooks were presented with explanations. In addition, at the end of the book there are advertisements of the authorization firm, which was founded by the well-known physician, Dr. Burhan Fehim, who bore the expenses of the publication. Dr. Burhan Fehim was the representative of the Radium Document Firm, which authorized the

radium practices and provided services to the other physicians about this subject. There are also illustrated advertisements related to the devices of international firms on the last five pages of the book.

The author of the book "Radyumla Tedavi Esasları" Reşid Süreyyâ (Ahmed Raşid) was born in Niğde Bor (Picture 3). Resid Sureyya Gursey was not only a multifaceted scientist, but also an internist, x-ray specialist and aesthetician. In addition to medicine, he published various works in mathematics, physics, and languages, created various works of literature and paintings and worked as an educator. Since he had PhD degrees in mathematics and physics from important international universities, he tried to combine his knowledge with his medical knowledge. In France (Sorbonne University) and in England (University of Cambridge), where he was sent for radiology training, he received education and worked with well-known people such as Marie Curie, Paul Langevin and J.J Thomson. There are known to be some unpublished works apart from his published works on various subjects (Table 2). Dr. Remziye Hisar (1904-1992), who was the first female chemist with a PhD degree in Turkey, was Reşit Sürreyâ's wife and both of their children are well-known scientists. Reşid Süreyyâ Gürsey died in U.S.A on August 27th, 1962 (Kurdoğlu, 1967; Etker, 2013).

The book "Radyumla Tedâvi Esasları" starts with a preface of one and a half pages written by the author with the title of "ilk söz". In this preface, Reşit Süreyya criticizes medical books in general. He claimed that these books were composed of information collected from other related resources without forming any framework. Consequently, even though these books provide some information to the reader, they were insufficient to provide information, especially about practice. He also claimed that unacceptable mistakes about "radium treatment" could be found in almost all of the books written about this subject. He, therefore adopted the rule "To explain my subject accurately. In order to do that, not to write anything unrelated to the subject". Although some information was repeated throughout the book, he wanted it to be known that these repetitions were intentional for better comprehension. He showed the information about an atom as an example of the conscious repetition. He argued that the physician, who performs the radium treatment, should have all the information and skills, otherwise s/he and the patient could suffer from unavoidable consequences. Since he had to publish this book as a small book, he stated that he wrote the book by trying to make a good summary of the related information. He also stated that this book was a first for his country based on its characteristics. He suggested that the need for information will increase and transform as the application became more common. In the preface, it could be seen that this book consists of the study notes he made to understand this complicated subject during his studies in Madame Curie's laboratory in Europe. He finished the preface by thanking his friend Doctor Burhanettin Fehim, who bore the expenses of the publication.

The book consists of eight chapters (*Preface; First Section: Radium; Practice, Reason; What is already known in firn chemistry; Second Section: Materials; Points to consider when buying tubes of radium; Application of radium treatment; Comparison of x-ray and radium treatments*). The first four chapters contain information about the physics and chemistry of radium and x-ray. The fifth chapter was explained as introducing the second section of the book after which information about the practical use is offered.

A high number of pictures can be found in the fifth chapter and with these pictures the author elaborated the information related to practice. For example, important information about the calculation of radiation amount, the fullness amount of the needle for every milligram of the radium, the size of the needle, determination of the radiation dose, and putting radium into range were explained and pictures were included. In this chapter, practical knowledge is presented, such as the reason for radiotherapy, its relationship with surgical treatment, the list of cases where no surgical treatment is possible and therefore radiotherapy is recommended (Table 3).

In the section dealing with the general principles of radium application, the application methods of radium, method preferences for different diseases and protection methods for external application are introduced in detail.

1. Application into cavities: Uterus, intestinal, breast cancers

2. Application into masses: Since operations are sometimes necessary in order to reach the cancerous areas, it can be disadvantageous. If it is applied with radon, the costs will decrease. For this method, beta ray should be completely filtered and the needles containing radium should be of a type that can remove the cell. This method was used for tongue cancers. In some case, beta is not filtered.

3. External application: Just as in application to masses, to skin cancer (in form of a disc as mentioned in cervical cancers), it is applied by lining tubes side by side and administering cross-rays. If this method is applied, radium treatment is superior to all the other treatments. In order to be protected, the tubes should always be held with forceps rather than hands and tubes should be stored in boxes covered in lead of 1-2 cm thickness when not in use. These boxes should be stored in partially lead covered boxes and be placed in a location as far away from the physician as possible.

The information provided in Chapter 7 of the book is about the application of radium for treatment purposes, its effect mechanism and diseases which are suitable for radium or x-ray treatments, and is summarized below.

Application of radium treatment: In this chapter, the effect mechanisms of x-ray and gamma rays are not that different from each other, the shape and features of their sources are different, x-rays are the shorter versions of gamma rays and finally the effect mechanism of x-rays.

Effect mechanism of the x-ray: It was stated that in order for the x-rays to be effective, they should penetrate the living cell, the effect of large and small rays are not the same; large rays would penetrate faster and therefore liquids in every tissue would absorb the rays and surrounding tissues would be activated. He likened a small amount of ray to a small amount of sugar in a lot of water. It is stated that since cells which are more sensitive to light are damaged first, an inflammatory response occurs, that x-ray only affects the germs at high quantities and that the tissues in the body and the corresponding cells are affected more. It is even claimed that at some stages of the cell cycle, the same cells show different sensitivity, with the selectiveness of this sensitivity more obvious at lower doses of rays, and thus gamma rays are medically more effective than x-rays.

It is discussed that it is used for genitals, uterus fibromas, myomas, prostate wounds, angiomas (especially superficial ones), lymphangiomas, pubis, abdominal wall, and papillomas on the throats of adults and children.

Breast fibroadenomas should be removed surgically. In the treatment of breast cancer, x-ray treatment is preferred

It was stated that both x-ray and radium treatments were successful for treating various diseases such as, skin diseases acne, exanthema, hemangiomas, lympangiomas, Hodgkin's disease, intertrigo, inflammatory lupus, sometimes common lupus, neurofibromas and sarcoids. To change the amount and location area or bacilli in the skin created by the disease, the beam (x-ray use) is applied to the lymph nodes to overcome the effect of the organ. An effect on leukaemia has been reported with the effect on masses or the beam used in this way.

<u>It has been claimed that gynaecological diseases</u>, especially chronic infections (chronic metritis) are treatable by radium treatment and throat infections are also known to have been cured.

Reșit Süreyya specified the preference reasons and flaws of radium and x-ray treatments. A summary of these points can be found below.

At the end of the book the author explained that his aim was not to invalidate one or the other method, but rather to show how they support each other and that physicians can use whichever is more appropriate for each case. He also claimed that cancers develop resistance to the ray after a while and thus the more destructive rays should be applied at the end of treatment. It was suggested that treatment should not begin with radium, but a high dose of x-ray treatment should be applied as soon as possible and then followed by radium treatment (Table 4).

Discussion

The book, which was written by a Turkish physician in 1927, covers the areas of use of radium, the mechanism of the effect and a comparison with x-ray treatment. With the inclusion of "modern medicine" practices in that period of the Young Turkish Republic, the book is considerably detailed and shows parallels with other practices of that era in the world. The author combined the available contemporary information with his personal experiences and shared it with the reader in plain language.

The book contains brief theoretical information about the atom and radium, the points to consider when buying and storing radium, the principles of the application of radium treatment and summarized information about the benefits and risks of the treatment and warnings specific to practice. All these subjects were covered in a manner appropriate to scientific methodology.

This book essentially explains the use of radium in brachytherapy, which is known as one of the radiotherapy methods used for cancer treatment. In addition to external radiotherapy, this is a method of radiotherapy in which the radiation source is planted inside or near (brachy) the tumor (Kuter, 2002; Denmeade, 2002). Current techniques are based on the experience of previous use of brachytherapy for treatment. The concepts of hypo fraction and personal irradiation have recently developed due to the more intense radiation of brachytherapy to the tumoral mass and the slightly toxic effects on normal tissues. These developments have led to the use of intensity modulated radiotherapy, stereotactic radiotherapy, 4D radiotherapy and image-guided radiotherapy applications, which are now more frequently used in clinical practice (Lederman, 1981; Kuter, 2002). The basis of these techniques can be considered to be the observations obtained from the brachytherapy method.

The treatment of cancer with radiation has advanced as the separate discipline of radiation oncology. Radiotherapy or brachytherapy can be used alone or together with surgical treatment. Current practice is to apply tumor treatment with x- and gamma rays with high technology devices at sensitive settings, in order to keep side-effects to a minimum. The dosage of the ray is calculated according to the patient and disease. The sessions are applied at intervals. Although the author stated intermittent application to be a disadvantage of the treatment, the application of radiotherapy under specialist supervision at intervals is more beneficial to the patient and has fewer side-effects. The difficulties of setting the correct dosage of x-rays and application are

mostly overcome by current technology. In the past, radium was found in many forms to provide ease at application, although it was not possible to calculate the dose of high energy rays with that technology. Radium was still used during the 1950s, especially for gynecological cancers (Ernst, 1956). Today, the application of radium is limited due to the side-effects on normal tissues. There are studies in literature which have shown that radium-223 dichloride might be useful for prostate cancers with bone metastasis. With chloride, the substance was rendered mimetic of calcium and it was attempted to make it specific to newly-formed bone tissues. It was considered that this method might be useful for bone metastasis (Coleman, 2016; Kairemo and Joensuu, 2015). With this exception, radium is not used in radiotherapy, whereas x-rays, have found a broad area of use in radiation oncology and screening in parallel to the technological developments.

Based on the fast developments in radiation oncology, it might be assumed that in the future the applications will be more effective with fewer side-effects. In fact, in addition to the developments in proton treatment, studies of carbon ions providing an effective cancer control with acceptable side-effect rates can foresee many possible developments in future radiation treatment. Similarly, the particular ability of protons and neutrons to determine the metabolic and biological features of a tumor, gives rise to ideas of the development of new methods to diagnose cancer (Lederman, 1981; Kuter, 2002).

This book, which was written almost a century ago, is a document that sheds light on the beginning of radiation oncology history in our country. The importance of this study is its contribution to the comprehension of physicians and future physicians about the importance of the profession and the provision of a new vision of medical practices, medical books and the features of the profession from almost a century ago.

Author	Book	Publication Year
İsmail Süleyman,	Röntgen ve Radyum Şuaatının Tatbikat ve Menafi-i Tıbbiyesi	1905
Mehmed Şemseddin [Günaltay]	Fennin en son keşfiyatından	1912
İzzet Fikrî	Radyum ve Tatbikâtı Tıbbiyesi	1914
Lenk, Robert: Çeviri: Selahaddin Mehmed	Röntgen tedavisi rehberi: Şuubat-ı saire ve mütehassısları ve pratisyen etıbba için	1924
Laborde Simon: Çeviri: Salahaddin Mehmed ve Şükrü Derviş	Radyum ve radyum tedavisi	1927

Reşit Süreyya	Radyumla tedavi esasları	1927
Şükrü Yusuf	Elektrikle teşhis ve tedavi	1927
Gürkan Kazım İsmail ve Tarık Temel	Huvaysal-ı safravî radyolojisi	1928

Table 2. Some of the Published Books Written by Reşid Süreyyâ Gürsey

Books		
Edebiyât-1 Cedide (1912)		
Bir Tılsımın Nakışları (Poetry Book-1929)		
Geceden Şarkılar (Poetry Book-1941)		
Radyumla Tedâvi Esasları		
Riyâziye Esasları (Basic Mathematics)		
Fizik Meseleleri (Physics Problems)		
Fizik Bakaloryası (Physics Problems)		
Harp Zehirleri Kimyası		
Top ve Mermi Sesleri		
Sesle Mevzi Tayini Aletleri		

 Table 3. The Principles of Radiotherapy

The Principles of Radiotherapy:

Why do we need to kill the cell? First, this cancerous cell is a malignant cell. Therefore, radiotherapy is applied. Radiotherapy is applied sometimes based on surgical treatment, sometimes with surgical treatment and when surgical treatment is not possible it can be applied by itself. Based on important statistics, the cases where radiotherapy is suggested even though surgical treatment is possible are:

About Radiotherapy:

1- All skin epitheliums regardless of the nature and shape of the cancer

2- All cervical epitheliums regardless of the nature and shape of the cancer (even uterus epitheliums to some extent)

3- All oral cavity epitheliums regardless of the nature and shape of the cancer

4- All throat epitheliums and all external throat cancers regardless of the nature and shape of the cancer

5- All lip epitheliums regardless of the nature and shape of the cancer

- 6- All common sarcomas regardless of their position
- 7- Some epitheliums of testicle
- 8- Some epitheliums of bladder
- 9- Prostate cancer
- 10- Eyelid and same epitheliums
- 11- Esophagus epitheliums

*In other cases surgical treatment and radium results are considered equivalent to each other. However, surgical treatment is better for early stage breast cancer and matter, intestinal cancer.

Table 4. Preference Reasons and Flaws of Radium and X-ray Treatments

Flaws of Radium Treatment
1- Since radium is very expensive, great
amounts of radium can only be purchased by
big institutions. Private physicians have very
small amounts of radium, so they cannot
make broad applications. However, this flaw
can be eliminated by the government.
2- In some cases radium treatment cannot be

treatment it is hard to apply the desired ap amount and type of rays to the desired point.

3- The scattering amount of radium rays, especially after it is filtered, is very low compared to x-rays. As well as its general burning effect being less compared to x-rays, its specific effect to lesions is good.

4- Pre-surgery ray treatment with radium takes 3 weeks, whereas the same procedure takes 2 months with x-ray. Since it is important to carry out the surgery as soon as possible, this feature of radium is important. Thus, x-ray cannot be used (as neoadjuvant) especially for Ohmic organs such as the uterus.

5- Another significant reason for preference is that x-ray can be applied to a lesion at intervals, when the patient can only see the doctors at certain times. Whereas when radium is applied to the patient, it affects the patient day and night for days. This is not just about buying time. The sensitivity of cancerous cells to rays differs over time. Each cell shows sensitivity to rays more during a specific time (during division). In order to affect the cell during the sensitive period, the ray should constantly penetrate the cell. In x-ray treatment it is highly possible that the sensitive periods of the cell occur during sleep and as the patient is not exposed to rays at that specific time, the cells

applied (i.e. During pregnancy)

3- In order to place needles or tubes into the masses, surgery may be necessary. If surgery is not suitable, it is possible to exchange radium treatment with x-ray treatment. In such cases, nonsurgical x-ray treatment is preferred to keep the patient strong,

would not be affected by the rays.		
Preference Reasons for X-ray Treatment	Flaws of X-ray Treatment	
 1- The same type of ray can be applied to broad areas. Efforts should be made to obtain the same type of rays. 2- There is no need for surgery, so the patient would not become weak. 	1- It is not possible to give the same type of ray to an area even with x-rays. Even though the amount is the same, it is not possible that the purity of the substance is always the same, which means that it is not possible to create the beam in the same way. However, this is possible in radium treatment.	
3- Radium can have side effects such as enteritis, which takes a long time to recover, whereas the side effects of x-ray are mild and temporary. Inexplicable, idiosyncratic reactions may occur during both treatments. Some argue that the rays should be applied gradually to accustom the body.	 2- Despite many measurement techniques, these are complex and not easily applied, so the exact amount of each ray applied from the source may be difficult to accurately record. It is also difficult to measure the ray amount touching the surface and reaching the lesion. 	
	3- Since gamma rays are more effective for neoplasia cells, this flaw of the x-ray is important.	

Picture 1: It was believed that drinking radium water from special cups was good for many diseases, such as arthritis and even wrinkles.

Picture 2. 'Radyumla Tedavi Esasları' Inner Cover

Picture 3. Doctor Reşid Süreyyâ Gürsey

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