Chapter One

Introduction

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1. Introduction

1.1 Background

More than 14 million new cases of cancer are diagnosed globally each year; radiation therapy (RT) has the potential to improve the rates of cure of 3.5 million people and provide palliative relief for an additional 3.5 million people. These conservative estimates are based on the fact that approximately 50 percent of all cancer patients can benefit from RT in the management of their disease. [1]

Soon after Roentgen's discovery of X-rays in 1895, ionizing radiation was applied to the treatment of cancer, with remarkable results. Carefully controlled doses of ionizing radiation induce damage to the DNA in cells, with preferential effects on cancer cells compared with normal tissues, providing treatment benefits in most types of cancer and saving lives. RT is now recognized as an essential element of an effective cancer care program throughout the world, regardless of countries' economic status. RT is used to cure cancers that are localized; it also can provide local control—complete response with no recurrence in the treated area—or symptom relief in cancers that are locally advanced or disseminated. It is frequently used in combination with surgery, either preoperatively or postoperatively, as well as in combination with systemic chemotherapy before, during, or subsequent to the course of RT.[2]

Because radiation affects normal tissues and tumors, achieving an acceptable therapeutic ratio—defined as the probability of tumor control versus the probability of unacceptable toxicity—requires that the radiation dose be delivered within very tightly controlled tolerances with less than 5 percent deviation. This controlled production and precise application of radiation requires specialized equipment that is maintained and operated by a team of trained personnel. The team includes, at a minimum, radiation oncologists to prescribe the appropriate dose, medical physicists to ensure accurate dose delivery, and radiation technologists to operate the equipment and guide patients through the radiation process. Radiation oncologists work within multidisciplinary teams with medical and surgical oncologists to coordinate a multidisciplinary approach to the management of cancer. A comprehensive cancer center provides the full scope of RT services, ranging from externally applied beams of X-rays to the placement of radiation-emitting sources within tumors.[(3]

Chapter Two literature Review

Chapter Two

2. Literature Review

2.1 Cancer

Cancer is a disease in which some of the body's cells grow uncontrollably and spread to other parts of the body. Cancer can start almost anywhere in the human body, which is made up of trillions of cells. Normally, human cells grow and multiply (through a process called cell division) to form new cells as the body needs them. When cells grow old or become damaged, they die, and new cells take their place. (7)

Sometimes this orderly process breaks down, and abnormal or damaged cells grow and multiply when they shouldn't. These cells may form tumors, which are lumps of tissue. Tumors can be cancerous or not cancerous (benign). Cancerous tumors spread into, or invade, nearby tissues and can travel to distant places in the body to form new tumors (a process called metastasis). Cancerous tumors may also be called malignant tumors. Many cancers form solid tumors, but cancers of the blood, such as leukemias, generally do not. Benign tumors do not spread into, or invade, nearby tissues. When removed, benign tumors usually don't grow back, whereas cancerous tumors sometimes do. Benign tumors can sometimes be quite large, however. Some can cause serious symptoms or be life threatening, such as benign tumors in the brain. (8)

2.2 Differences between Cancer Cells and Normal Cells

Cancer cells differ from normal cells in many ways. For instance, cancer cells: (9)

- Grow in the absence of signals telling them to grow. Normal cells only grow when they receive such signals.

- Ignore signals that normally tell cells to stop dividing or to die (a process known as programmed cell death, or apoptosis).
- Invade into nearby areas and spread to other areas of the body. Normal cells stop growing when they encounter other cells, and most normal cells do not move around the body.
- Tell blood vessels to grow toward tumors. These blood vessels supply tumors with oxygen and nutrients and remove waste products from tumors.
- Hide from the immune system. The immune system normally eliminates damaged or abnormal cells.
- Trick the immune system into helping cancer cells stay alive and grow. For instance, some cancer cells convince immune cells to protect the tumor instead of attacking it.
- Accumulate multiple changes in their chromosomes, such as duplications and deletions of chromosome parts. Some cancer cells have double the normal number of chromosomes.
- Rely on different kinds of nutrients than normal cells. In addition, some cancer cells make energy from nutrients in a different way than most normal cells. This lets cancer cells grow more quickly.

2.3 Types of cancer

Cancers are named for the area in which they begin and the type of cell they are made of, even if they spread to other parts of the body. For example, a cancer that begins in the lungs and spreads to the liver is still called lung cancer.

There are also several clinical terms used for certain general types of cancer: [10]

- **Carcinoma:** is a cancer that starts in the skin or the tissues that line other organs.
- **Sarcoma:** is a cancer of connective tissues such as bones, muscles, cartilage, and blood vessels.
- **Leukemia:** is a cancer of the bone marrow, which creates blood cells.
- **Lymphoma and myeloma:** are cancers of the immune system.

Learn more about specific types of cancer with the resources below: [11]

- Bladder cancer
- Kidney cancer
- Liver cancer
- Lung cancer
- Signet cell cancer
- Skin cancer
- Gallbladder cancer
- Gastric cancer
- Thyroid cancer
- Salivary gland cancer
- Secondary cancer

Fig.2 Types of cancer

2.4 Types of Cancer Treatment

There are many types of cancer treatment. The types of treatment that you receive will depend on the type of cancer you have and how advanced it is some people with cancer will have only one treatment. But most people have a combination of treatments, such as surgery with chemotherapy and radiation therapy:

- **Biomarker Testing for Cancer Treatment:**

Biomarker testing is a way to look for genes, proteins, and other substances (called biomarkers or tumor markers) that can provide information about cancer. Biomarker testing can help you and your

1. **Brachytherapy**

Involves radioactive material that is implanted in the body. Dozens of tiny "seeds" containing radioactive iodine are placed at the tumor site with a special needle or catheter. This is done as an outpatient procedure. Brachytherapy is used for treatment of prostate, cervical, endometrial, vaginal and breast cancers. (31)

2. **Intraoperative radiation therapy (IORT)**

Is used to treat an exposed tumor during cancer surgery. IORT delivers a high dose of radiation to a surgically exposed treatment area. Surrounding healthy organs and tissues are protected by lead shields. This type of radiation can be used for certain gastrointestinal cancers and other cancers that are challenging to remove during surgery. (32)

3. **Stereotactic radiosurgery (SRS)**

Fig.5 IORT Radiation

Is not actually surgery. Instead, it uses dozens of tiny radiation beams to treat tumors in the head and neck with a single radiation dose. MD Anderson uses the Gamma Knife® SRS system. Gamma Knife is used to treat cancer that has spread to the brain or head or neck area, as well as tumors in the base of the skull, malignant gliomas, acoustic neuromas, pituitary tumors and meningiomas. (33)

2.5.3 External beam radiation therapies are delivered through a specialized machine directly to the cancer site

These include the following types of radiation therapy:

1. **Proton therapy**

Uses a beam of protons to deliver radiation directly to the tumor. A proton beam conforms to the shape and depth of a tumor while sparing healthy tissues and organs. At the MD Anderson Proton Therapy Center, we provide advanced radiation to treat cancers of the prostate, lung, head and neck, liver, esophagus and brain, as well as for the treatment of lymphoma, pediatric cancers and other rare tumors. [(34]

2. **MRI**

Linear accelerator is used to track soft tissue-based tumors in real time during radiation. During treatment, the MRI is constantly obtaining images. This allows for real-time control of the radiation beam during treatment. This provides the ability to adapt the radiation delivery as needed at each treatment. This technique is used for multiple cancer types with a soft tissue component, such as head and neck cancers and gastrointestinal cancers. [(35)]

3. **Stereotactic body radiation therapy (SBRT)**

Has a narrower beam of radiation. It allows us to more precisely target the tumor. SBRT may be a good option for patients who are not candidates for surgery, and it can be used for a variety of cancer types, including lung cancer, pancreatic cancer, liver cancer, and cancers that have spread to the bones. [(36)]

2.6 Pharmacological properties

Systemic radiation therapy uses radioactive drugs (called radiopharmaceuticals or radionuclides) to treat certain types of cancer, including thyroid, bone, and prostate cancer. These are liquid drugs made up of a radioactive substance. They can be given by mouth or put into a vein; they then travel throughout the body. [37]

2.6.1 Radiopharmaceuticals

Radiopharmaceuticals include a group of radioactive agents used for either diagnostic or therapeutic interventions. Although the administration of radiopharmaceuticals is often systemic, they are likely to localize to specific tissues because of their biomolecular properties, i.e., the areas of hyperintensity observed on positron emission tomography (PET) scans that indicate a high tissue metabolic demand. Radiopharmaceuticals actively emit radiation, which makes their storage more difficult than non-radioactive pharmaceuticals. Compounds used for diagnostic interventions usually either emit beta particles (positrons or electrons) or gamma rays, while compounds that emit Auger electrons or alpha particles (helium nuclei) are generally for therapeutic interventions. [38]

Radio-imaging involves the use of incredibly low concentrations of radiotracers (sub-micro quantities). Radio-imaging is currently used to analyze tissue physiology, detect disease, and monitor treatments; however, new uses are being discovered with the advent of personalized medicine. [38]

Radiotherapeutic agents use the radiation emitted from the nuclide to kill the target cells or serve palliative purposes. Radiation is toxic to tissues in the body: the brain, spinal cord, kidneys, and bone marrow are especially susceptible. Many radiopharmaceuticals are delivered systemically, and this means that ideally, the pharmaceuticals should selectively prefer the tumor tissue relative to normal healthy tissue. Many various specific radionuclides are in common use. [38]

2.6.2 Clinical Significance

Radiopharmaceuticals are vital to healthcare. They are instrumental in imaging, and in the United States alone, millions of nuclear medicine procedures are performed annually. They are instrumental in the treatment of many malignancies and even many benign tumors. (39)

Designing radiopharmaceuticals is a rigorous and complicated process that relies on many different factors. Selecting the appropriate nuclide is critical, as the specific nuclide has a specific half-life and decay mode. These both impact the localization and utility of the radiopharmaceutical. Other factors, such as molecular stability, ease, and production cost, are also important factors. Specific radiopharmaceuticals like radium-223 are useful for treating painful bone metastases in prostate cancer patients with castration-resistant bone metastases and have been approved by FDA for this use. (40)

2.7 Mechanism of action of radiation therapy

Radiation therapy uses particles or waves moving at a high frequency to target the DNA of cells in the body and change the way they are able to replicate. If the DNA required for mitosis and replication is damaged, the cells are unable to replicate as usual and the growth of a cancerous tumor is inhibited. This type of therapy manipulates the fact that cancerous cells usually replicate more quickly than normal cells in the body. As the DNA can only be damaged when the cells are undertaking the replication process – not in the G0 phase – the majority of normal cells that take longer to replicate are less affected than the cancerous cells. Radiation therapy uses low and high linear energy transfer (LET) radiations to efficiently kill the tumor cells while minimizing dose (biological effective) to normal tissues to prevent toxicity. (41)

2.8 The date of its appearance

Radiotherapy has its origins in the aftermath of the discovery of x-rays in 1895 and of radioactivity in 1896. Through scientific discoveries, trial and error, and technology advances, standardised approaches in external beam radiotherapy and brachytherapy were developed. Also, the development of the fields of radiobiology and radiation metrology was particularly important in making radiotherapy an effective treatment modality for cancer therapy. [42]

External beam radiotherapy began with superficial and orthovoltage therapy with x-ray tubes and teletherapy with sealed radioactive sources. St Bartholomew's Hospital pushed the limits of technology with the 1 MV x-ray tube in the 1940's. Megavoltage therapy matured in the 1950's with the development of the Cobalt-60 machine along with the medical linear accelerator. The betatron and microtron have also been used in radiotherapy. Hospital-based particle therapy arrived in 1989 and there are currently 57 particle therapy facilities worldwide in operation. [43]

Brachytherapy using sealed sources began with Radium-226 (1901), and then followed brachytherapy with Radon-222 seeds, Caesium-137, Iridium-192 and Cobalt-60 sources, while other isotopes including Iodine-125 and Gold-198 have proved effective. Brachytherapy with beta sources such as Strontium-90 and Ruthenium-106 has niche uses. Various manual loading systems have been superseded by modern high-dose-rate Iridium-192 and Cobalt-60 afterloader systems and automated systems for delivery of Iodine-125 seeds to the prostate. [44]

2.9 Beginning of radiation therapy

Radiotherapy can be traced back about 125 years to the discovery of X-rays (1895) by a Germany physicist named W. C. Roentgen. After X-rays were discovered, it did not take long before X-rays were used in cancer treatments. On January 29, 1896, just three days after announcement of the discovery of X-rays, the E. H. Grubb company, a vacuum tube manufacturer, applied X-rays for the first time in cancer treatment at the suggestion of doctor Ludlam. A single treatment was performed for about one hour in breast cancer patients. [45] In 1900, T. Stenbeck and T. Sjogren treated patients with skin cancer at the tip of their nose. In 1903, Senn first attempted treatment in a leukemia patient. [46] In 1896, Despeignes began using radiotherapy in France. Patients with stomach cancer were irradiated 15 to 30 minutes with 80 fractions and it was reported that the disease improved and pain was relieved. [47]

2.9.1 Beginning of radiation therapy in Iraq

In Iraq, the first establishment of radiotherapy services dates back to the 1920s when the Radiology Institute was established in Baghdad. [48] This institute was the only place in Iraq that was offering diagnostic and therapeutic radiation services until the late 1950s, when a deep X-ray therapy unit was installed in Mosul in 1959. The establishment of the Oncology and Nuclear Medicine Institute in Baghdad was in 1969, and in Mosul and in Basra, it was in 1978. [49]

2.10 The purpose of using radiation therapy

Radiation therapy is an essential tool for treating cancer and is often used with other therapies, such as chemotherapy or tumor removal surgery. The main goals of radiation therapy are to shrink tumors and kill cancer cells.

There are many reasons why doctors may choose to treat cancer with radiation. They use it to: [50]

- Destroy all cancer cells

- Shrink the tumor
- Stop cancer from coming back
- Treat cancer symptoms

2.11 Side effects of radiation therapy

Radiation to the brain can cause these short-term side effects: [51]

- Headaches
- Hair loss
- Nausea
- Vomiting
- Extreme tiredness (fatigue)
- Hearing loss
- Skin and scalp changes
- Trouble with memory and speech
- Seizures

Aim of study

In the current study, the primary objective was to estimate the most common side effects in cancer patients undergoing radiotherapy in Babylon Governorate, Iraq. A secondary objective was to evaluate possible relationships of side effects with the patient's age and gender.

Chapter Three Materials and Methods

Chapter Three

3. Materials and Methods

The study was a retrospective, survey-based, and cross-sectional study

Survey and data collection. The study included a paper questionnaire targeting cancer patients who are undergoing Radiotherapy and attending the oncology center at Marjan Medical City Hospital in Al-Hilla, Babylon, Iraq.

Later, an online-based questionnaire was shared in order to include the largest possible number of cases. The study lasted for three months, from 19 December, 2022 to 27 April, 2023.

Chapter Four

Results and Discussion

2.7 Mechanism of action of radiation therapy

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References

1. Maier P, Hartmann L, Wenz F, Herskind C. Cellular Pathways in Response to Ionizing Radiation and Their Targetability for Tumor Radiosensitization. Int J Mol Sci. 2016 Jan 14;17(1).

2. Barton M B, Jacob S, Shafiq J, Wong K, Thompson S R. others. 2014. ―Estimating the Demand for Radiotherapy from the Evidence: A Review of Changes from 2003 to 2012.‖ Radiotherapy & Oncology 112 (1): 140–44.

3. Gospodarowicz M, Trypuc J, D'Cruz A, Khader J, Omar S, Knaul F. 2015. ―Cancer Services and the Comprehensive Cancer Center.‖ In Disease Control Priorities (third edition): Volume 3, Cancer, edited by Gelband H, Jha P, Sankaranarayanan R, Horton S, editors. . Washington, DC: World Bank.

4. Weintraub SM, Salter BJ, Chevalier CL, Ransdell S. Human factor associations with safety events in radiation therapy. J Appl Clin Med Phys. 2021 Oct;22(10):288-294.

5. National Cancer Institute (NIH), 2019.
6. Berger M, Yang Q, Maier A. X-ray Imaging. In: Maier A, Steidl S, Christlein V, Hornegger J, editors. Medical Imaging Systems: An Introductory Guide [Internet]. Springer; Cham (CH): Aug 3, 2018. pp. 119–145.
7. Vander Heiden M.G., DeBerardinis R.J. Understanding the intersections between metabolism and cancer biology. Cell. 2017;168(4):657–669.
8. Lambert A.W., Pattabiraman D.R., Weinberg R.A. Emerging biological principles of metastasis. Cell. 2017;168(4):670–691.
9. Lambert A.W., Pattabiraman D.R., Weinberg R.A. Emerging biological principles of metastasis. Cell. 2017;168(4):670–691.
10.Visvader J.E. Types of cancer. Nature. 2011;469(7330):314–322.
11.Greaves M. Evolutionary determinants of cancer. Canc Discov. 2015;5(8):806–820.
12.Blumenthal D, Abrams M, Nuzum R. The Affordable Care Act at 5 years. New England Journal of Medicine. 2015;372(25):2451–2458.
13.Chui PL, Abdullah KL, Wong LP, Taib NA. Complementary and alternative medicine use and symptom burden in women undergoing chemotherapy for breast cancer in Malaysia. Cancer Nurs. 2018;41:189–99.
14.Cañete MD, Valle-Martos R, Martos R, Cañete R, Valle M, Jiménez-Reina L. Effects of growth hormone therapy on metabolic parameters, adipokine and endothelial dysfunction in prepuberal children. Acta Paediatr. 2019 Nov;108(11):2027-2033.
15.Nye EA, Edler JR, Eberman LE, Games KE. Optimizing ColdWater Immersion for Exercise-Induced Hyperthermia: An Evidence-Based Paper. J Athl Train. 2016 Jun 02;51(6):500-1.

16.Verhoeven D, Stoppelenburg AJ, Meyer-Wentrup F, Boes M. Increased risk of hematologic malignancies in primary immunodeficiency disorders: opportunities for immunotherapy. Clin Immunol. 2018 May;190:22-31.
17.Allison RR, Mota HC, Sibata CH. Clinical PD/PDT in North America: an historical review. Photodiagnosis Photodyn Ther. 2004;1:263–277.
18.Maier P, Hartmann L, Wenz F, Herskind C. Cellular Pathways in Response to Ionizing Radiation and Their Targetability for Tumor Radiosensitization. Int J Mol Sci. 2016 Jan 14;17(1).
19.Naji A, Eitoku M, Favier B, et al. Biological functions of mesenchymal stem cells and clinical implications. Cell Mol Life Sci 2019; 76(17): 3323–3348.
20.Purushotham A D, Lewison G, Sullivan R. 2012. ―The State of Research and Development in Global Cancer Surgery.‖ Annals of Surgery 255 (3): 427–32.
21.Adjei IM, Blanka S. Modulation of the tumor microenvironment for cancer treatment: a biomaterials approach. J Funct Biomater 2015; 6: 81–103.
22.Barton M B, Jacob S, Shafiq J, Wong K, Thompson S R. others. 2014. ―Estimating the Demand for Radiotherapy from the Evidence: A Review of Changes from 2003 to 2012.‖ Radiotherapy & Oncology 112 (1): 140–44. doi:10.1016/j.radonc.2014.03.024. Epub May 12.
23.Gunderson L L, Tepper J E. 2012. Clinical Radiation Oncology. 3rd ed. Philadelphia, PA: Saunders; London: Elsevier.
24.Gospodarowicz M, Trypuc J, D'Cruz A, Khader J, Omar S, Knaul F. 2015. ―Cancer Services and the Comprehensive Cancer Center.‖ In Disease Control Priorities (third edition): Volume 3, Cancer,

edited by Gelband H, Jha P, Sankaranarayanan R, Horton S, editors. . Washington, DC: World Bank.
25.Fisher B J, Daugherty L C, Einck J P, Suneja G, Shah M M. others. 2014. ―Radiation Oncology in Africa: Improving Access to Cancer Care on the African Continent.‖ International Journal of Radiation Oncology, Biology, Physics 89 (3): 458–61.
26.Abdel-Wahab M, Bourque J M, Pynda Y, Izewska J, Van der Merwe D. others. 2013. ―Status of Radiotherapy Resources in Africa: An International Atomic Energy Agency Analysis.‖ The Lancet Oncology 14 (4): e168–75.
27.Gandhi AK, Sharma DN, Rath GK, et al. Early clinical outcomes and toxicity of intensity modulated versus conventional pelvic radiation therapy for locally advanced cervix carcinoma: a prospective randomized study. Int J Radiat Oncol Biol Phys. 2013;87:542–548.
28.Gill S, Thomas J, Fox C, Kron T, Rolfo A, Leahy M, Chander S, Williams S, Tai KH, Duchesne GM, Foroudi F. Acute toxicity in prostate cancer patients treated with and without image-guided radiotherapy. Radiat Oncol. 2011;6:145.
29.Feng FY, Kim HM, Lyden TH, Haxer MJ, Feng M, Worden FP, Chepeha DB, Eisbruch A. Intensity-modulated radiotherapy of head and neck cancer aiming to reduce dysphagia: early dose-effect relationships for the swallowing structures. Int J Radiat Oncol Phys. 2012;68:1289–1298.
30.M Teoh, C H Clark, K Wood, S Whitaker, A Nisbet, Volumetric modulated arc therapy: a review of current literature and clinical use in practice, Br J Radiol, 2011 Nov;84(1007):967-96.
31.Cyrus Chargari, Eric Deutsch, Pierre Blanchard, Sebastien Gouy, Hélène Martelli, Florent Guérin, Brachytherapy: An overview for

clinicians, CA Cancer J Clin 2019 Sep;69(5):386-401.
32.Ahmed Elashwah, Abdullah Alsuhaibani, Ali Alzahrani, Ayman Zaki Azzam, Belal Moftah, The Use of Intraoperative Radiation Therapy (IORT) in Multimodality Management of Cancer Patients: a Single Institution Experience, J Gastrointest Cancer 2022 Mar 15, 00786-9.
33.Suh JH. Stereotactic radiosurgery for the management of brain metastases. N Engl J Med. 2010 Mar 25;362(12):1119-27.
34.Ganz JC. The journey from proton to gamma knife. Prog Brain Res. 2014;215:67-75.
35.Westbrook C., Roth C.K., Talbot J. 4th edition. John Wiley & Sons, Inc.; London: 2011. MRI in Practice.
36.Elysia K Donovan, Anand Swaminath, Stereotactic body radiation therapy (SBRT) in the management of non-small-cell lung cancer: Clinical impact and patient perspectives, Lung Cancer (Auckl), 2018 Mar 16;9:13-23.
37.Bartholomä MD. Radioimmunotherapy of solid tumors: Approaches on the verge of clinical application. J Labelled Comp Radiopharm. 2018 Jul;61(9):715-726.
38.Hong AS, Levin D, Parker L, Rao VM, Ross-Degnan D, Wharam JF. Trends in Diagnostic Imaging Utilization among Medicare and Commercially Insured Adults from 2003 through 2016. Radiology. 2020 Feb;294(2):342-350.
39.Zhou SF, Zhong WZ. Drug Design and Discovery: Principles and Applications. Molecules. 2017 Feb 13;22(2)
40.Gupta N, Devgan A, Bansal I, Olsavsky TD, Li S, Abdelbaki A, Kumar Y. Usefulness of radium-223 in patients with bone metastases. Proc (Bayl Univ Med Cent). 2017 Oct;30(4):424-426.
41.Niemantsverdriet M., van Goethem M.-J., Bron R., Hogewerf W.,

Brandenburg S., Langendijk J. A., et al.. (2012). High and low LET radiation differentially induce normal tissue damage signals. Int. J. Radiat. Oncol. Biol. Phys. 83, 1291–1297.
42.Rontgen WC Uber eine neue Art von Strahlen. Vorl¨aufige Mitteilung. Vol. 30. Sitzung: Sitzungsberichte¨der physikalischmedicinischen Gesellschaft zu W¨urzburg; 1985. pp. 132–141.
43.Grubbe EH. Priority in the therapeutic use of X-rays. Radiology´ 1933;21:156–162.
44.Boone MLM, Lawrence JH, Connor WG, et al. Introduction to the use of protons and heavy ions in radiation therapy:historical perspective. Int. J. Radiat. Oncol. Biol. Phys. 1977;3:65–69.
45.Case JT, Buschke F. History of radiation therapy . New York: Grune & Stratton; 1958:13-41.
46.Lederman M. The early history of radiotherapy: 1895-1939. Int J Radiat Oncol Biol Phys. 1981;7:639-648.
47.Holsti LR. Development of clinical radiotherapy since 1896. Acta Oncol. 1995;34:995-1003.
48.M. Al-Ghazi, Cancer care in a war zone: radiation oncology in Iraq, Int J Radiat Oncol Biol Phys, 96 (2016), p. E413.
49.L. Mula-Hussain, Cancer care in Iraq: a descriptive study, (1st ed.), LAP LAMBERT Academic Publishing, Saarbrucken-Germany 2012 .
50.Gunderson LL, Tepper JE, editors. Clinical radiation oncology. 5th ed. Philadelphia, PA: Elsevier; 2021.
51.Baskar R, Lee KA, Yeo R, Yeoh KW.. Cancer and radiation therapy: side effect and future directions. Int J Med Sci 2012;9 3 :193-9.