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MINISTRY OF HIGHER EDUCATION AND SCIENTIFIC RESEARCH
جـامـعـة عمّـــار ثـلـيـــجـــي بالأغـــواط
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FACULTY OF SCIENCES
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Department OF Material Sciences

Master thesis

Domain: Material Sciences

Field: Physics

Option: Medical physics

Presented by:
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THEME

Helical and Direct Irradiation in Tomotherapy

Dosimetric Comparison Study of Breast Cancer Treatment

Graduated in 26/06/2019

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Dedication

I dedicate this thesis which has been made by love for medical physics field to:

My dear parents Mommy: NAIMA and daddy ABDALLAH for their great education to me and their efforts and helps during all my study path

My dear sister HADJER and her husband MUSTAPHA and their baby ZINOU

My dear brothers OUSSAMA and SAFOANE

My future life partner AROUSSA

All my family and friends and lovers

All medical physicists through the world for their efforts to perform patient's life quality.

Big salutations and respect

I love you all

Ilyas BENABDALLAH

Acknowledgement

I would first like to thank my thesis supervisor **Mr. REDJEM FETHI** professor in material sciences department of AMMAR TELEDJI University for his advices and help in directing this work.

Thanks to the president of my graduation session professor in material sciences department of AMMAR TELEDJI University **Dr. KHANCHOUL Salah**

Thanks to jury members of my graduation session professors in material sciences department of AMMAR TELEDJI University **Mr. ZERGUINI HOCINE** and **Mrs. AISSOUS BASMA.**

I would also to thank my supervisor the medical physicist at SIDI ABDALLAH center of carcinology-Algiers.

Mr. HAMID BEMAAMER for his great help and accompaniment during all my time at the center and after. Also, a big salutation and thanks to the medical physicist **Mrs. MERIEM ALLEL** from the same center for her extra help and standing leading me to understand many concepts inside the center especially in dosimetric planning.

Special thanks to my best friend **Mr. HOCINE BOUHDIBA** for his great help and standing beside me.

Thanks to the idea leader of this theme the medical physicist at ELAZHAR center of carcinology - Algiers **Mr. ZINEDDINE LAGHRIBI**.

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Abbreviations List

DNA: Deoxyribonucleic Acid.

GTV: Gross Tumor Volume.

CTV: Clinical Target Volume.

PTV: Planning Target Volume.

IMC: Internal Mammary Chanel.

EBRT: External Beam Radiation Therapy.

GY: Gray

DVH: Dose Volume Histogram.

MRI: *Magnetic resonance imaging*.

CT: computed Tomography.

LINAC: Linear Accelerator.

MLC: Multi leaf collimator.

DQA: Delivery Quality Assurance.

NCRP: National Council on Radiation Protection.

TNM: Tumor. Nodes. Metastasis.

DCIS: Ductal Carcinoma In Situ.

LCIS: Lobular Carcinoma In Situ.

IMRT: Intensity Modulated Radiation Therapy.

IGRT: Image Guidance Radiation Therapy.

FWHM: *Full Width at Half Maximum*

OAR: Organ at Risk.

MF: Modulation Factor.

LET: Linear Energy Transfer.

TH: TomoHelical.

TD: TomoDirect.

3D-CRT: Three Dimensional Conformal Radiation Therapy.

ART: Adaptive Radiation Therapy.

VMAT: Volumetric modulated arc therapy

IORT: Intraoperative radiation

SRS: Stereotactic radiosurgery

ROI: Region of Interest.

DIR: Deformable Image Registration.

TPS: Treatment Planning System.

DLVs: Dose Limiting Volumes.

IVDT: Image Value to Density Table.

ICRU : International Commission on Radiation Units.

AVER: Average.

RTOG: Radiation Therapy Oncology Group.

CI: Conformity Index.

HI: Homogeneity Index.

GE: General Electric.

CSAC: Centre of Sidi Abdallah of Carcinology.

General Introduction

Radiation therapy has been used as a cancer treatment for more than 100 years, beginning shortly after the discovery of x-rays in 1895 by Wilhelm Roentgen. Radiation is still one of the most effective cancer treatments available today. Radiation oncologists make use of highly sophisticated, precise, and intricate instruments, such as stereotactic devices, linear accelerators, brachytherapy, and radiopharmaceuticals, to precisely target tumors with ionizing radiation.

During the past 50 years, the most common form of radiotherapy has been external beam radiation therapy (EBRT). Conventional EBRT uses a beam of high energy x-rays or photons directed at the tumor from one to several different directions, so that radiation is focused on a target and surrounding healthy tissue is shielded. EBRT is typically delivered via a linear accelerator, a machine which produces and focuses photons towards the target, with photons exerting their effects by ionization of molecules in tissues directly within their path. One of the most recent high technologies of EBRT is Tomotherapy [1].

The word Tomotherapy has emerged from a Greek prefix – tomo, which means slice, so the radiation is transported slice by slice. Tomotherapy is an advanced system by which powerful and precise radiation beams are continuously produced to treat inoperable tumors. The inbuilt computed tomography scanning helps in confirming the size and position of the tumor prior the treatment.

In the other side we know that cancer occurs as a result of mutations, or abnormal changes, in the genes responsible for regulating the growth of cells and keeping them healthy. The genes are in each cell's nucleus, which acts as the "control room" of each cell. Normally, the cells in our bodies replace themselves through an orderly process of cell growth, healthy new cells take over as old ones die out. But over time, mutations can "turn on" certain genes and "turn off" others in a cell. That changed cell gains the ability to keep dividing without control or order, producing more cells just like it and forming a tumor. One of the most common types of cancer is Breast cancer.

Breast cancer is always caused by a genetic abnormality (a "mistake" in the genetic material). However, only 5-10% of cancers are due to an abnormality inherited from mother or father. Instead, 85-90% of breast cancers are due to genetic abnormalities that happen as a result of aging process and other factors such as late first pregnancy and life style in general. In which about 41,760 women in the U.S. are expected to die in 2019 from breast cancer. Women under 50 have experienced larger decreases. These decreases are thought to be the result of treatment advances, earlier detection through screening, and increased awareness [2].

The goal of this study is to evaluate the Tomotherapy system and showing its capacity and efficacity in treating breast cancer, reaching to the main goal of radiotherapy which is providing a better life's quality for the patient. For this we have planned a special study structure consist of four chapters, in which:

In the first chapter: we have talked about general basics of physics such as the mechanism of X-ray production and its interactions with matter, then its effect on biological tissues (radiobiology), and general concepts about cancer treatments.

In the second chapter: we have talked about Breast cancer pathology as the problem that can threat many women's life, by including actual statistics and facts, then talking about risk factors and breast cancer stages, then about breast cancer treatments and the side effects of the radiation therapy.

In the third chapter: we have talked about the Tomotherapy system and its details including the new technologies and characteristics of cancer treatments which make the deference by comparing with conventional radiotherapy techniques, then we talk about the patient workflow in Tomotherapy service.

In the fourth chapter: we have presented our results which are about dosimetric comparison between planes of the tow modes of delivery in Tomotherapy, the TomoDirect and the TomoHelical, we discuss our obtained results and finally we conclude.

Physics, Radiobiology and Cancer Treatment Basics

I.1 Introduction

X-rays were discovered by Roentgen in 1895 while studying cathode rays (stream of electrons) in a gas discharge tube. He observed that another type of radiation was produced (presumably by the interaction of electrons with the glass walls of the tube) that could be detected outside the tube. This radiation could penetrate opaque substances, produce fluorescence, blacken a photographic plate, and ionize a gas. He named the new radiation x-rays [3].

I.2 Physics Basics

I.2.1 The x-ray tube

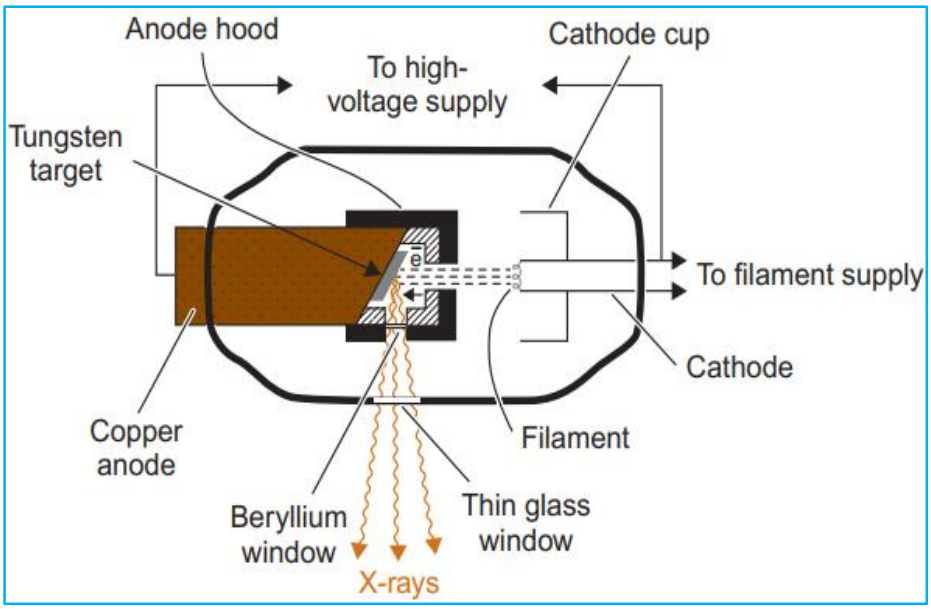

Figure I-1 Schematic diagram of a therapy x-ray tube with a hooded anode.

Figure I-1 is a schematic representation of a conventional x-ray tube. The tube consists of a glass envelope which has been evacuated to high vacuum. At one end is a cathode (negative electrode) and at the other an anode (positive electrode), both hermetically sealed in the tube.

The cathode is a tungsten filament which when heated emits electrons, a phenomenon known as thermionic emission. The anode consists of a thick copper rod, at the end of which is placed a small piece of tungsten target. When a high voltage is applied between the anode and the cathode, the electrons emitted from the filament are accelerated toward the anode and achieve high velocities before striking the target. The x-rays are produced by the sudden deflection or acceleration of the electron caused by the attractive force of the tungsten nucleus.

I.2.2 Physics of X-Ray Production

There are two different mechanisms by which x-rays are produced. One gives rise to bremsstrahlung x-rays and the other characteristic x-rays.

I.2.2.1 Bremsstrahlung

The process of bremsstrahlung (braking radiation) is the result of radiative "collision" (interaction) between a high-speed electron and a nucleus. The electron while passing near a nucleus may be deflected from its path by the action of Coulomb forces of attraction and lose energy as bremsstrahlung, a phenomenon predicted by Maxwell's general theory of electromagnetic radiation. According to this theory, energy is propagated through space by electromagnetic fields. As the electron, with its associated electromagnetic field, passes in the vicinity of a nucleus, it suffers a sudden deflection and acceleration. As a result, a part or all of its energy is dissociated from it and propagates in space as electromagnetic radiation. The mechanism of bremsstrahlung production is illustrated in Figure I-2.

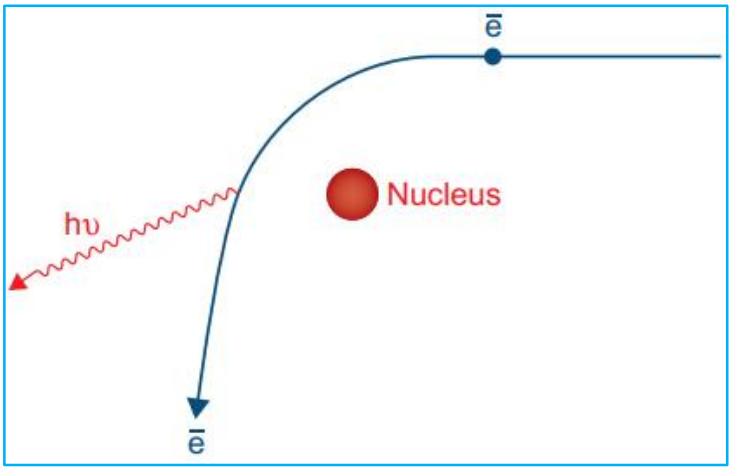

Figure I-2 Illustration of the bremsstrahlung process.

I.2.2.2 Characteristic X-Rays

Electrons incident on the target also produce characteristic x-rays. The mechanism of their production is illustrated in Figure I-3. An electron, with kinetic energy E0, may interact with the atoms of the target by ejecting an orbital electron, such as a K, L, or M electron, leaving the atom ionized. The original electron will recede from the collision with energy E0 – ΔE, where ΔE is the energy given to the orbital electron. A part of ΔE is spent in overcoming the binding energy of the electron and the rest is carried by the ejected electron. When a vacancy is created in an orbit, an outer orbital electron will fall down to fill that vacancy. In so doing, the energy is radiated in the form of electromagnetic radiation. This is called characteristic radiation.

It should be noted that, unlike bremsstrahlung, characteristic x-rays are emitted at discrete energies. If the transition involved an electron descending from the L shell to the K shell, then the photon emitted will have energy $h\upsilon = E_K - E_L$, where E_K and E_L are the electron-binding energies of the K shell and the L shell, respectively [3].

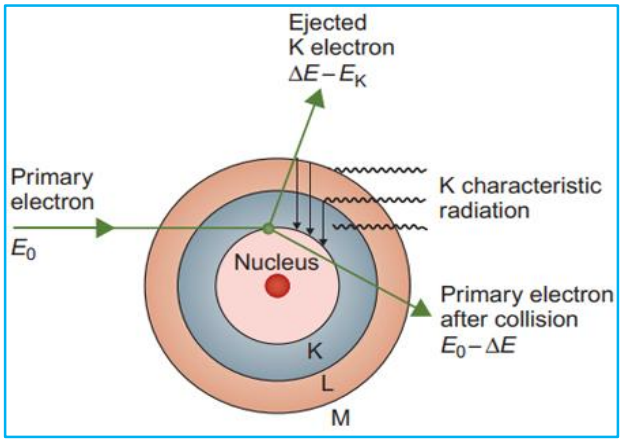

Figure I-3 Diagram to explain the production of characteristic

I.2.3 Interactions of Photons with Matter

I.2.3.1 Photoelectric Effect

The photoelectric effect is a phenomenon in which a photon is absorbed by an atom, and as a result one of its orbital electrons is ejected (Figure I-4). In this process, the entire energy ($h\upsilon$) of the photon is first absorbed by the atom and then essentially all of it is transferred to the atomic electron. The kinetic energy of the ejected electron (called the photoelectron) is equal to $h\upsilon - E_B$, where E_B is the binding energy of the electron. Interactions of this type can take place with electrons in the K, L, M, or N shells.

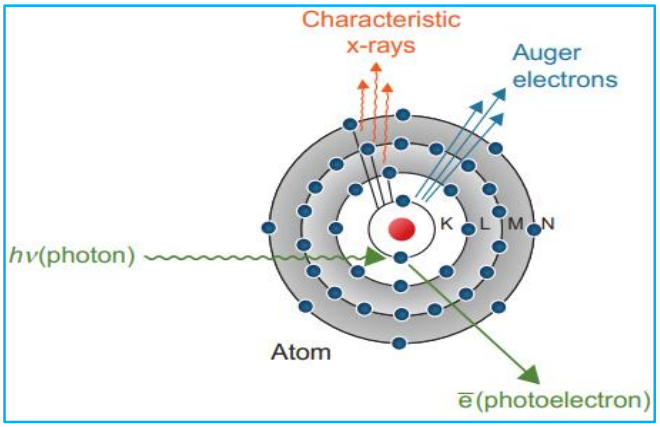

Figure I-4 Illustration of the photoelectric.

After the electron has been ejected from the atom, a vacancy is created in the shell, thus leaving the atom in an excited state. The vacancy can be filled by an outer orbital electron with the emission of a characteristic x-ray.

I.2.3.2 Compton Effect

In the Compton process, the photon interacts with an atomic electron as though it were a "free" electron, that is, the binding energy of the electron is much less than the energy of the bombarding photon. In this interaction, the electron receives some energy from the photon and is emitted at an angle θ (Figure I-5). The photon, with reduced energy, is scattered at an angle ϕ.

The Compton process can be analyzed in terms of a collision between two particles, a photon and an electron. By applying the laws of conservation of energy and momentum, one can derive the following relationships:

$$E = h\upsilon_0 \frac{\alpha(1-\cos\phi)}{1+\alpha(1-\cos\phi)}$$

Equation I-1 Energy of scattered electron

where $h\upsilon_0$, and E are the energies of the incident photon, and scattered electron, respectively.

and $$\alpha = \frac{h\upsilon_0}{m_0 c^2}$$

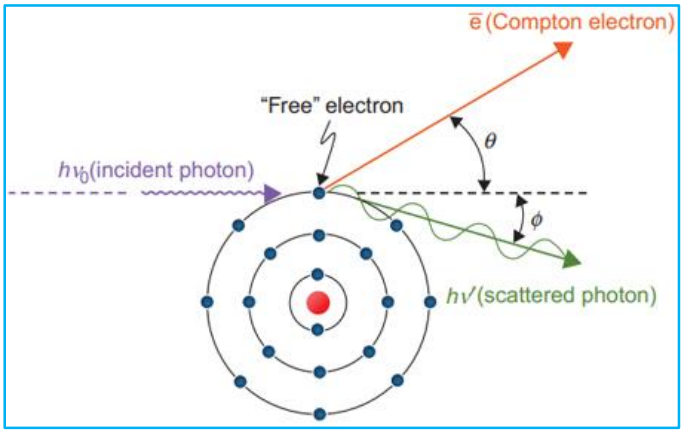

Figure I-5 Diagram illustrating the Compton

I.2.4 Pair Production

If the energy of the photon is greater than 1.02 MeV, the photon may interact with matter through the mechanism of pair production. In this process (Figure I-6), the photon interacts strongly with the electromagnetic field of an atomic nucleus and gives up all its energy in the process of creating a pair consisting of a negative electron (e-) and a positive electron (e+). Because the rest mass energy of the electron is equivalent to 0.51 MeV, a minimum energy of 1.02 MeV is required to create the pair of electrons. Thus, the threshold energy for the pair production process is 1.02 MeV.

The photon energy in excess of this threshold is shared between the particles as kinetic energy. The total kinetic energy available for the electron–positron pair is given by ($h\upsilon$ – 1.02) MeV [4].

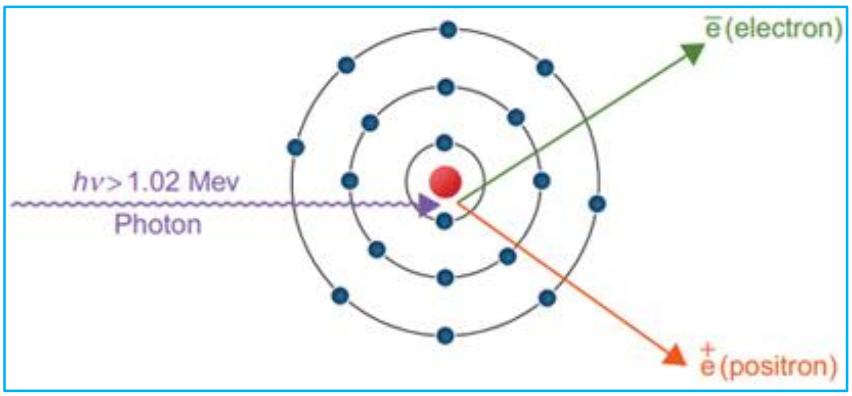

Figure I-6 The Diagram illustrating the pair production .

Note:

According to (Figure I-7), Below 0.1 MeV, we find almost totally photoelectric processes occurring, then between 0.1 MeV and 2.5 MeV we can detect both photoelectric and Compton processes and finally, as the energy level rises above to between 2.5 MeV and 100 MeV, we can observe both Compton scattering and pair production [5].

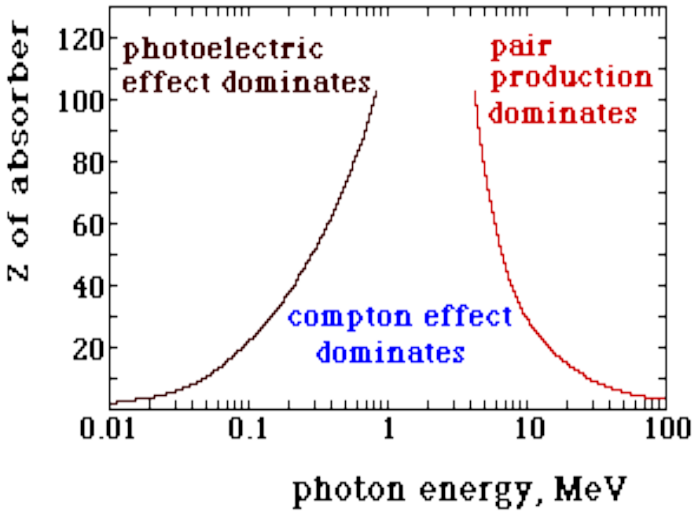

Figure I-7 Energy Dependent Photoelectric Effect, Compton Scattering and Pair.

I.3 Radiobiology Basics

I.3.1 Irradiation of Cells

When cells are exposed to ionizing radiation the standard physical effects between radiation and the atoms or molecules of the cells occur first and the possible biological damage to cell functions follows later. The biological effects of radiation result mainly from damage to the DNA,

which is the most critical target within the cell; however, there are also other sites in the cell that, when damaged, may lead to cell death. When directly ionizing radiation is absorbed in biological material, the damage to the cell may occur in one of two ways: direct or indirect.

I.3.2 Direct Action in Cell Damage by Radiation

In direct action the radiation interacts directly with the critical target in the cell. The atoms of the target itself may be ionized or excited through Coulomb interactions, leading to the chain of physical and chemical events that eventually produce the biological damage. Direct action is the dominant process in the interaction of high LET particles with biological material.

I.3.3 Indirect action in cell damage by radiation

In indirect action the radiation interacts with other molecules and atoms (mainly water, since about 80% of a cell is composed of water) within the cell to produce free radicals, which can, through diffusion in the cell, damage the critical target within the cell. In interactions of radiation with water, short lived yet extremely reactive free radicals such as H_2O^+ (water ion) and OH- (hydroxyl radical) are produced. The free radicals in turn can cause damage to the target within the cell.

The free radicals that break the chemical bonds and produce chemical changes that lead to biological damage are highly reactive molecules because they have an unpaired valence electron.

The steps involved in producing biological damage by the indirect action of X rays are as follows:

- Step 1: Primary photon interaction (photoelectric effect, Compton effect and pair production) produces a high energy electron.
- Step 2: The high energy electron in moving through tissue produces free radicals in water.
- Step 3: The free radicals may produce changes in DNA from breakage of chemical bonds.
- Step 4: The changes in chemical bonds result in biological effects.

Step (1) is in the realm of physics; step (2) is in chemistry; steps (3) and (4) are in radiobiology.

I.3.4 Fate of Irradiated Cells

Irradiation of a cell will result in one of the following nine possible outcomes:

- No effect.
- Division delay: The cell is delayed from going through division.
- Apoptosis: The cell dies before it can divide or afterwards by fragmentation into smaller bodies, which are taken up by neighboring cells.

- Reproductive failure: The cell dies when attempting the first or subsequent mitosis.
- Genomic instability: There is a delayed form of reproductive failure as a result of induced genomic instability.
- Mutation: The cell survives but contains a mutation.
- Transformation: The cell survives but the mutation leads to a transformed phenotype and possibly carcinogenesis.
- Bystander effects: An irradiated cell can send signals to neighboring unirradiated cells and induce genetic damage in them.
- Adaptive responses: The irradiated cell is stimulated to react and become more resistant to subsequent irradiation.

I.3.5 Radiation Damage

I.3.5.1 Classification of radiation damage

Radiation damage to mammalian cells is divided into three categories:

- Lethal damage, which is irreversible, irreparable and leads to cell death.
- Sub-lethal damage, which can be repaired in hours unless additional sub-lethal damage is added that eventually leads to lethal damage.
- Potentially lethal damage, which can be manipulated by repair when cells are allowed to remain in a non-dividing state.

I.3.5.2 Somatic and genetic effects

The effects of radiation on the human population can be classified as either somatic or genetic:

- Somatic effects are harm that exposed individuals suffer during their lifetime, such as radiation induced cancers (carcinogenesis), sterility, opacification of the eye lens and life shortening.
- Genetic or hereditary effects are radiation induced mutations to an individual's genes and DNA that can contribute to the birth of defective descendants.

I.3.5.3 Stochastic and deterministic (non-stochastic) effects

The harmful effects of radiation may be classified into two general categories: stochastic and deterministic (previously called non-stochastic). The National Council on Radiation Protection and Measurements (NCRP) defines these effects as follows:

- A stochastic effect is one in which the probability of occurrence increases with

increasing dose but the severity in affected individuals does not depend on the dose (induction of cancer, radiation carcinogenesis and genetic effects). There is no threshold dose for effects that are truly stochastic, because these effects arise in single cells and it is assumed that there is always some small probability of the event occurring even at very small doses.

- A deterministic effect (tissue reaction) is one that increases in severity with increasing dose, usually above a threshold dose, in affected individuals (organ dysfunction, fibrosis, lens opacification, blood changes and decrease in sperm count). These are events caused by damage to populations of cells, hence the presence of a threshold dose [6].

I.4 Radiotherapy and treatment Basics

I.4.1 Caner and Radiotherapy concepts

Cancer: a general term for more than 100 diseases that have uncontrolled, abnormal growth of cells that can invade and destroy healthy tissues. [Basic Radiation therapy Terms, n.d.].

Tumor: an abnormal lump or mass of tissue. Tumors are either benign (not cancer) or malignant (cancer) [7].

Primary Tumor: is the original site where the tumor was first discovered or originated. This is like having a single mass that's in the lung. This would be the primary source of lung cancer.

Metastatic Tumor: is a tumor that's spread to another part of the body as a result of the original tumor. This would be like having a mass in the liver or the adrenal gland that came or was metastatic from the primary lung tumor [7].

The TNM system: for describing the anatomical extent of disease is based on the assessment of three components: T – The extent of the primary tumor, N – The absence or presence and extent of regional lymph node metastasis, M – The absence or presence of distant metastasis The addition of numbers to these three components indicates the extent of the malignant disease, thus: T0, T1, T2, T3, T4 - N0, N1, N2, N3 - M0, M1 [8].

x-ray: a form of radiation that can be used either at low levels to make an picture of the inside of the body on film or at high levels to kill cancer cells.

radiation: energy carried by waves or a stream of particles. Types of radiation used to treat cancer include x-ray, electron beam, alpha and beta particle, and gamma ray.

Radioactive substances include forms of cobalt, radium, iridium, cesium, iodine, strontium, samarium, phosphorus, and palladium [7].

Kerma: is a measure of energy transferred from radiation to matter and is an acronym for kinetic energy released in matter. It is related to, but not the same as absorbed dose. Kerma is measured by the SI unit, the gray (joules per kilogram).

Absorbed Dose: absorbed dose, or simply dose, is the quotient of $\frac{d\mathrm{E}}{dm}$ where $d\mathrm{E}$ is the mean energy imparted by ionizing radiation to material of mass dm [4]. The SI unit for absorbed dose is gray (Gy) and is defined as: 1 Gy = 1 J/kg.

Simulation: a process involving special x-ray pictures that is used to plan radiation treatment so that the area to be treated is precisely located and marked

Radiation oncologist: a doctor who specializes in using radiation to treat cancer.

Medical oncologist: a doctor who is specially trained in the diagnosis and treatment of cancer and who specializes in the use of chemotherapy and other drugs to treat cancer.

Radiation physicist: a person trained to ensure that the radiation machine delivers the right amount of radiation to the treatment area. This person works with the radiation oncologist and dosimetrist to design, plan, and calculate the proper dose for radiation treatment.

Dosimetrist: a person who plans and calculates the proper radiation dose for treatment.

Fractions: the smaller, divided doses of radiation that are given each day.

Treatment field (or port): the place on the body at which the radiation beam is aimed.

Linear accelerator (Linac): a machine that creates high-energy radiation to treat cancers using electricity to form a beam of fast-moving subatomic particles. Also called mega-voltage (MeV) linear accelerator or a linac.

External radiation (EBRT): radiation therapy that uses a machine located outside of the body to aim high-energy rays at cancer cells.

Conformal radiation therapy (3D-CRT): a newer type of radiation treatment that uses a special computer to help shape the beam of radiation to match the shape of the tumor and delivers the beam from different directions. This reduces the amount of exposure to nearby healthy tissues.

Intensity modulated radiation therapy (IMRT): an advanced method of conformal radiation therapy in which the beams are aimed from many directions and the intensity (strength) of the beams is controlled by computers. This allows more radiation to reach the treatment area while reducing the radiation to healthy tissues.

Volumetric modulated arc therapy (VMAT) is a novel radiation therapy technique that delivers the radiation dose continuously as the treatment machine rotates. This technique accurately shapes the radiation dose to the tumor while minimizing the dose to the organs surrounding the tumor. VMAT works similarly to intensity-modulated radiation therapy (IMRT) in the way the radiation dose is varied throughout treatment.

Intraoperative radiation (IORT): a type of external radiation therapy used to deliver a large dose of radiation to the tumor and surrounding tissue during surgery.

Stereotactic radiosurgery (SRS): a type of radiation treatment that gives a large dose of radiation to a small tumor area, usually in a single session. It is mostly used for brain tumors and other tumors inside the head. Though it is not surgery, it is able to focus the radiation on small areas. There are different types of equipment for this, such as the X-Knife, Cyber Knife, Clinac, and Gamma Knife. Sometimes doctors give the radiation in many smaller treatments to deliver the same or slightly higher dose. This is sometimes called fractionated radiosurgery or stereotactic radiotherapy [7].

I.4.2 Common Types of Cancer Treatment

I.4.2.1 Surgery

Many people with cancer have surgery, especially if the cancer seems to be contained in one area (localized). Surgery may be used to remove it along with any nearby tissue that might contain cancer cells.

Sometimes it's hard to tell how much surgery is needed until the surgeon sees the extent of the cancer during the operation. Surgery is most successful when the tumor has not spread to other areas. Surgery offers the greatest chance of a cure for many types of cancer. It may also be used to treat problems caused by cancer, such as taking out a tumor that's blocking the intestine.

Other treatments, such as radiation therapy and chemotherapy, may be used along with surgery. They may be given before or after the surgery.

I.4.2.2 Radiation therapy

Like surgery, radiation therapy is used mostly to treat localized cancers – those contained in one area. Radiation destroys cancer cells or damages them so they can't grow. It can be used alone or along with surgery or chemotherapy. More than half of all people with cancer get radiation at some point.

I.4.2.2.1 How is radiation given?

Radiation is given by two ways: either high-energy rays are aimed from a machine (external radiation) or implants are put into the body near the tumor.

External radiation (EBRT): Getting external radiation is painless, much like having an x-ray taken. It's usually done in an outpatient setting, and the treatments take very little time. Treatment is most often given 5 days a week for 5 to 8 weeks, depending on the size, place, and type of cancer being treated.

I.4.2.2.2 Radiation implants

In some cases, radiation may be given through implants placed inside the body. Another name for radiation given as an implant is brachytherapy.

This type of radiation uses small containers of radiation that are placed in or near the tumor. Implants allow a person to get a higher total dose of radiation to a smaller area and in a shorter amount of time than with external radiation.

I.4.2.2.3 Side effects of radiation therapy

Side effects vary from patient to patient. The most common side effects are feeling tired, skin changes in the area of treatment, and some loss of appetite. Other side effects usually are related to the treatment of specific areas, such as hair loss after radiation treatment to the head.

Most side effects go away in time, but some might last or might not show up until years later.

I.4.2.3 Chemotherapy

Chemotherapy: is treatment with strong drugs that are most often given by mouth or by injection. In most cases, more than one chemo drug is used. Unlike radiation therapy or surgery, chemo drugs can treat cancers that have spread throughout the body because they travel through the bloodstream. It's given for different reasons, depending on the type of cancer and its stage.

Chemo can be used to:

- Cure the cancer.
- Keep it from spreading.
- Kill cancer cells that may have already spread.
- Slow the cancer's growth.
- Relieve symptoms caused by cancer.
- Shrink a tumor before surgery is done to remove it.
- Lower the risk of cancer coming back after surgery.

I.4.2.4 Hormone Therapy

Hormone therapy is a cancer treatment that slows or stops the growth of cancer that uses hormones to grow.

Hormone therapy is used to:

- Treat cancer: Hormone therapy can lessen the chance that cancer will return or stop or slow its growth.
- Ease cancer symptoms: Hormone therapy may be used to reduce or prevent symptoms
- in men with prostate cancer who are not able to have surgery or radiation therapy.

I.4.2.5 Targeted Therapy

Targeted therapy is the foundation of precision medicine. It is a type of cancer treatment that targets the changes in cancer cells that help them grow, divide, and spread. As researchers learn more about the cell changes that drive cancer, they are better able to design promising therapies that target these changes or block their effects.

I.4.2.6 Immunotherapy

Immunotherapy, also called biologic therapy, is a type of cancer treatment that boosts the body's natural defenses to fight cancer. It uses substances made by the body or in a laboratory to improve or restore immune system function. Immunotherapy may work by:

- Stopping or slowing the growth of cancer cells.
- Stopping cancer from spreading to other parts of the body.
- Helping the immune system work better at destroying cancer cells [9].

I.5 Conclusion

It is so important to understand the processes of treating cancer which begins in physics level by the interaction of radiation with the matter, then the chemical transformation of the DNA, which lead to biological changes of the cells may lead to its death. Also knowing the technologies exist in radiotherapy field and the characteristics of using treatment by radiation for cancer [10].

Challenge of Breast Cancer Pathology

II.1 Introduction

About 1 in 8 U.S. women (about 12%) will develop invasive breast cancer over the course of her lifetime. in 2019, an estimated 268,600 new cases of invasive breast cancer are expected to be diagnosed in women in the U.S, along with 62,930 new cases of non-invasive (in situ) breast cancer.

About 85% of breast cancers occur in women who have no family history of breast cancer. These occur due to genetic mutations that happen as a result of the aging process and life in general, rather than inherited mutations [11].

II.2 The Breasts

Inside a woman's breast are 15 to 20 sections (lobes). Each lobe is made of many smaller sections (lobules). Lobules have groups of tiny glands that can make milk.

After a baby is born, breast milk flows from the lobules through thin tubes (ducts) to the nipple. Fibrous tissue and fat fill the spaces between the lobules and ducts. (Figure II-1).

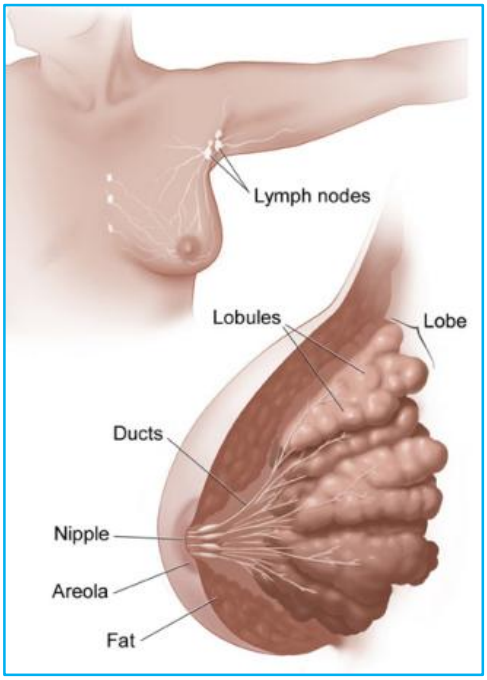

Figure II-1 The lobes and ducts inside the breast and the lymph nodes near the breast.

II.3 Cancer Cells

Cancer begins in cells, the building blocks that make up all tissues and organs of the body, including the breast. Normal cells in the breast and other parts of the body grow and divide to form new cells as they are needed. When normal cells grow old or get damaged, they die, and new cells

take their place. Sometimes, this process goes wrong. New cells form when the body doesn't need them, and old or damaged cells don't die as they should. The buildup of extra cells often forms a mass of tissue called a lump, growth, or tumor.

Tumors in the breast can be **benign** (not cancer) or **malignant** (cancer):

A. **Benign tumors:**
   - Are usually not harmful.
   - Rarely invade the tissues around them.
   - Don't spread to other parts of the body.
   - Can be removed and usually don't grow back.

B. **Malignant tumors:**
   - May be a threat to life
   - Can invade nearby organs and tissues (such as the chest wall)
   - Can spread to other parts of the body
   - Often can be removed but sometimes grow back.

Breast cancer cells can spread by breaking away from a breast tumor. They can travel through blood vessels or lymph vessels to reach other parts of the body. After spreading, cancer cells may attach to other tissues and grow to form new tumors that may damage those tissues.

For example, breast cancer cells may spread first to nearby lymph nodes. Groups of lymph nodes are near the breast under the arm (axilla), above the collarbone, and in the chest behind the breastbone.

When breast cancer spreads from its original place to another part of the body, the new tumor has the same kind of abnormal cells and the same name as the primary (original) tumor. For example, if breast cancer spreads to a lung, the cancer cells in the lung are actually breast cancer cells. The disease is metastatic breast cancer, not lung cancer. For that reason, it's treated as breast cancer, not lung cancer [12].

II.4 Facts about Breast cancer

- Each year, approximately 70,000 men and women age 15 to 39 are diagnosed with cancer in the US. Breast cancer is the most common cancer for women in this age group.
- Every year, more than 1,000 women under age 40 die from breast cancer.
- Breast cancer is the most common form of cancer in women who are pregnant or have recently given birth, occurring once in every 3,000 pregnancies. An estimated 30% or more

of all breast cancer in young women is diagnosed in the few years after a woman has had a baby.

- Compared to older women, young women generally face more aggressive cancers and lower survival rates. More and more evidence tells us that breast cancer before age 40 differs biologically from the cancer faced by older women.
- The incidence of metastatic breast cancer at the time of initial diagnosis is apparently rising in women under the age of 40 [13].
- Breast cancer needs a wide range of treatments, including surgery, radiation therapy, chemotherapy, and hormonotherapy [14].
- Brest cancer takes a long time to be full treated, an "average case" of early-stage breast cancer could take a year for diagnosis and treatment with short-term recovery.(March 15 & 2019, n.d.)
- Breast cancer has a critic localization (close to heart and lung), especially for the left side breast [15].
- Breast cancer most commonly spreads to the bones, liver, lungs, and brain. It is still called breast cancer, even after it has spread. Metastatic breast cancer is not curable, but it is treatable [16].

II.5 Breast Cancer Types

There are many types of breast cancer. The most common types are ductal carcinoma in situ, invasive ductal carcinoma, and invasive lobular carcinoma. The following terms are used to describe the extent of the cancer:

- In situ breast cancers have not spread.
- Invasive or infiltrating cancers have spread (invaded) into the surrounding breast tissue.

The most common kinds of breast cancer are carcinomas, and are named basing on where they form and how far they have spread. These general kinds of breast cancer below can be further described with the terms outlined above.

II.5.1 In situ cancers

Ductal carcinoma in situ (DCIS; also known as intraductal carcinoma), is a non-invasive or pre-invasive breast cancer.

Lobular carcinoma in situ (LCIS; may also be called lobular neoplasia), This breast change is not a cancer, though the name can be confusing. In LCIS, cells that look like cancer cells are growing

in the lobules of the milk-producing glands of the breast, but they don't grow through the wall of the lobules.

II.5.2 Invasive (infiltrating) breast cancer

Breast cancers that have spread into surrounding breast tissue are known as invasive breast cancer. There are many different kinds of invasive breast cancer, but the most common are called invasive ductal carcinoma and invasive lobular carcinoma [17].

II.6 Causes and risk factors of Breast cancer

There are a number of factors that have been shown to increase a woman's risk of developing breast cancer:

Age: The majority of breast cancer cases occur in women over the age of 50.

Family history: If a woman has a personal or family history of breast cancer, she is at increased risk of developing breast cancer.

Clinical history: Women who have previously suffered with benign breast cancer are at greater risk of developing breast cancer in the future.

A late first pregnancy: Women who have a late first pregnancy (after the age of 35) are more likely to develop breast cancer.

Prolonged hormonal exposure: a long menstrual life or possibly use of hormone replacement therapy after the menopause expose women to an increased risk of developing breast cancer.

Lifestyle factors: For example, being overweight or obese after the menopause, physical inactivity, a high fat diet and high alcohol consumption can play an important role in the development of breast cancer [18].

Radiation exposure: Undergoing radiation treatment for a cancer that is not breast cancer increases the risk of breast cancer later in life [14].

II.7 Breast cancer Stages

Cancer is staged according to the size of the tumor and whether it has spread to lymph nodes or other parts of the body. There are different ways of staging breast cancer. One way is from Stage 0 to 4, but these may be broken down into smaller stages.

Stage 0: Known as ductal carcinoma in situ (DCIS), the cells are limited to within a duct and have not invaded surrounding tissues.

Stage 1: At the beginning of this stage, the tumor is up to 2 centimeters (cm) across and it has not affected any lymph nodes.

Stage 2: The tumor is 2 cm across and it has started to spread to nearby nodes.

Stage 3: The tumor is up to 5 cm across and it may have spread to some lymph nodes.

Stage 4: The cancer has spread to distant organs, especially the bones, liver, brain, or lungs [14].

Generally, there are three main stages of breast cancer:

Early stage: which refers to cancer that is confined to the fatty tissue of the breast.

Locally advanced: which has spread to underlying tissue of the chest wall.

Advanced or metastatic: where the tumor has spread to other parts of the body.

Approximately one third of breast cancer cases are diagnosed after the cancer has spread beyond the primary tumor site (metastasized) (Figure II-2) [18].

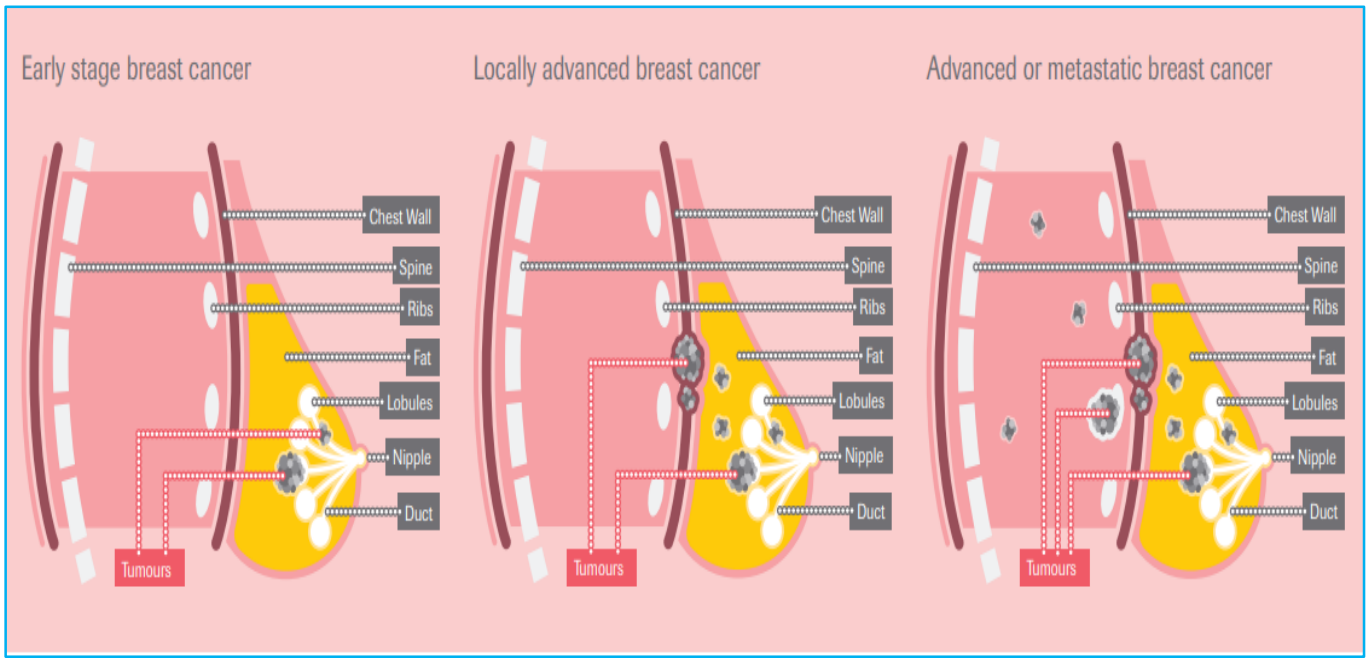

Figure II-2 Illustration of breast cancer staging.

II.8 Breast Diagnosis

A diagnosis often occurs as the result of routine screening, or when a woman approaches her doctor after detecting symptoms.

Some diagnostic tests and procedures help to confirm a diagnosis.

II.8.1 Imaging tests

A mammogram: is a type of x-ray commonly used for initial breast cancer screening. It produces images that can help detect any lumps or abnormalities. A suspicious result can be followed up by further diagnosis. However, mammography sometimes shows up a suspicious area that is not cancer. This can lead to unnecessary stress and sometimes interventions.

An ultrasound scan: can help differentiate between a solid mass or a fluid-filled cyst.

An MRI scan involves injecting a dye into the patient, so find out how far the cancer has spread.

II.8.2 Biopsy

A sample of tissue is surgically removed for laboratory analysis. This can show whether the cells are cancerous, and, if so, which type of cancer it is, including whether or not the cancer is hormone-sensitive.

Diagnosis also involves staging the cancer, to establish:

- The size of a tumor.
- How far it has spread.
- Whether it is invasive or non-invasive.
- Whether it has metastasized, or spread to other parts of the body.

Staging will affect the chances of recovery and will help decide on the best treatment options [14].

II.9 Breast cancer treatment

Treatment will depend on:

- The type of breast cancer.
- The stage of the cancer.
- Sensitivity to hormones.
- The patient's age, overall health, and preferences.

Treatment Types: the main treatment options include:

- Radiation therapy.
- Surgery.
- Biological therapy, or targeted drug therapy.
- hormone therapy.
- Chemotherapy.

Factors affecting a person's choice will include the stage of the cancer, other medical conditions, and their individual preference.

II.9.1 Surgery:

If surgery is needed, the choice will depend on the diagnosis and the individual. Types of surgery include:

Lumpectomy: This involves removing the tumor and a small amount of healthy tissue around it. This can help prevent the spread of the cancer. This may be an option if the tumor is small and likely to be easy to separate from the tissue surrounding it.

Mastectomy: A simple mastectomy involves removing the lobules, ducts, fatty tissue, nipple, areola, and some skin. Radical mastectomy will remove muscle from the chest wall as well as the lymph nodes in the armpit.

Sentinel node biopsy: Removing one lymph node can stop the cancer spreading, because if breast cancer reaches a lymph node, it can spread farther through the lymphatic system into other parts of the body.

Axillary lymph node dissection: If there are cancer cells on a node called the sentinel node, the healthcare professional may recommend removing several lymph nodes in the armpit to prevent the spread of disease.

Reconstruction: Following breast surgery, a surgeon can perform a reconstruction to recreate the breast so that it looks similar to the other one. They can do this at the same time as performing a mastectomy, or at a later date. They may use a breast implant, or tissue from another part of the patient's body.

II.9.2 Radiation therapy

Controlled doses of radiation are targeted at the tumor to destroy the cancer cells. A person may undergo this from around a month after surgery, along with chemotherapy. This works to kill any remaining cancer cells.

Each session lasts for a few minutes, and a person may need three to five sessions per week for 3-6 weeks, depending on the aim and the extent of the cancer.

The type of breast cancer will dictate what type of radiation therapy, if any, is the most suitable.

Adverse effects include fatigue, lymphedema, darkening of the breast skin, and irritation of the breast skin.

II.9.3 Chemotherapy

A doctor may prescribe cytotoxic drugs may be used to kill cancer cells, if there is a high risk of recurrence or spread. This is called adjuvant chemotherapy.

If a tumor is large, a specialist may choose to administer chemotherapy before the surgery to shrink the tumor and make its removal easier. This is called neo-adjuvant chemotherapy.

Chemotherapy can also treat cancer that has metastasized, or spread to other parts of the body, and it can reduce some symptoms. This is especially true in the later stages. It can also reduce estrogen production, as estrogen can encourage the growth of some breast cancers.

Adverse effects of chemotherapy may include:

- Nausea.
- Vomiting.
- Loss of appetite.
- Fatigue.
- Sore mouth.
- Hair loss.
- A slightly higher susceptibility to infections.

Medications can help control many of these side effects [14].

II.10 Side Effects of radiotherapy in breast cancer treatment

Radiotherapy can cause side-effects. Side-effects happen because radiotherapy affects normal cells as well as cancer cells. side-effects will generally be limited to the area being treated.

Normal cells are able to recover, but they might be damaged in the short or long term by the effects of radiation. Most side-effects are temporary, but some might be permanent. Some side-effects might even occur months or years after treatment.

Each person reacts differently to treatment, but certain side-effects are more common than others.

Common Side Effects:

- Skin reactions:

Most people have some redness around the area being treated. The skin may also:

- Become pinker or darker over time.
- Feel tender, dry, itchy and sore.
- Peel or flake as treatment goes on.

- Blister or become moist and weepy.

Skin reactions usually begin around 10 to 14 days after starting treatment, but can happen later or after it has finished.

- Swelling of the breast.
- Pain in the breast or chest area.
- Hair loss in the armpit.
- Sore throat.
- Tiredness and fatigue.
- Lymphedema.
- Change in breast shape, size and color.
- Tenderness over the ribs.

II.11 Late side effects

Some side effects can develop months or years after the end of radiotherapy. However, improvements with the equipment and accuracy in marking the exact areas to be treated have made many of these side effects much less common. Serious side effects are very rare and experts agree that the benefits of radiotherapy in reducing the chances of breast cancer returning outweigh the risk of possible side effects.

II.11.1 Hardening of tissue

Radiotherapy to the breast or under the arm can cause hardening of the tissue. This is known as fibrosis. If the fibrosis is severe, the breast can become noticeably smaller as well as firmer. This is rare but may happen several months or years after radiotherapy has finished.

II.11.2 Broken blood vessels

You may see tiny broken blood vessels under the skin. This is known as telangiectasia. It's permanent and there's no treatment for it.

II.11.3 Effects on the lung or heart

Sometimes after treatment to the breast or chest wall area, part of the lung behind the treatment area can become inflamed, causing a dry cough or shortness of breath. This usually heals by itself over time. More rarely, fibrosis of the upper lung can occur, causing similar side effects.

Although particular care is taken to avoid unnecessary radiotherapy to the tissues of the heart, if radiotherapy is given on the left side you may be at risk of heart problems in future.

Breath hold technique is thought to reduce the risk of any possible damage to the heart and lungs.

II.12 Other effects

Other side effects that can occur later include:

- Weakening of the bones in the treated area, which can lead to rib and collarbone fractures.
- Damage to the nerves in the arm on the treated side, which may cause tingling, numbness, pain, weakness and possibly some loss of movement
- developing another type of cancer in the future [19].

II.13 Conclusion

more than 250,000 women living in the United States today were diagnosed with breast cancer under age 40 [13].

With treatment, a woman who receives a diagnosis of stage 0 or stage 1 breast cancer has an almost **100 percent** chance of surviving for at least 5 years.

If the diagnosis is made at stage 4, the chance of surviving another 5 years is around 22 percent.

Regular checks and screening can help detect symptoms early, then women should discuss their options with a doctor. the way will assure a highly healing rate [14].

Tomotherapy and treatment procedures

III.1 Introduction

Radiation therapy, a non-invasive procedure that destroys and damages cancer cells to stop them from growing, is one the most common treatments for cancer. About half of all cancer patients will have some type of radiation therapy as part of their treatment plan [20].

Tomotherapy, the first technology of its kind, provides 3-D imaging of a tumor immediately prior to delivering radiation. With cancer patients lying on a platform, the machine takes an image of a tumor to verify its size, shape and location. Minutes later, it delivers a halo of radiation to the tumor in a spiral pattern around the patient, while minimizing contact with healthy tissue and avoiding the complications so often associated with standard radiation treatment.

Tomotherapy was discovered, developed and patented by UWCCC (University of Wisconsin Carbone Cancer Center) researchers, who first used it to treat patients in 2003.

The tomotherapy machine combines two devices into one that seamlessly detects and defines cancer tumors, then delivers appropriate doses of radiation [21].

III.2 Tomotherapy Treatment

The tomotherapy® System is a clinically proven, effective treatment platform for tumors throughout the body and can improve patients' quality of life. One of the most innovative and precise radiation therapy systems available, the tomotherapy System enables clinicians to customize treatment plans to each patient's unique needs, and relies on integrated imaging to verify tumor position to ensure accurate radiation delivery at each treatment.

The tomotherapy System is a radiation delivery system that efficiently treats cancer anywhere in the body. Designed like a CT scanner, the Tomotherapy System uses integrated imaging to enhance treatment accuracy and a unique beam delivery approach to improve treatment precision. Together, these features enable clinicians to customize treatments for each patient, minimizing exposure to surrounding healthy tissue, which can result in fewer side effects.

The Tomotherapy System can be used for virtually any case for which radiation therapy is prescribed, including those involving large tumors or multiple tumors throughout the body.

The tomotherapy System may be used as the only treatment, or in combination with surgery and/or chemotherapy. Hundreds of scientific papers have been written on the use of the tomotherapy

System in clinics worldwide. Many shows that its unique design results in superior treatment plans and improved clinical outcomes compared with traditional radiation therapy (Figure III-1).

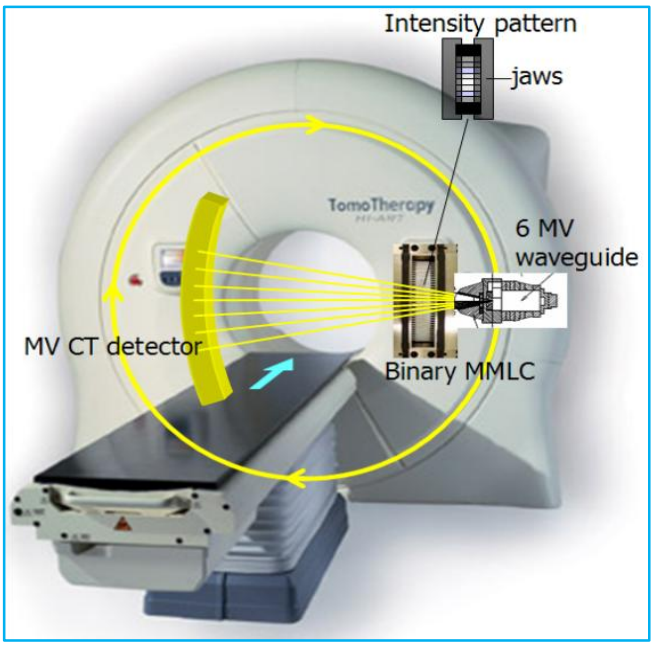

Figure III-1 Illustration of Tomotherapy Machine.

III.3 Intensity-Modulated Radiation Therapy (IMRT)

In IMRT, very small beams, or beamlets, are aimed at a tumor from many angles. During treatment, the radiation intensity of each beamlet is controlled by a device called a multileaf collimator (MLC). The collimator is a computer-controlled mechanical device that modulates the shape and amount of radiation delivered by blocking out some areas and filtering others through movement of the leaves. The beam's intensity is thus modulated to distribute the intended radiation dosage precisely in complex shapes and patterns (Figure III-2). As a result, the radiation dose is shaped to the tumor geometry and bends around important healthy tissues in a manner that would be impossible with conventional radiation techniques.

Figure III-2 Real image of Tomotherapy multileaf collimator (MLC).

III.4 Image Guidance Radiation Therapy (IGRT)

For any conformal radiotherapy system to be effective, the anatomical position of the tumor and surrounding healthy tissues must be accurately defined and localized. tomotherapy has the ability to perform a quick CT scan before each treatment starts, to ensure the patient is aligned accurately with the treatment plan. (Figure III-3). In addition to localizing the target, physicians can also monitor changes in tumor volume and anatomy during the treatment course. For example, when a tumor responds to treatment over a several week treatment course, changes in tumor anatomy or in surrounding tis sues can occur. If not recognized, the target volume may shift outside of the originally planned target, resulting in a geographic miss, potentially compromising local control or cure. With tomotherapy, review of CT imaging ensures that geographic misses do not occur.

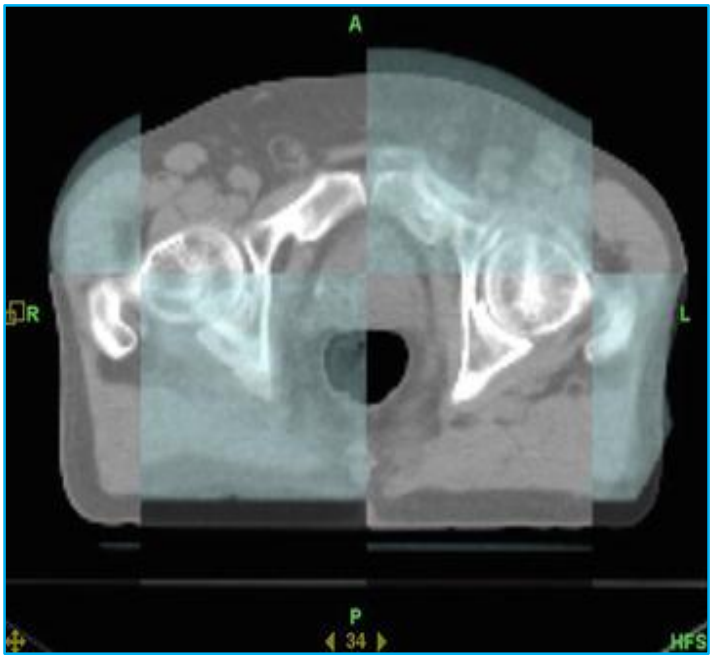

Figure III-3 Real Daily CT image of tomotherapy machine to get the fit tumor position.

III.5 IG-IMRT

Image-guided, intensity-modulated radiation therapy (IG-IMRT) is a radiation treatment guided by imaging equipment – such as CT, ultrasound or X-rays – taken in the treatment room just before radiation is given. During IG-IMRT, the images are used as a final check to ensure accurate delivery of the radiation treatment [22].

III.6 Characteristics Tomotherapy System

III.6.1 Radiation source

The beam intensity is 6 MV (LINAC mounted on CT gantry**).**

III.6.2 TomoEDGE - Dynamic Jaws

- Jaws define the field size along the y-axis: 1.05, 2.50, or 5.02 cm. FWHM at isocenter (For dynamic jaws plans, the jaws gradually open and close at the superior and inferior ends of the target). (Figure III-4).

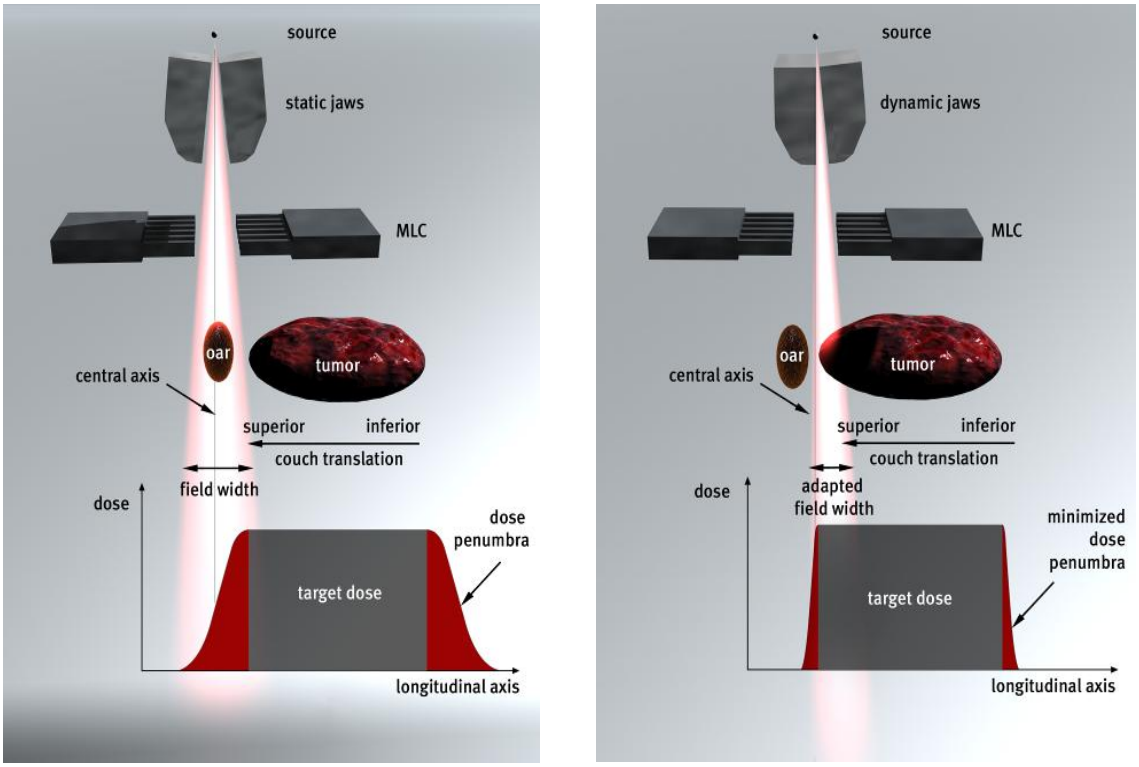

Figure III-4 Illustration of regular tomotherapy delivery (left), and the TomoEDGE.

- Leaves open and close to shape the intensity distribution across the beam.

III.6.2.1 Jaw Mode

- Fixed mode means jaws do not move during delivery.
- Dynamic mode means jaws use a running start and stop to shape the superior and inferior of penumbra.

III.6.2.2 Jaws for Prostate Cancer

Fixed Jaw Mode

- 2.5 cm jaw used to balance quality and treatment time.
- 3.4-minute treatment.

Dynamic Jaw Mode

- 90 second treatment.

- Improved OAR Sparing.

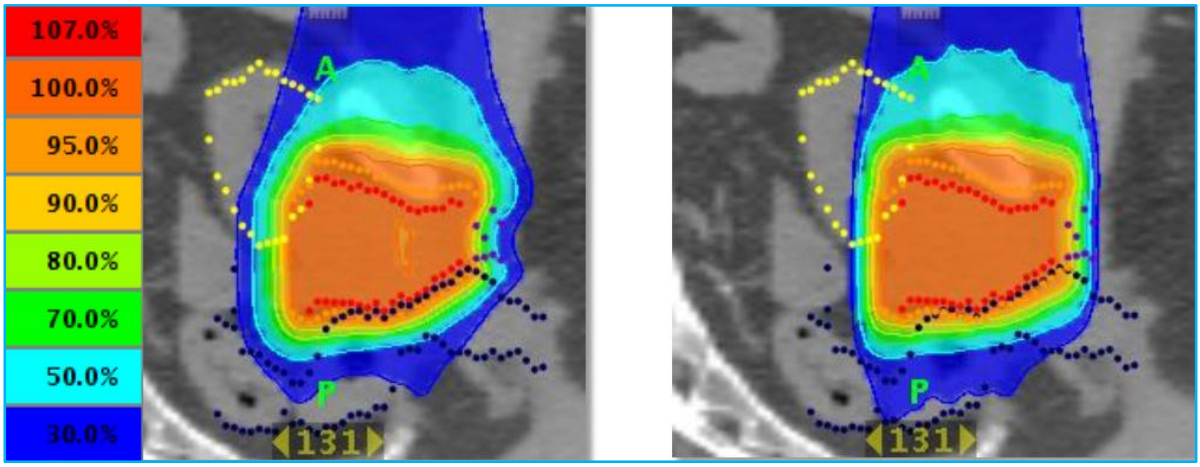

Figure III-5 Prostate dosimetric illustration of fixed jaw mode (left), and the dynamic jaw mode (right).

III.6.2.3 Jaws for Multiple Metastases

Fixed Jaw Mode

- 5 cm jaw used to deliver fast treatment.

Dynamic Jaw Mode

- Same treatment time.
- Jaws open and close for each target.

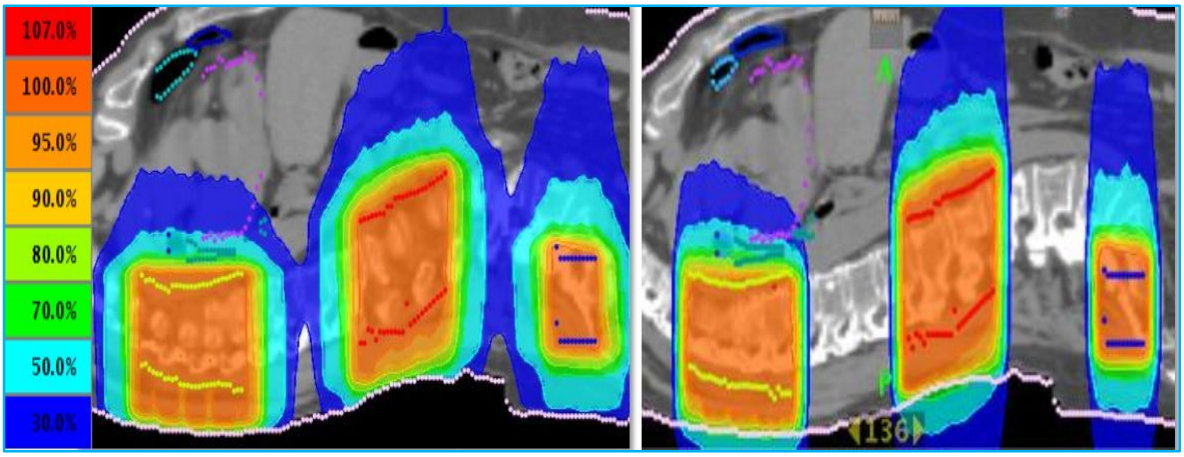

Figure III-6 Dosimetric illustration of multiple metastases of fixed jaw mode (left), and dynamic jaw mode (right).

III.6.3 Binary MLC

- There are 64 binary interlaced leaves (tongue and groove side profile), 10 cm leaf thickness in beam direction. (Figure III-7).

- Leaves are open, closed, or switching very quickly between states ~11–17 m sec transit time.
- For all plans generated on the planning system, leaves are closed for the first 10 sec of beam-on time to allow for output ramp-up.

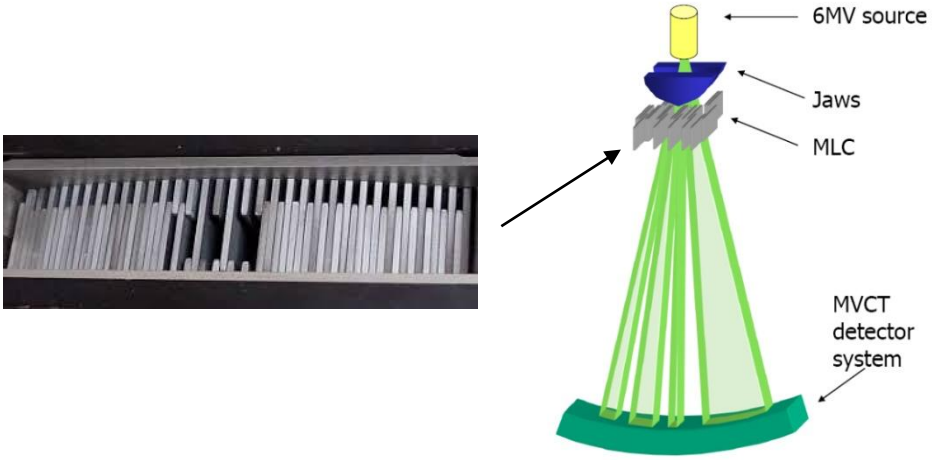

Figure III-7 Illustration of binary multileaf collimator (MLC) of Tomotherapy machine.

III.6.4 Pitch

Determines the amount of primary beam overlap along the Y axis. (Figure III-8).

- **For TomoHelical treatments:** Pitch = Couch Distance Traveled per Gantry Rotation/Field width (e.g., if the table travels 1.25 cm in one gantry rotation and the field width is 2.50 cm, the pitch is 0.5).
- **For TomoDirect treatments:** Pitch = Distance traveled by the couch between beam projections.

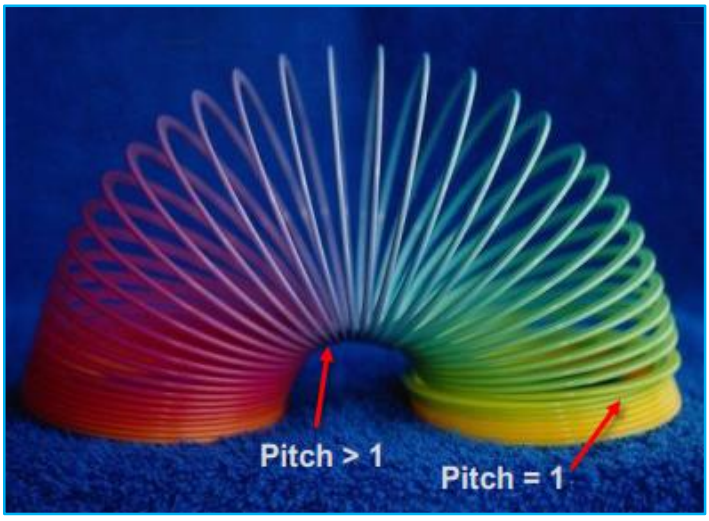

Figure III-8 Illustration of pitch concept.

III.6.5 Field width (cm)

The longitudinal thickness of radiation field at machine isocenter. Inferior and superior boundaries are defined by the full-width at half-maximum values.

III.6.6 Modulation Factor (MF)

Limits the range of leaf-open times (modulated intensities) that are allowed in the optimized plan.

- Range 1–5.
- Possible to change MF during optimization process.
- Directly affects treatment time.

III.6.7 Projections, Beamlets, and Rays

III.6.7.1 Projections

- 51 projections (beam angles) per rotation, spanning 7.06° (=360°/51) each.
- Each leaf may physically open and close up to one time per projection.
- The percentage of time for which a leaf is open determines the intensity.
- If a leaf is open for only a portion of a projection, the machine delivery will center the open time on the projection angle.
- The couch and gantry move continuously during treatment, but for calculation purposes, the couch and gantry are sampled at three equidistant positions per projection (‘super-sampling’).

III.6.7.2 Beamlets and Rays

- 64 beamlets per projection (one for each MLC leaf).
- A single gantry rotation has 51 x 64 = 3,264 beamlets.
- A treatment with 30 rotations would have 97,920 beamlets.
- Each beamlet is divided into multiple rays for dose calculations.

III.6.8 Lateral dose profile

One of the most important differences of the tomotherapy system compared to other radiation therapy systems is that it does not have a flattening filter, which would make the dose at depth more uniform. This results in the characteristic conical-shaped transverse (in-slice) fluence profile shown in Figure III-9.

The main reason for allowing the nonuniform profile is that helical tomotherapy is a dedicated IMRT system, without a need for the flat dose profile. The multileaf collimator can be used to

modulate the treatment field to produce a flat dose distribution. On the other hand, the absence of the flattening filter increases the dose output in the center of the field by approximately two-fold compared to the edge of the field. This leads to an increased average dose rate and consequently reduced treatment times for patients [23].

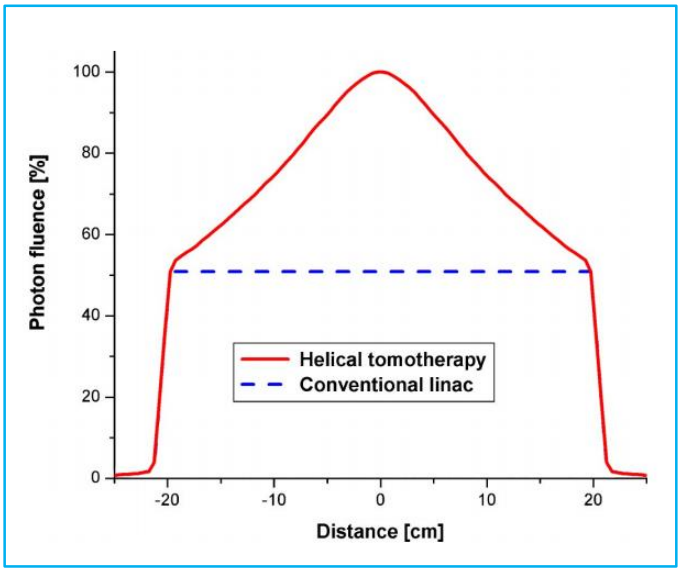

Figure III-9 The transverse dose profile of the helical tomotherapy treatment comparing with the transvers dose profile of other treatments.

III.6.9 TomoHelical Treatment Delivery Mode

The TomoHelical delivery mode provides IMRT and 3D-CRT treatment delivery in a continuous (360°) helical pattern. The TomoHelical mode is suited to the majority of clinical situations, where rotational delivery and beam modulation enhance target dose conformality and uniformity.

The user is able to create a treatment plan that defines dose goals and constraints for target and avoidance structures, the level of modulation for the plan, as well as the fractionation schedule. During treatment delivery, the linear accelerator completes multiple 360° rotations around the patient while the couch passes through the bore of the system, initiated by a single turn of the operator console key (Figure III-10).

Fixed jaw and optional dynamic jaw (TomoEDGE™) modes are available with TomoHelical. With TomoEDGE, field width varies during delivery to increase dose gradient outside the target.

Targets of up to 135 cm in length can be treated, with no need to reposition the patient and with no field junctioning.

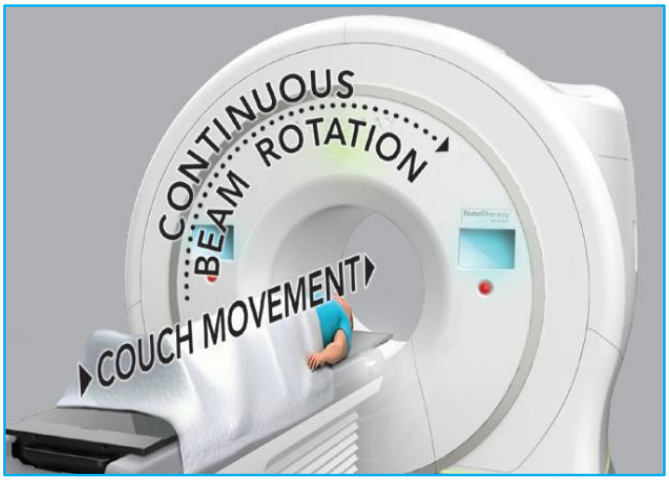

Figure III-10 The gantry rotates around the patient in TomoHelical delivery mode, delivering radiation in a continuous spiral pattern

III.6.10 TomoDirect Treatment Delivery Mode

The TomoDirect delivery mode provides IMRT and 3D-CRT treatment via a discrete angle, non-rotational delivery mode. TomoDirect allows creation of treatment plans that include between 2 and 12 target-specific gantry angles. TomoDirect complements TomoHelical in situations where a fixed-angle delivery is most appropriate (Figure III-11).

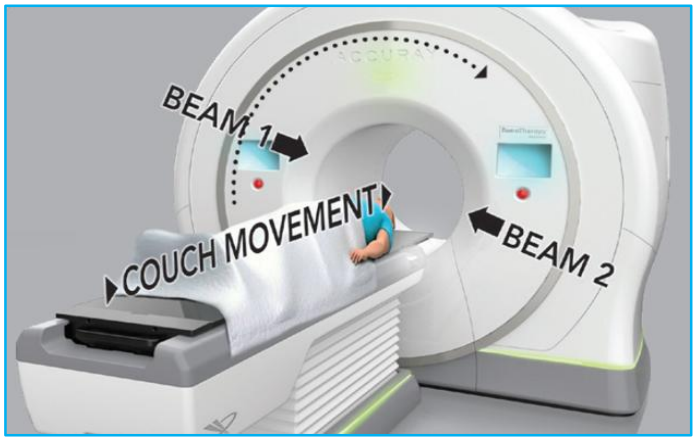

Figure III-11 2 – 12 discrete gantry angles can be used in TomoDirect delivery mode.

During treatment delivery, beams are delivered sequentially with the couch passing through the bore of the system at an appropriate speed for each beam. The complete treatment delivery is initiated by a single turn of the operator console key.

Fixed jaw and optional dynamic jaw (TomoEDGE) modes are available with TomoDirect. With TomoEDGE, field width varies during delivery to increase dose gradient outside the target. Targets of up to 135 cm in length can be treated, with no need to reposition the patient and with no field junctioning.

III.6.11 Adaptive Radiation Therapy

- Dose Monitoring.
- Re-Planning.
- Delivery Verification.

Adaptive radiation therapy (ART) is introduced to fully address any inter-fraction variations. ART is a state-of-the-art approach that uses a feedback process to account for patient-specific anatomic or biological changes during the treatment, thus delivering highly individualized radiation therapy for cancer patients.

Standard IGRT practice involves the acquisition of a volumetric image prior to each treatment fraction, which is then co-registered with the planning image to calculate a couch shift, if needed, to restore the relative location of the target volume within the treatment ports. Couch shifts however can only correct for translational errors and partially for rotational errors (Figure III-12). If substantial non-translational inter-fraction anatomic changes arise, such as changes in the size or shape of the tumor volume or OARs, or overall patient weight gain or loss, they may be identified in the daily IGRT image, which in turn can serve as the basis for a revised radiotherapy plan. Further, using robust rigid and deformable image registration (DIR) tools, the cumulative dose distribution throughout the treatment course can be quantified.

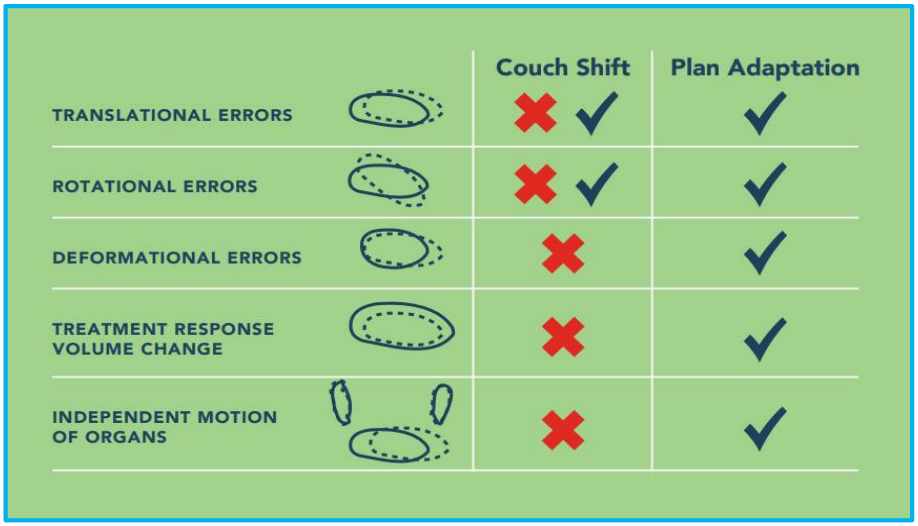

Figure III-12 A diagram illustrating the limitations of relying on couch shifts alone for plan adaptation for various inter-fraction changes to the region of interest.

In the current practice, however, analyzing inter-fraction changes from daily IGRT images is subjective, qualitative, and labor intensive. An observer on the radiotherapy team (e.g., radiation therapist, medical physicist, or reviewing physician) determines a need for ART simply by visually

inspecting the IGRT image and grossly identifying macroscopic anatomic changes relative to the original planning image, often without rigorously evaluating the dosimetric impact. Software tools that can analyze inter-fraction anatomic changes and evaluate the resulting dosimetric effects based on the IGRT image in an automatic manner are highly desirable. With such tools, determining a need for ART thus becomes objective and quantitative. The automated image registration includes no observer bias and the automated calculations of region of interest (ROI) volume and dose changes trigger predefined thresholds when clinically significant deviation occurs [24].

III.7 How is the Tomotherapy System different than conventional radiation therapy systems?

III.7.1 Precision Through Unique Delivery Modes

The Tomotherapy System is the only radiation system specifically designed for IG-IMRT. Leveraging a CT scanner-based platform, TomoHelical Mode enables continuous delivery from 360^0 degrees around the patient with highly conformal and homogeneous dose to the tumor. A clinician can also choose to deliver treatment from specific fixed angles via TomoDirect Mode.

III.7.2 Precision Through Daily Imaging

The Tomotherapy System is designed to accommodate all forms of patient and tumor motion with daily imaging. The Tomotherapy System uses daily CTrue imaging to guide the treatment each day. So, doctors can continually adjust patient treatment based on even the smallest changes in patient anatomy.

III.7.3 Why Does Precision Matter?

Technological advancements have enabled manufacturers of external-beam radiation therapy equipment to improve the precision of their delivery systems. In general:

- The radiation beam needs to enter and exit the body.
- The device design limits how radiation beams can be directed into the body.
- The device may deliver some radiation to tissue surrounding the tumor because of tumor motion during treatment.

Based on a CT scanner platform, the Tomotherapy System provide continuous delivery of radiation from 360^0 degrees around the patient, or delivery from clinician-specified beam angles.

These unique features, combined with daily 3D image guidance, enable physicians to deliver highly accurate, individualized dose distributions that precisely conform to the shape of the patient's tumor while minimizing dose to normal, healthy tissue, resulting in fewer side effects for patients.

The Tomotherapy System is capable of treating all standard radiation therapy indications including breast, prostate, lung, and head and neck cancers, in addition to complex treatments, such as total marrow irradiation (Figure III-13).

Figure III-13 Treatment of Various and complex areas with Tomotherapy system.

III.8 Tomotherapy Patient Workflow

When the patient decide to start tomotherapy treatment after the diagnosis and the staging of his cancer, he's going to pass through many stations each one has a proprieties and a trained team to work in, starting with CT simulation, then contouring, then dosimetry planning, after the treatment verification, then verification of patient position on the coach, finally the treatment delivery to patient (Figure III-14).

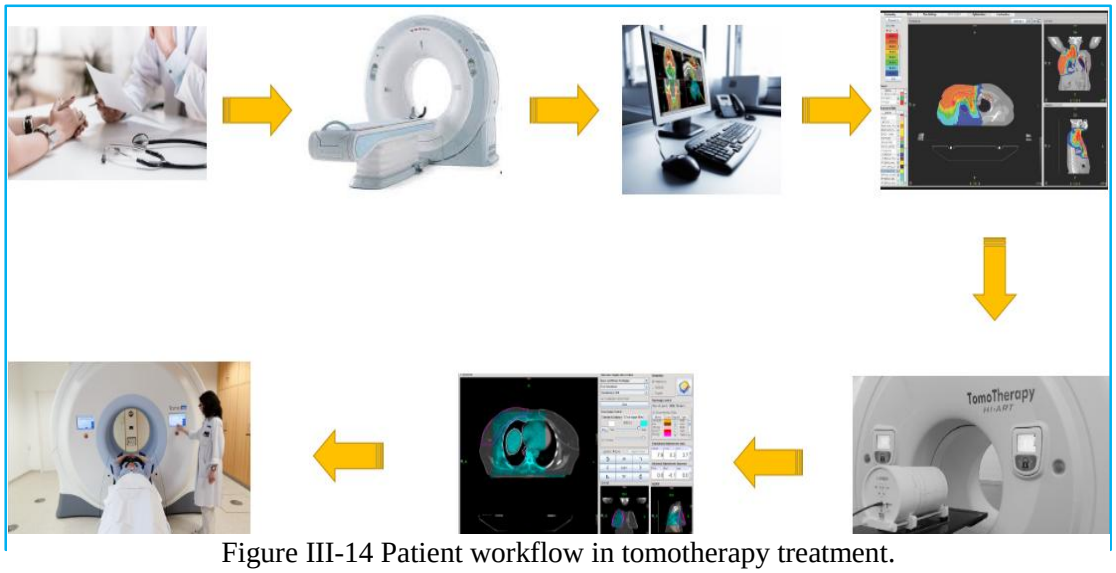

Figure III-14 Patient workflow in tomotherapy treatment.

III.8.1 3-D Imaging

This step of the process is analogous to the generic first step of radiation therapy planning as shown in Figure III-15.

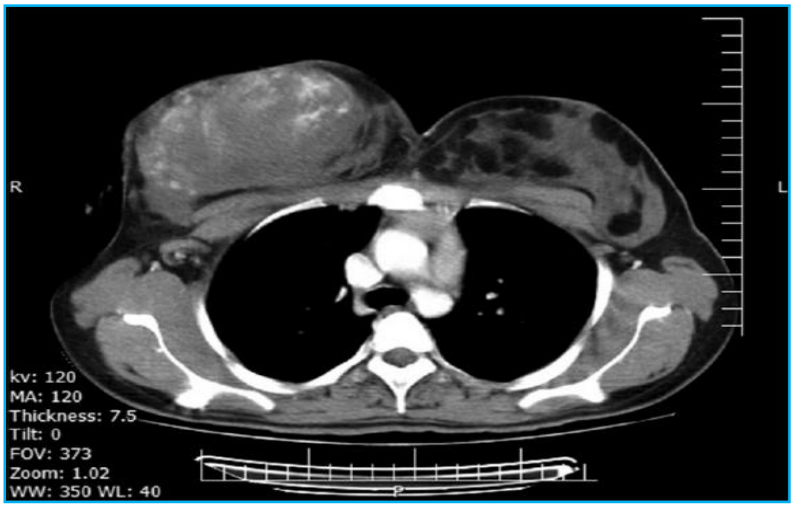

Figure III-15 CT image of breasts.

This imaging is generally performed with standard diagnostic imaging equipment or CT-simulators (Figure III-16). Under special circumstances or emergency situations (out of regular working hours), the megavoltage CT capabilities on the tomotherapy unit could be used to generate this image data for treatment planning and dose delivery purposes on short notice.

Figure III-16 GE CT simulator.

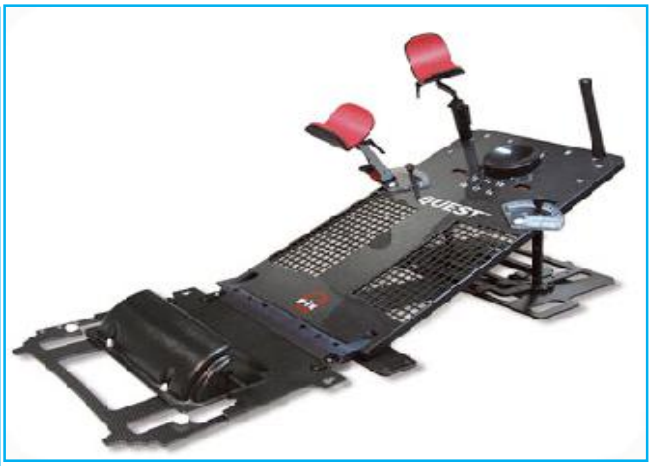

Figure III-17 Means of restraint for breast cancer imaging (Breast Board).

For some pathologic cases it may also add some means of restraint in order to take a fixed and comfortable position for the patient, in breast cancer situation we add a special equipment named a " Breast Board "to set the head, the shoulders and the hands (Figure III-17).

And for each patient we save the position references points in order to set the patient in the same position when he is on the treatment machine coach (Figure III-18).

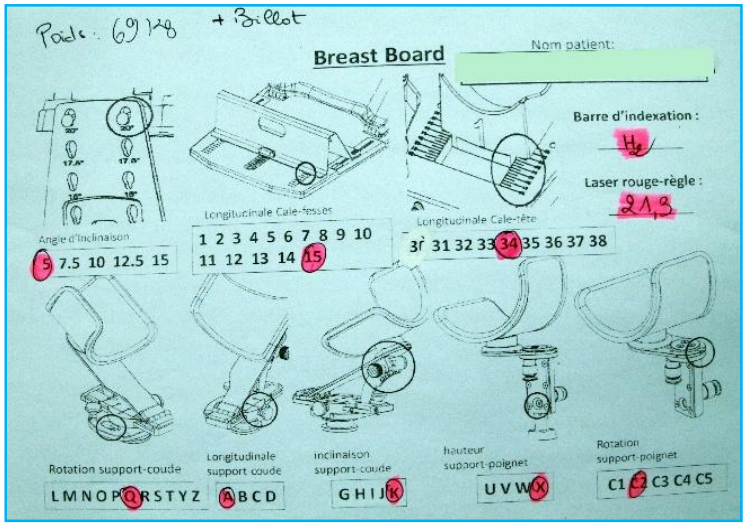

Figure III-18 Sheet of position references for breast cancer imaging.

III.8.2 Definition of Target Volume and Organs at Risk

With this 3-D image data set, the radiation oncologist needs to contour the target volumes (GTV, CTV, PTV) as well as the organs at risk (OAR). (Figure III-19) This could be done at the CT-simulator or on a conventional 3-D treatment planning computer after the image data set has been transferred to the treatment planning system.

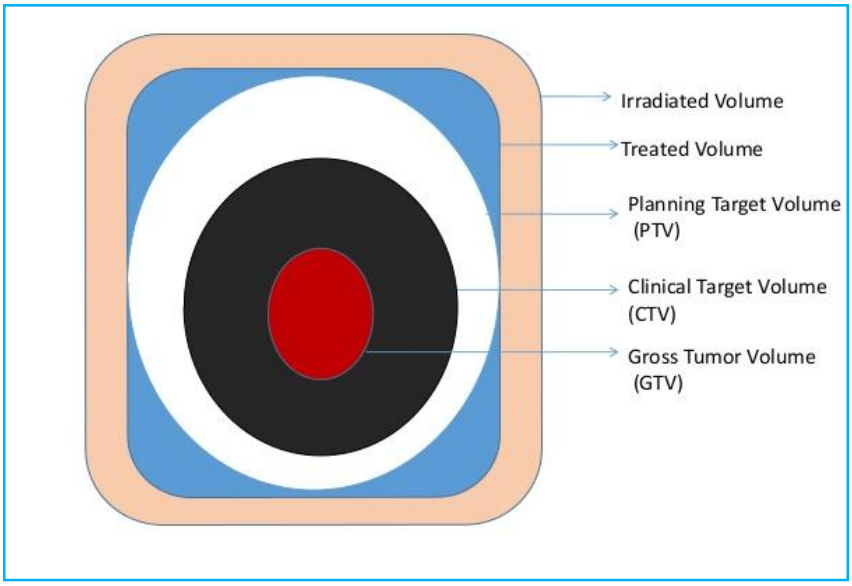

Figure III-19 Target Volumes contoured by the radiation oncologist.

Or using the smart contouring system which has many new features than the conventional include the automatic contouring of organs, it exist as a software "Raystation Launcher" its interface shown in the image below (Figure III-20).

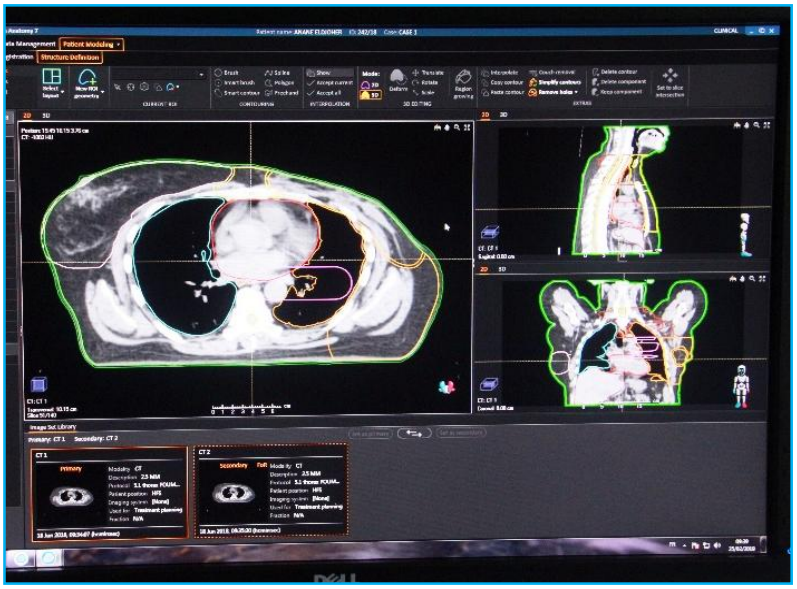

Figure III-20 Software interface of the smart contouring system "Raystation Launcher".

III.8.3 Treatment planning system (TPS)

After the definition of target volumes and organs at risk the radiation oncologists will transfer patient data from their station to the station of physicists to start treatment planning, the associated software with tomotherapy system has a running setup named "planning station", where the dosimetry will be prepared for each patient by the team of physicists. The planning station interface include mainly techniques steps to reach at the end to optimal pre-delivered dose (contouring, ROIs, plan setting, beam angles, optimization, fractionation). The tomotherapy treatment planning system provides "inverse planning" capabilities and determines the leaf positions for all the gantry angles and couch positions. The computation is carried out until all the constraints are satisfied or have been optimized. A typical tomotherapy treatment will involve the delivery of tens of thousands or even hundreds of thousands of pencil beams of radiation. Each of these pencil beams also affects many thousands of volume elements in the patient. Thus, each optimization involves processing an enormous amount of data- clearly, this is a very complex computational process. The present version of computer hardware associated with tomotherapy optimization calculations involves an array of 32 parallel processors. Even then the optimization takes approximately one hour of computation time [25].

III.8.3.1 Contouring help Structures

The planning station include a contouring tab which is a space to work on adding or editing a help structure that can control our dose and eliminate the spill outside the target volumes (Figure III-21).

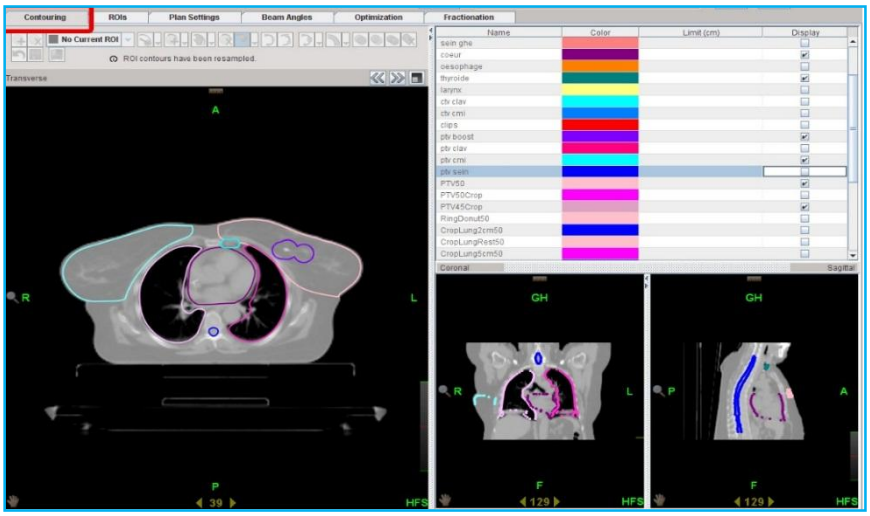

Figure III-21 The contouring tab include in planning station software.

III.8.3.1.1 Dose Limiting Volumes (DLVs)

Before starting the optimization process, we need as medical physicists to definite some additional volumes called "Dose Limiting Volumes (DLVs)", in order to control the dose outside of the targets and help us in optimization process (Figure III-22). To create help structures it's better to let margin from PTV (target) to allow the dose falling off, 1.0-1.5 cm margin can help to provide better dose control without affecting a target's minimum dose.

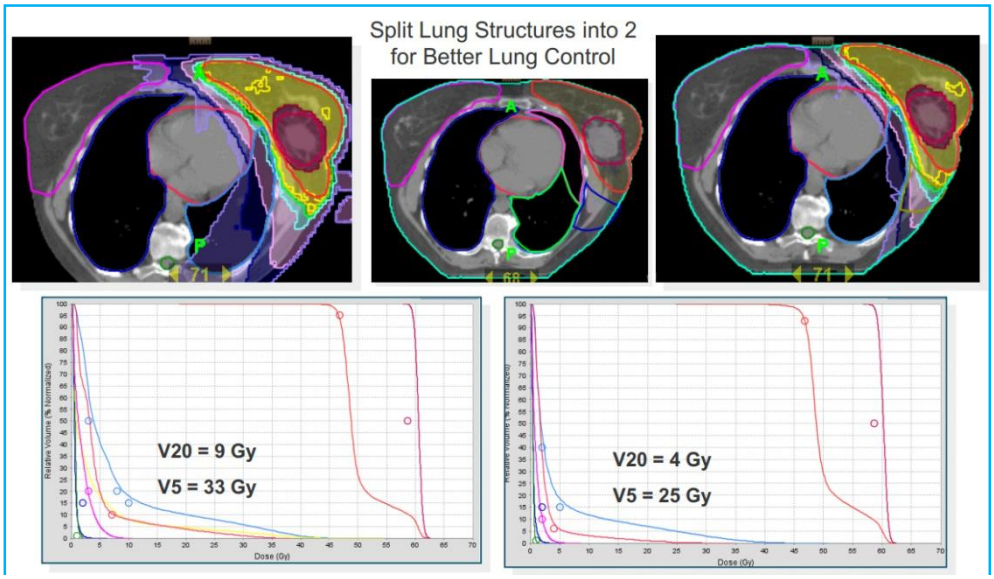

Figure III-22 Dosimetric and HDV illustrations show the deference between before (left) and after (right) using the help structures for controlling the dose outside the target volumes.

III.8.3.1.2 Rings

Another type of help structure called "Rin", the purpose of its creating is to help to eliminate the high dose (spill) outside of the PTV. we let as a typical margin size from PTV: 1.5–2.0 cm. then we assign this structure as an OAR volume. We should keep help structures out of the ring to work on optimization of each structure alone.

III.8.3.2 Region of Interests ROIs

In this tab and after selecting our help structure for optimization, we're going to chose the PTVs to be in targets constraints list, and the OAR in the region at risk constraints list, then we will set the overlap priorities which is a special concept used for optimization. All the volumes should be numbered and according to this number the system will consider the priority, in which a lower number represent a higher overlap priority (Figure III-23).

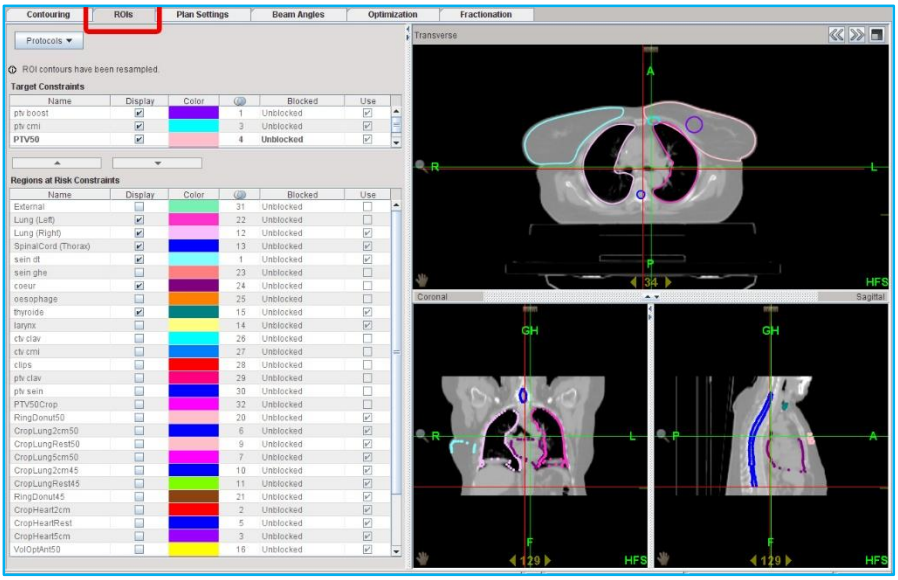

Figure III-23 The ROIs tab include in planning station software .

III.8.3.3 Plan Setting

After the working on ROIs and setting the priorities we continue to next tab in planning station software which is the choosing of plan setting, here are the parameters that should be taken in consideration (as shown in Figure III-24 of plan setting tab):

- Adjust the patient position.
- Set the red laser position.
- Select the delivery mode: {TomoHelical, TomoDirect)
- Select the plan mode: {IMRT, 3DCRT}.
- Select the field width: {1.0, 2.5, 5.0} cm.

- Select the jaw mode: {Fixed, Dynamic}.
- Enter the pitch value.
- Select the image value to density Table (IVDT).
- Replace the couch.

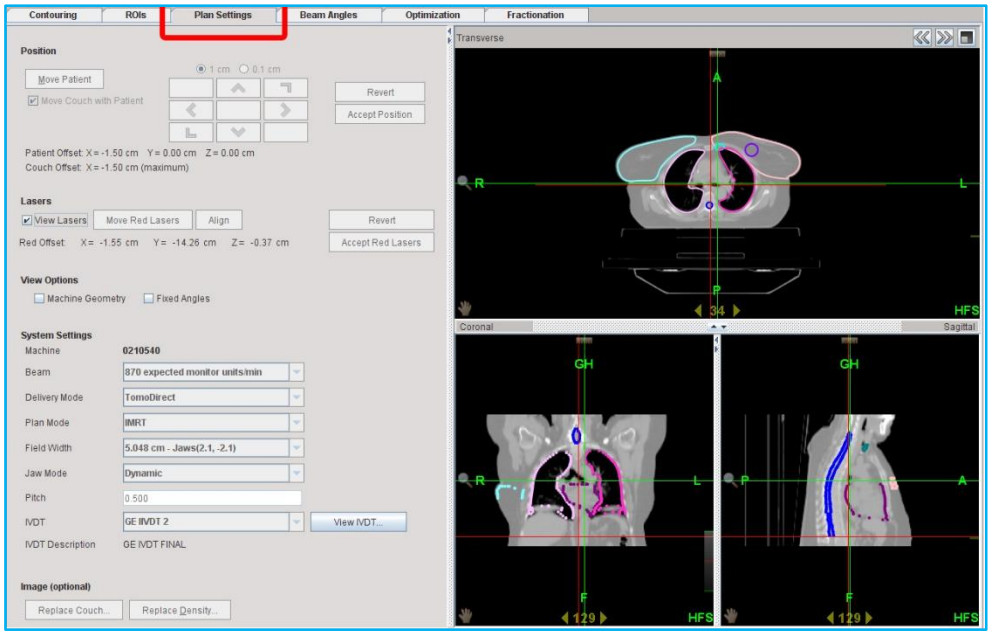

Figure III-24 The plan setting tab include in planning station software.

III.8.3.4 Beam angles

After we choose the plan setting and if the delivered mode that we've selected is the TomoDirect, the next step will be setting the beam angles, in which TomoDirect treatment procedures are delivered one beam angle at a time, with 2 to 12 beam angles for the plan. For multi-target treatments, we could select targets individually for each beam (Figure III-25). The system will automatically step through the different beam angles (without user action). Beam turns off for gantry and couch positioning between fragments, then comes on automatically when the system is ready. Opening the door between fragments will cause an interrupt, even if the Beam On light is not lit. The patient must remain immobile from the time of the registration image until all beam angles have been delivered.

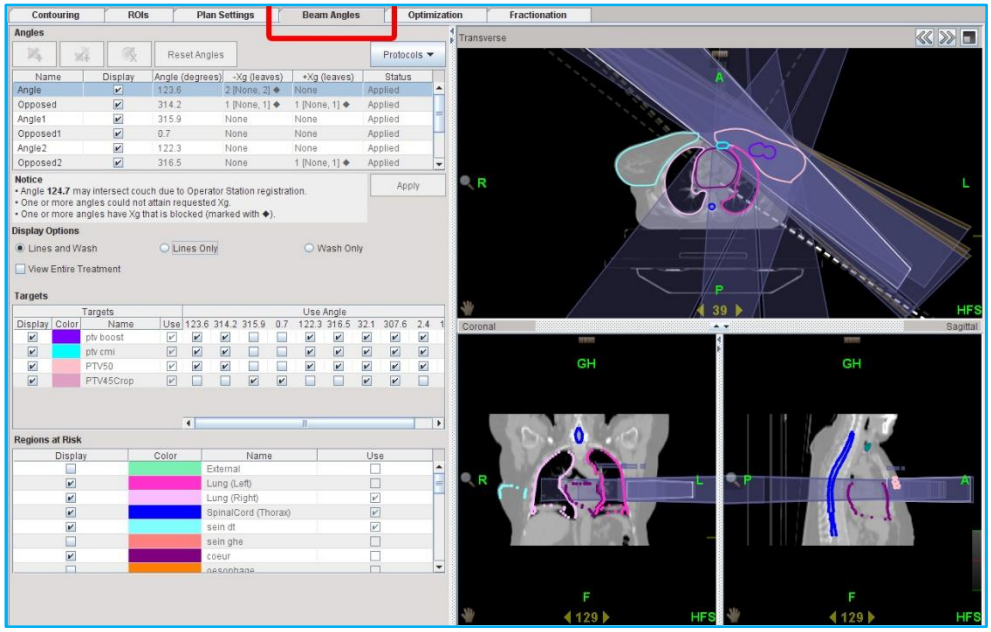

Figure III-25 The beam angles tab include in planning station software which is used only with the TomoDirect delivery mode.

III.8.3.5 Optimization

The next step after plan settings and beam angles (for TomoDirect mode) is the optimization process which represent the main step of treatment planning to get the challenge of arriving to the best calculated dosimetry on TPS software (Figure III-26), It may take hours of working depending on the pathological case.

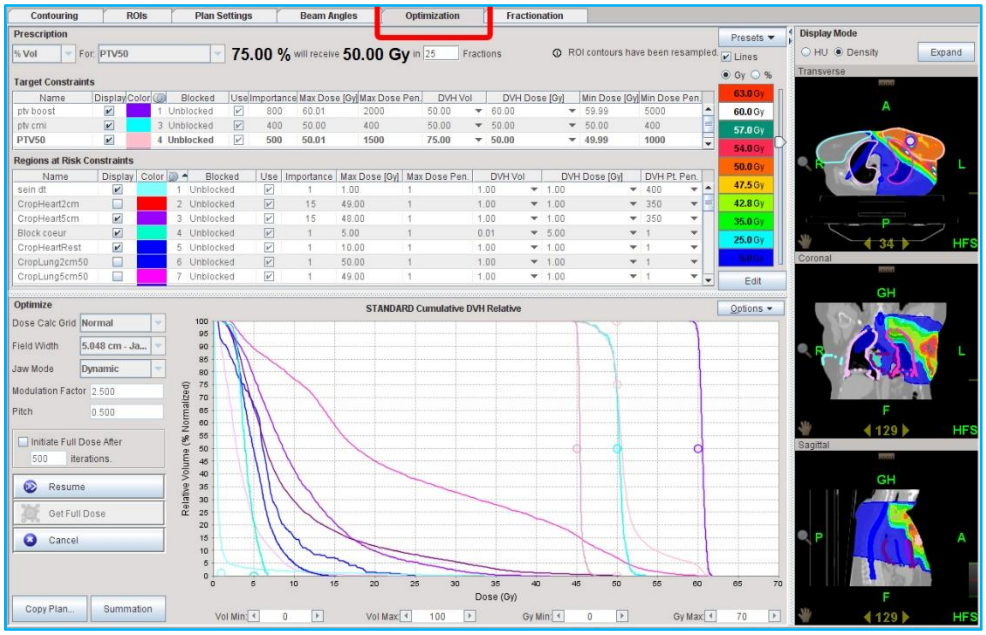

Figure III-26 The optimization tab include in planning station software.

To calculate an optimized treatment plan, the radiation oncologist needs to define the planning constraints or objectives, the prescribed dose to the target volume and the dose limitations to various organs at risk. For our dosimetric planning we've followed a list of prescription doses and constraints of OAR special for breast and chest area according to ICRU as shown in table 3.1 and table 3.2.

Target Volume	Prescription dose
Whole Breast	50Gy
Chest Wall	50Gy
Clavicle	45Gy
Supraclavicular	45Gy
Boost	60Gy

Table III-1 Prescription doses of target volumes of breast cancer according to ICRU protocols.

OAR	Dose Constraints
Contralateral Breast	V5<50%
	V7<35%
	V10<20%
	V20<15%
Heart	V15<20%
	V20<15%
	V25<10%
	AverD <5Gy
Homolateral Lung	V15<50%
	V20<35%
	V30<20%
	V35<15%
Contralateral Lung	V10<50%
	V12<35%
	V15<20%
Esophagus	V45<40%
Spinal Cord	MaxD<45Gy

Larynx	V30<60%
	V45<50%
	AverD<43,5Gy
Thyroid	V50<50%

Table III-2 The dose constraints of OAR for chest area according to ICRU protocols.

III.8.3.5.1 Main steps of optimization process

1. Entering prescription (primary DVH points)**,** as shown in Figure 3.25 the primary DVH point of prescription dose is 75% of the volume must receive 50Gy. This point has been selected by the radiation oncologist, and for constraints value will be entered by the physicist according to a special international protocol.
2. Entering other DVH points, Importances, Penalties, to respect dose constraints, in which optimization algorithm controls weighting by:
   - **A. Importance:** applies to all voxels in the structure. Adjust importance (relative to other structures) to achieve overall agreement between prescribed and actual plan dose in the structure.
   - B. **Penalty**: apply to those voxels that fail to meet constraints (max dose, min dose, or DVH constraints). Adjust penalties (relative to other structures) to enforce constraints. The efficacity of importance and penalty (Figure III-27).

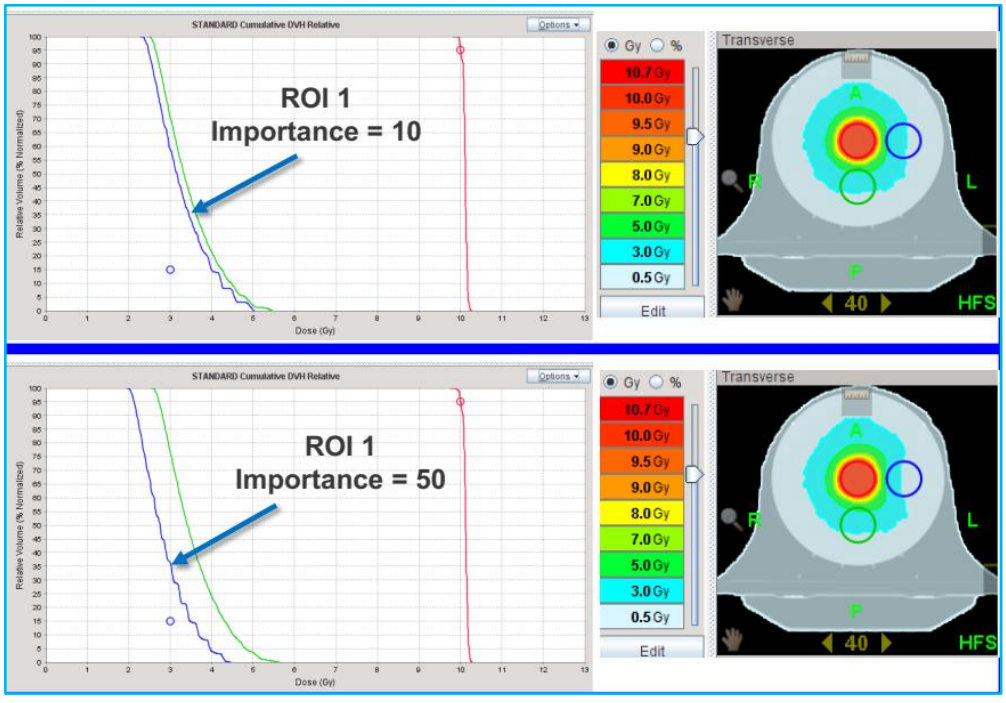

Figure III-27 DVH illustration shows the efficacity of "importance" in optimization process.

3. blocking structure option to allow a full beamlet directions (unblocked), or a directional beamlet passing (directional), or a blocked (complete). It's an optimization feature exist only in TomoHelical delivery mode as shown in the Figure III-28.

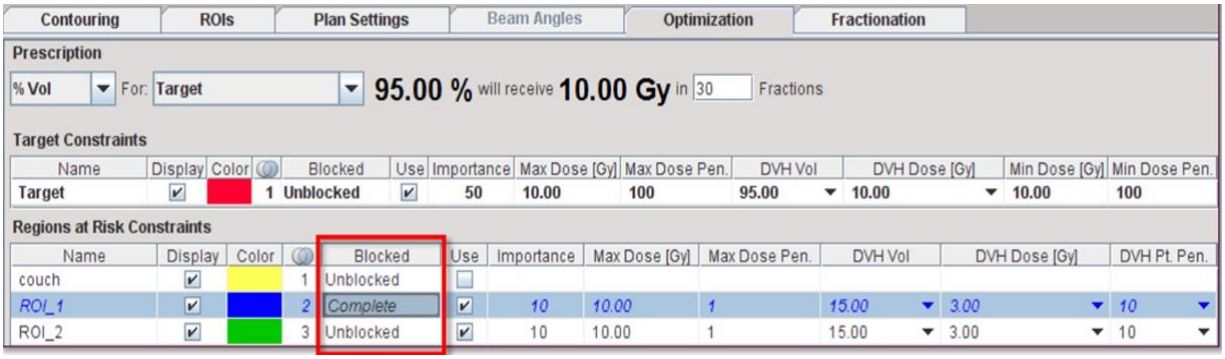

Figure III-28 Optimization tab shows the option of choosing the beamlets situations for each volume.

In which in "unlocked" option the beamlets are available to pass in all directions (even through the OAR volume), however in "directional" option the beamlets are available to pass only in the situation where the target volume located before the OAR, and in "complete" option the beamlets are blocked to pass through the OAR from the two directions either by passing through the OAR to the target or the inverse (passing through the target to the OAR) (Figure III-29).

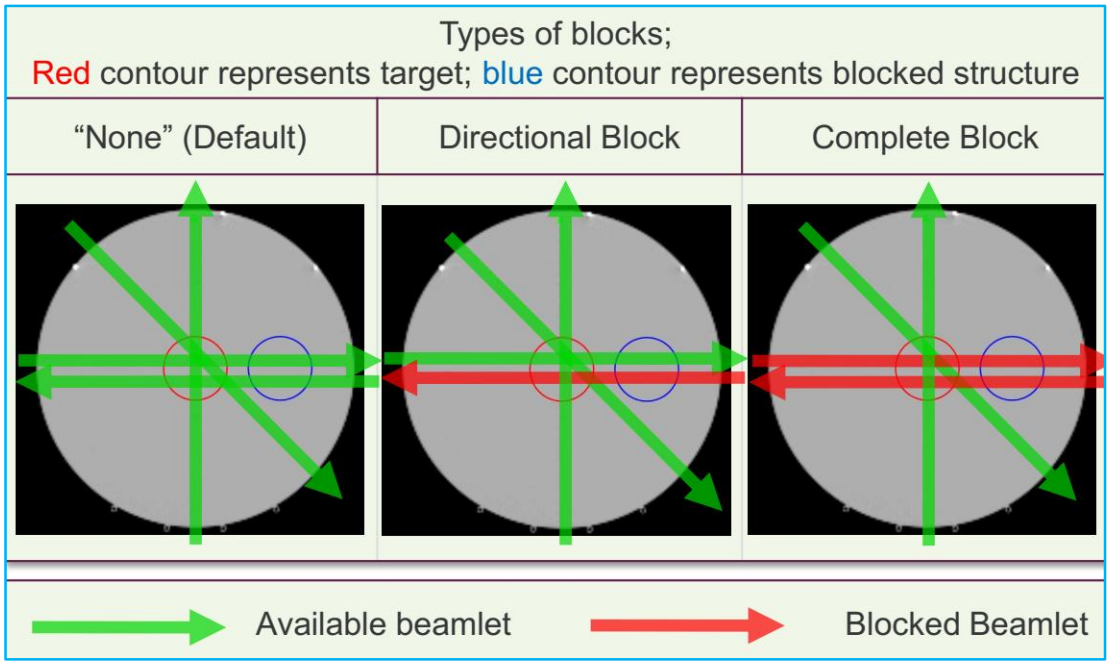

Figure III-29 Types of blocks illustration exist in optimization process on TPS.

In the DVH below (Figure III-30) we see clearly the efficacity of the option "blocking structure". The OAR (bleu volume) has better protection in the second image by using the complete block with conserving the dose of the target (red volume), while with no using blocks the dose will stay high for the organs at risk, that may not respect international dose constraints.

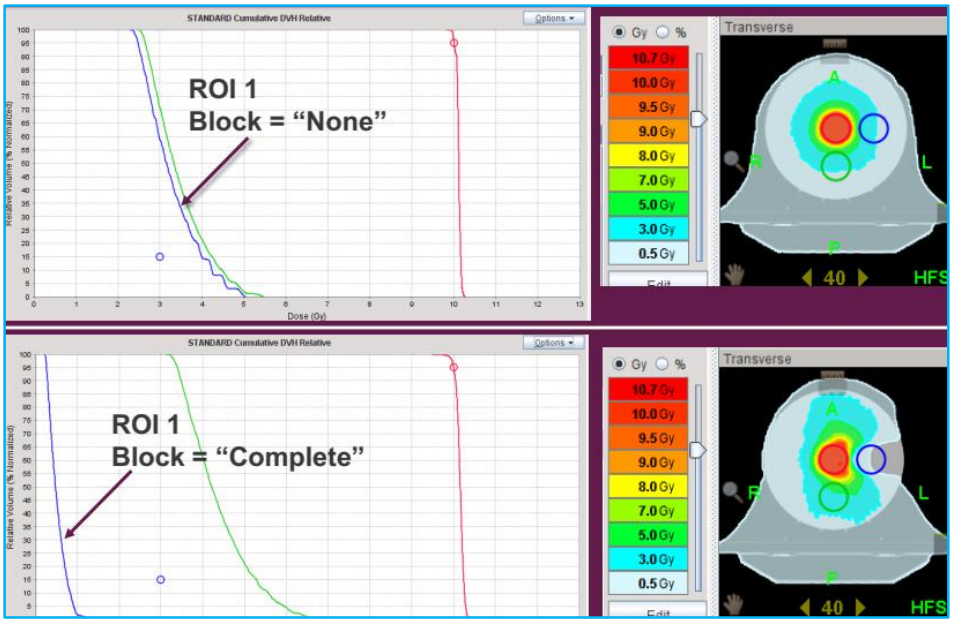

Figure III-30 DVH illustration shows the efficacity of " blocking structure" in optimization process.

III.8.3.6 Fractionations

Represent the final step of dose calculation on planning station software as shown in Figure III-31 include information like dose per fraction, number of fraction, time of treatment and some other options like:

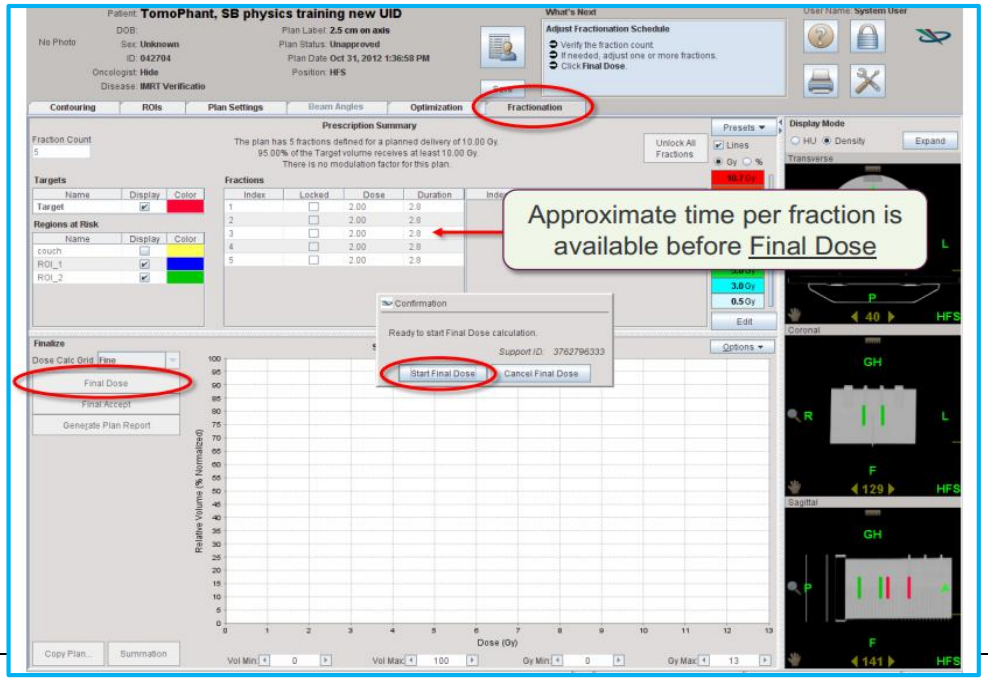

Figure III-31 Fraction tab include in planning station software.

- **Get Final Dose.**
- **Generate Report:** (draft reports are also available after final dose and before final accept).
- **Final Accept:** accepts the results of Final Dose (plan is locked and cannot be changed or modified after final accept).

III.8.4 Transfer of Planning Data to the Treatment Unit

Once the multileaf delivery configuration has been established by the treatment planning optimization calculation, the leaf positions for each gantry angle and couch position are transferred to the tomotherapy unit for delivery implementation.

III.8.5 Delivery Quality Assurance (DQA)

Verifies planned dose on TPS to the measured delivered dose on phantom, and check the range of identification between them which is represented by gamma index that it should be more than 95% (Figure III-32).

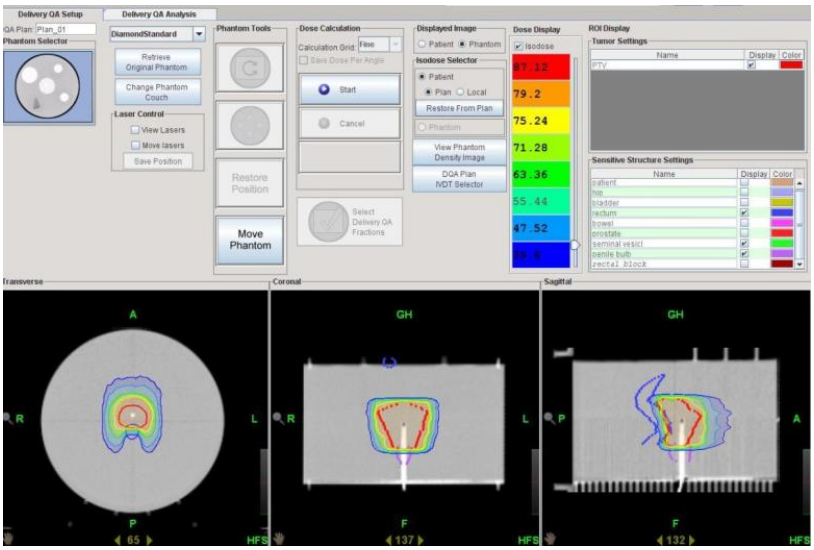

Figure III-32 Delivery qualité assurance software.

Also, the verification includes checking the multileaf collimator configurations. After the end of verifications, we can print a summary report contain quality assurance indexes including gamma (Figure III-33).

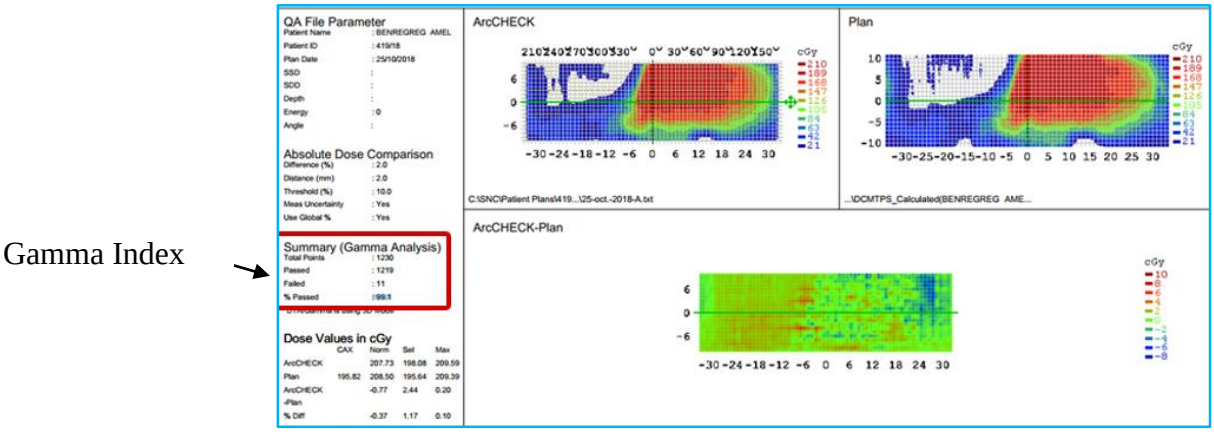

Figure III-33 Delivery quality assurance software.

III.8.6 Pre-Treatment Megavoltage CT (IGRT)

A pre-treatment CT scan is performed for the verification of the patient position and the location of the internal anatomy. This allows for the relocation of the patient or for the replanting of the multileaf collimator configuration to ensure dose delivery to the right tissues within the patient as shown in Figure III-34.

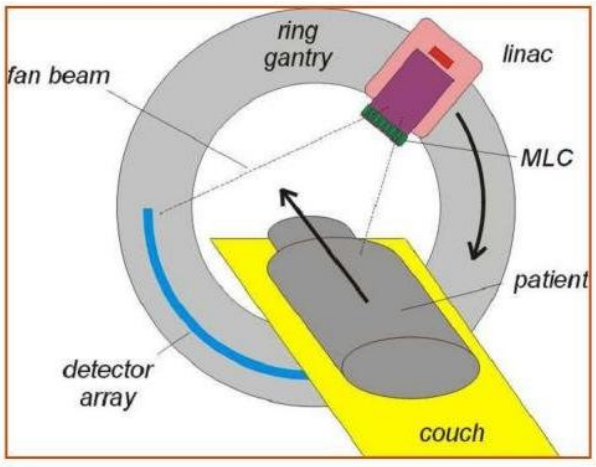

Figure III-34 Illustration shows the location of array detector in the ring gantry.

III.8.7 Tomotherapy Delivery

Once the above steps confirm the accurate location of the patient and the internal anatomy, the dose is delivered according to the planned multileaf configuration with the leaves moving in and out while the beam is on, the gantry is rotating and the couch is moving simultaneously.

III.8.8 Delivery Verification

While the patient is being treated, the detector array is actively measuring the radiation transmitted through the patient (for each pulse of the linac). This is used to determine actual radiation incident on the patient and can be used to verify dose delivery during or after treatment.

III.9 Conclusion

As it has shown above the Tomotherapy system has many new features comparing with the conventional treatments, in which we get many radiotherapy technologies and characteristics in one system and machine, this can make a deference in radiation treatment and in quality of patient's life.

Results and Discussion

IV.1 Introduction

Sidi Abdallah Centre of Carcinology (CSAC), where I have passed my internship is located on an area of 4500 m^2 amidst the green hills of the sanitary pole in the new city Sidi Abdallah – Algiers.

For the first time in Africa, the technique of Tomotherapy is available, in which it is based on combining between the scanning technology (CT) and the particle accelerator (Linac). This innovative technology allows the application of the latest treatment methods in radiotherapy field such as (IMRT, IGRT, TomoHelical, ...etc.).

The center has a GE simulator scanner with position accessories, and two Tomotherapy machines HDA (Helical, Direct and Adaptative) of Accuray, and surgery and chemotherapy equipment, in addition to Brachytherapy department which contain a stock of radioelements and applicators special for different pathologies (col-uterine, vaginal). All the equipment and devises are manipulated and controlled by a team which consists of " doctors, physicists and manipulators" trained in United States, France and Switzerland.

IV.2 My internship

I have passed an internships in CSAC- Algiers for two periods (from 04 to11 September 2018) and (From 27 January to 03 mars 2019), in this two periods I have learned a lot and inspired by the great physicist team (contain 5 physicist with a large experience in radiotherapy field), also we've been partners for doctors and manipulators to take a look for the associated specialties with the medical physics field inside the radiotherapy service.

I'm so proud to be the first intern in history of this private center in Algiers and the first master graduation study about the technique of tomotherapy in Algeria.

IV.3 Skills

After this internship and in the final path of the two years of study in master, here are some mainly skills I have been able to do which are concerned about working in radiotherapy service:

- Being able to do computed tomography month checks, and daily preparing of X-ray tube.
- Being able to work on help structures process in contouring and ROIs priorities on TPS.
- Being able to prepare a dosimetry planning on TPS for direct planning (3D-CRT technique) and inverse planning (planning station of Tomotherapy system).
- Being able to do some Tomotherapy week checks such as (modulated intensity).

- Having an average skill on manipulating on MRI and CT scanner.

IV.4 Patient selection

We have worked on many cases of patients and we have chosen 20 for our study, with the age range between (30 to 73 years old), with different stages of breast cancer (from T0 to T3) underwent a radical mastectomy or a lumpectomy (partial mastectomy).

In this planning study. All patients received post-mastectomy radiation therapy (PMRT), then the dosimetry has been prepared for each patient with the two modes of treating (Helical and Direct) to compare and chose the best mode of treating for each pathological case.

IV.5 Patient categories

We have classified our 15 chosen patient to three categories depending on the stage of cancer and the target volumes to be treated.

The first category includes 7 patients with simple case contain a breast or a chest wall as a PTV.

The second category includes 4 patients have a breast or a chest wall plus a boost as PTVs.

The third category includes 4 patients have as PTVs a breast or a chest wall plus a boost plus clavicle plus CMI (Internal mammary channel) plus axillary.

IV.6 Simulation, contouring, planning and the plan assessment

Patients were simulated using a General Electric (GE) computed tomography (CT) and positioned using a breast board (shown in chapter three), with their head turned to the contralateral side and the ipsilateral arm raised above their head. CT images with a 3.0 mm thickness were used to generate all the target volumes irradiation plans using TD and TH technique.

PTV of breast, chest wall, clavicle, boost and organ at risk (OAR) were defined and contoured by a radiation oncologist according to the recommendations of the breast cancer atlas for radiation therapy planning consensus definitions of RTOG (the Radiation Therapy Oncology Group), the volume contours and CT images were transferred to the Tomotherapy HDA system to create treatment plans.

Planning parameters used for TD and TH are: Field width: 5.048 cm; The plan mode: IMRT; The jaw mode: Dynamic; Pitch value: 0.287 for TH and 0.5 for TD; Modulation factor (MF): ranged from 1.5 to 3.

The dose to PTV was prescribed as 50 Gy (for the Breast, chest wall and IMC) in 25 fractions of 2.0 Gy daily.

As dose constraints for the PTV, D95% was defined as the minimum dose delivered to 95% of the PTV and D95% ≥ 95% of the prescribed dose were satisfied.

V95% (V47.5 Gy) was defined as the percentage of the PTV receiving at least 95% of the prescribed dose and V95% ≥ 95% were satisfied. For PTV, the parameter V107 (V53.5 Gy) was defined as the percentage of the PTV receiving in maximum 107% of the prescribed dose. The same dose prescription for targets and constraints for OARs were used to compare direct and helical plans, in which if the prescribed dose is 45 Gy (for the Clavicle) the minimum dose delivered to 95% of the PTV and D95% ≥ 95% is 42.75 Gy and receiving in maximum 107% of the prescribed dose 48.15 Gy, and if the prescribed dose is 60 Gy (for the Boost) the minimum dose delivered to 95% of the PTV and D95% ≥ 95% is 57 Gy, and receiving in maximum 107% of the prescribed dose 64.20 Gy.

The Conformity Index (CI) was used to evaluate the target dose conformity in our study. The CI was calculated according to following formula defined in ICRU (International Commission on Radiation Units and Measurements) CI= Volume of PTV covered by the reference dose / Volume of PTV. CI= 1.00 is for an ideal case.

The Homogeneity Index (HI) was used to analyze the uniformity of dose distribution in the target volume. HI is the ratio of the dose difference between D5% (the dose to 5% of the target volume) and D95% (the dose to 95% of the target volume) to D50% (the target median dose). While a higher HI value ranging from 0 to 1 represents worse homogeneity, and the lower value shows better conformity.

Effects on target and organ-at-risk (OAR) doses, and treatment time were assessed for each planning technique by one radiation oncologist.

IV.7 Results and Discussion

IV.7.1 The first category

IV.7.1.1 PTV: Breast or Chest Wall (Prescribed dose: 50Gy, 2Gy per fraction)

To check the Homogeneity and the conformity of the dose in our PTV we calculate the indexes of these two parameters for each patient in the two modes of delivery (Direct and Helical), results shown in Figure IV-1 and Figure IV-2.

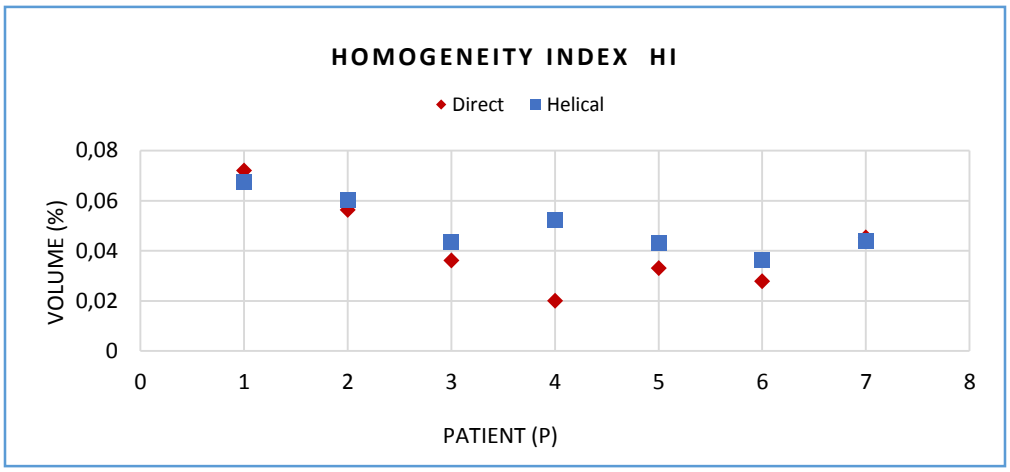

Figure IV-1 Homogeneity index calculated for each patient in the two modes of delivery.

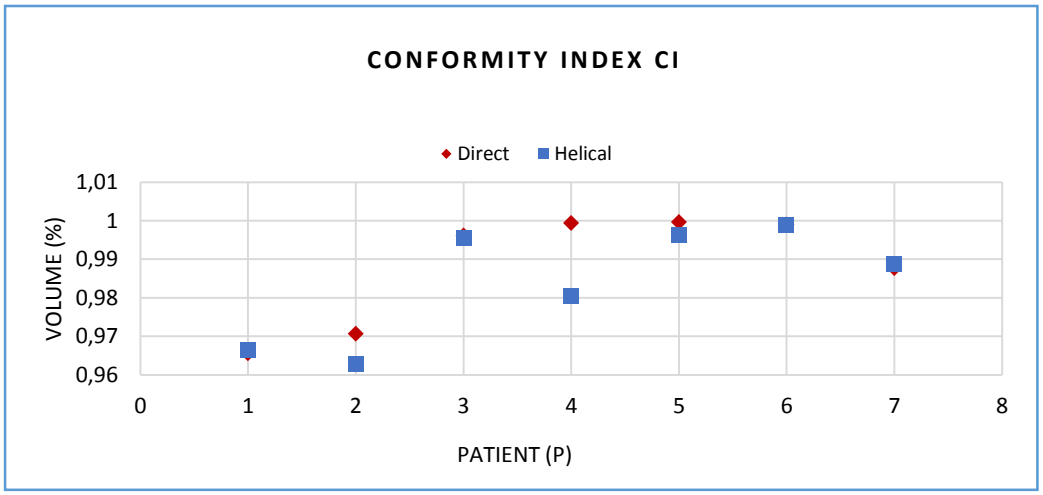

Figure IV-2 Conformity index calculated for each patient in the two modes of delivery.

IV.7.1.2 Organs at Risk

With getting the fit dose to our PTV which respecting the international dose constraints published by ICRU, we should also control and try to respect as possible as we can the dose constraints of OARs, and choosing the best way to deliver all the dose and protect the maximum the surrounding tissues. Figures below shows the different doses received by each organ at risk in the two modes of delivery.

Heart

The average dose received by Heart for each patient (4 with left-side breast target and 3 with right-side breast target), results shown in Figure IV-3 and Figure IV-4, in which the dose constraint is: Ave D<5Gy.

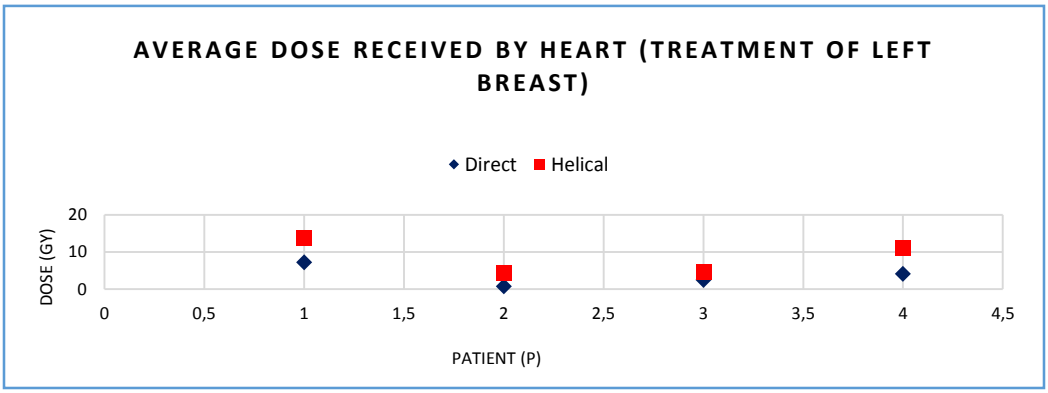

Figure IV-3 The average dose received by heart for the left-side breast in tow modes of delivery.

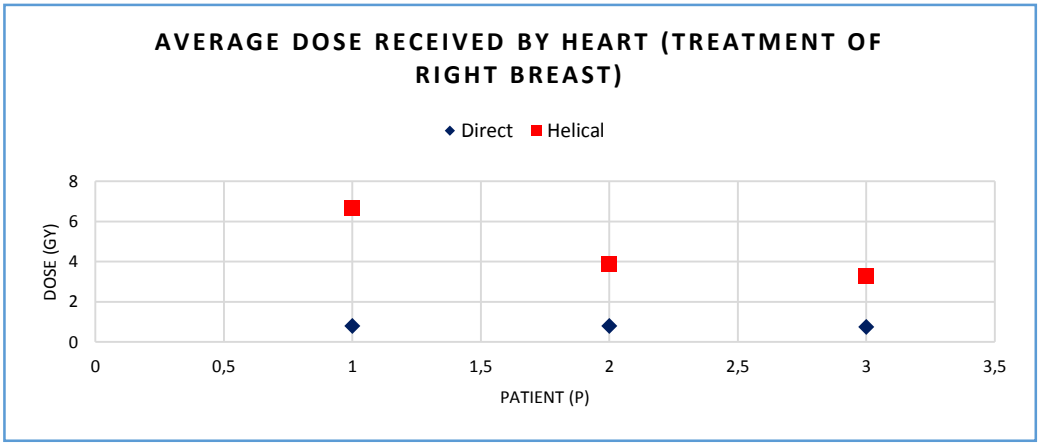

Figure IV-4 The average dose received by heart for the right-side breast in tow modes of delivery.

Contralateral Breast

Volumes received 5Gy of dose by the Contralateral Breast with the two mode of delivery shown in Figure IV-5, in which the dose constraint is: V5<50%.

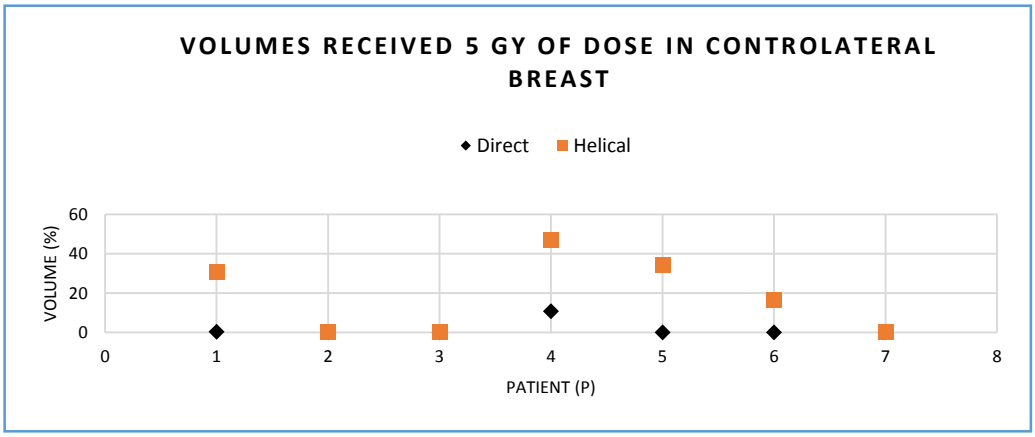

Figure IV-5 Volumes received 5Gy of dose by the Contralateral Breast in tow mode of

Contralateral Lung

Volumes received 10Gy of dose by the Contralateral Lung with the two mode of delivery shown in Figure IV-6, in which the dose constraint is: V10<50%.

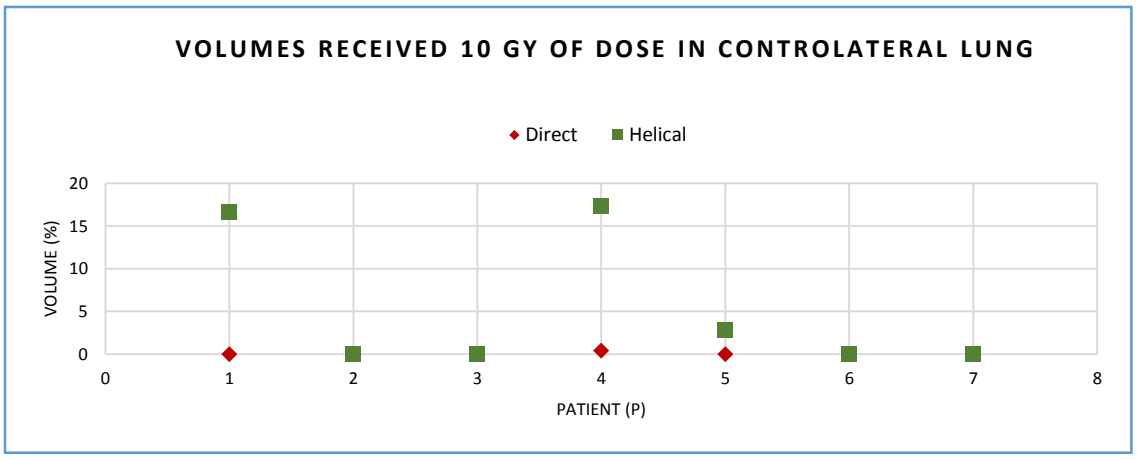

Figure IV-6 Volumes received 10Gy of dose by the Contralateral Lung in tow modes of delivery.

Ipsilateral Lung

Volumes received 15Gy of dose by the Ipsilateral Lung with the two modes of delivery shown in Figure IV-7, in which the dose constraint is: V15<50%.

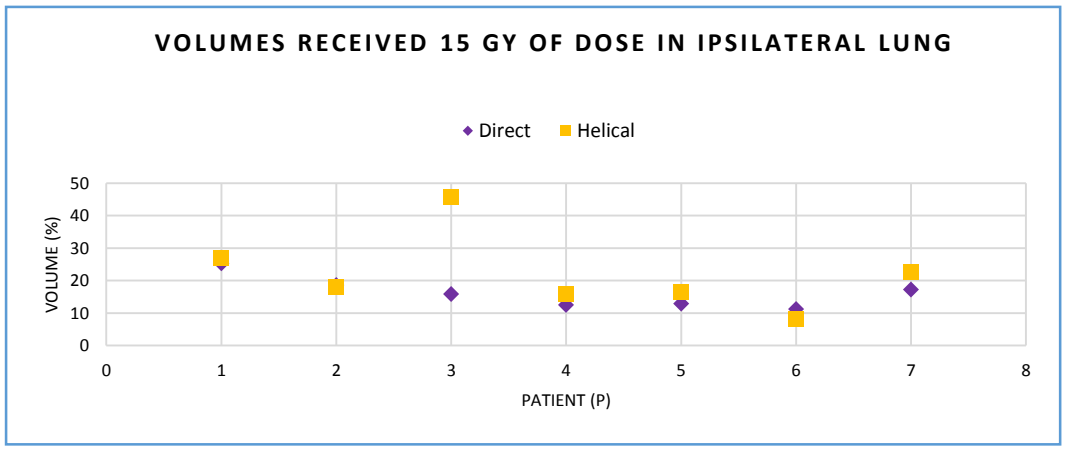

Figure IV-7 Volumes received 15Gy of dose by the Ipsilateral Lung in tow modes of delivery.

IV.7.1.3 Dose Distribution

A visual illustration of dose distribution for chest wall PTV shown for the two modes of delivery, Direct and Helical. (Figure IV-8).

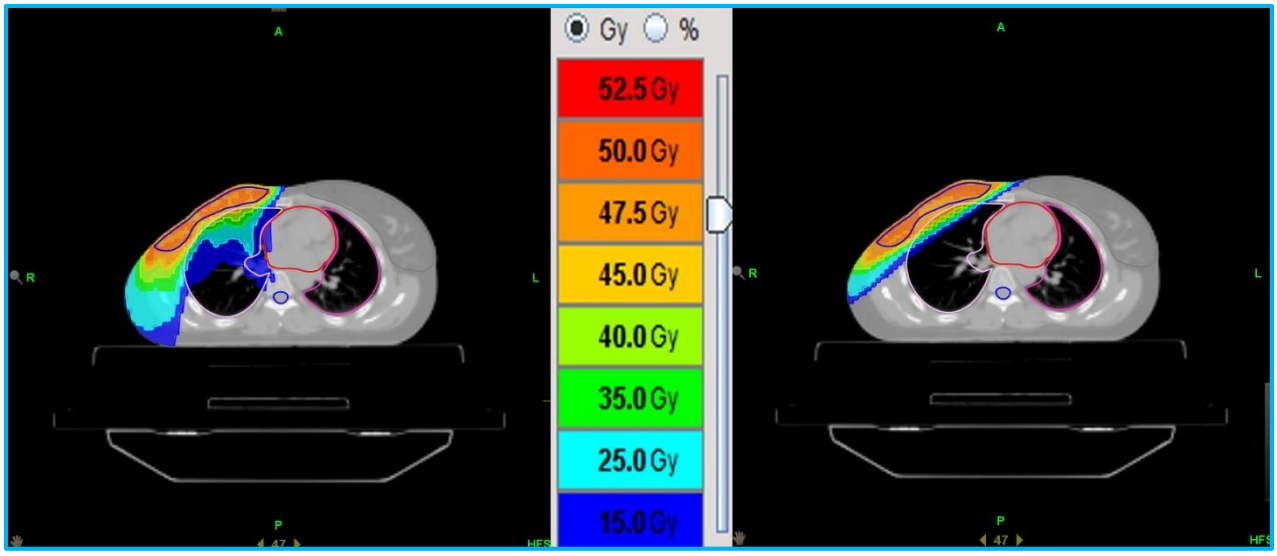

Figure IV-8 Illustration of dose distribution for chest wall in the two mode of delivery, Helical (left) and Direct(right).

IV.7.1.4 Histogram Dose Volume (HDV)

Illustration of HDVs for the same pathological case of dose distribution shown before for the tow delivery modes, Direct and Helical. (Figure IV-9).

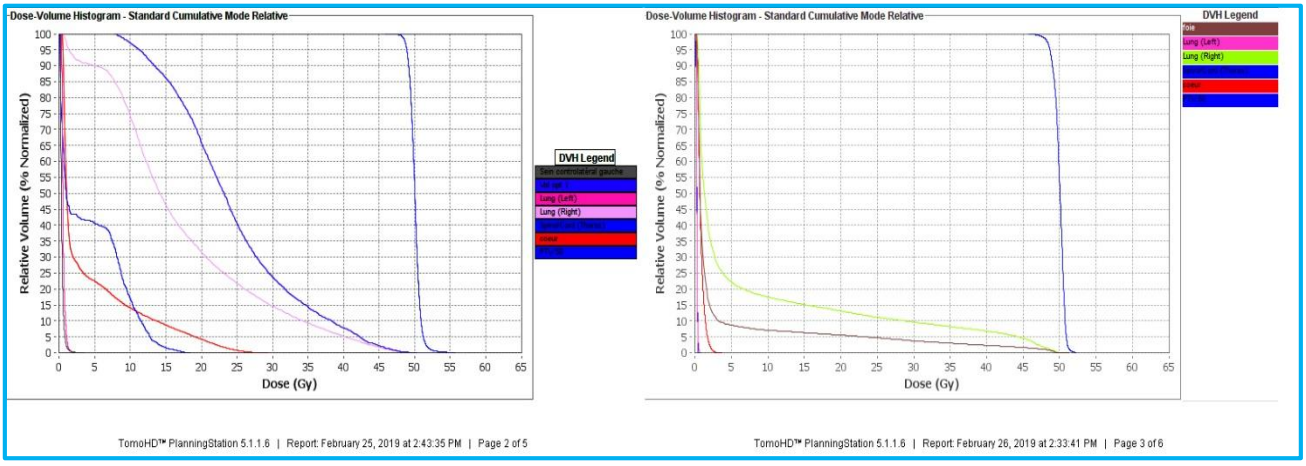

Figure IV-9 Illustration of HDVs for chest wall PTV in the two mode of delivery, Helical (left), and Direct(right).

IV.7.1.5 Discussion

According to the previous statistics data about the PTVs and OARs for simple pathological cases include only the breast or the chest wall, we observed the same variant situation in general, in which for the PTVs we noted that the homogeneity index values is lower in TomoDirect than in TomoHelical, where its ideal value of HI is zero, while for the conformity index the values are higher for TomoDirect than TomoHelical (or equal), where the ideal value of the CI is 1, that leads us to say

that the TomoDirect cover better the target volumes with the reference dose than the TomoHelical in case of breast or chest wall alone as a PTV.

And about the organs at risk as we have seen for the organs the heart, the contralateral breast, the contralateral lung, the ipsilateral lung, the TomoDirect provides the lower value of dose than the TomoHelical, in which protects better the surrounding tissues around the PTVs.

The visual illustration of dose distribution and the HDV confirm the same result from the comparison between the two modes of delivery which is that the TomoDirect cover the target better by the reference dose and protect the organs at risk without having a large dose diffusion in the out-side of the PTV than the TomoHelical.

IV.7.1.6 Conclusion

For the simple pathological cases include breast or chest wall as a PTV, TomoDirect assure better covering by the reference dose and better protecting in the same time for the organs at risk than TomoHelical, so it's recommended to choose TomoDirect as a delivery mode with like this category of patients.

IV.7.2 The second category

IV.7.2.1 PTV 1: Breast or Chest Wall (Prescribed dose: 50Gy, 2Gy per fraction)

For Checking the Homogeneity and the conformity of the dose in PTV 1 and PTV 2 we calculate the indexes of these two parameters for each patient in the two modes of delivery (Direct and Helical), results shown in Figure IV-10, Figure IV-11, Figure IV-12 and Figure IV-13.

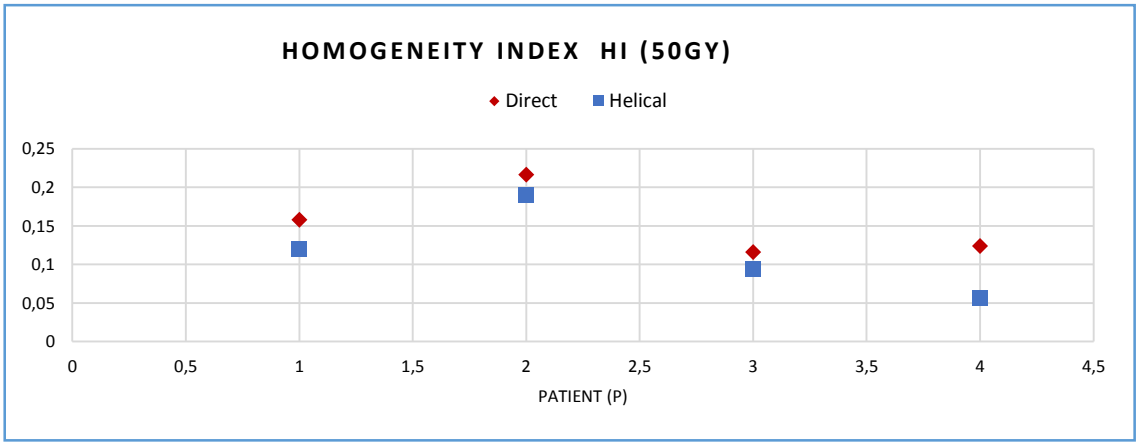

Figure IV-10 Homogeneity index calculated in PTV 1 for each patient in the two modes of delivery.

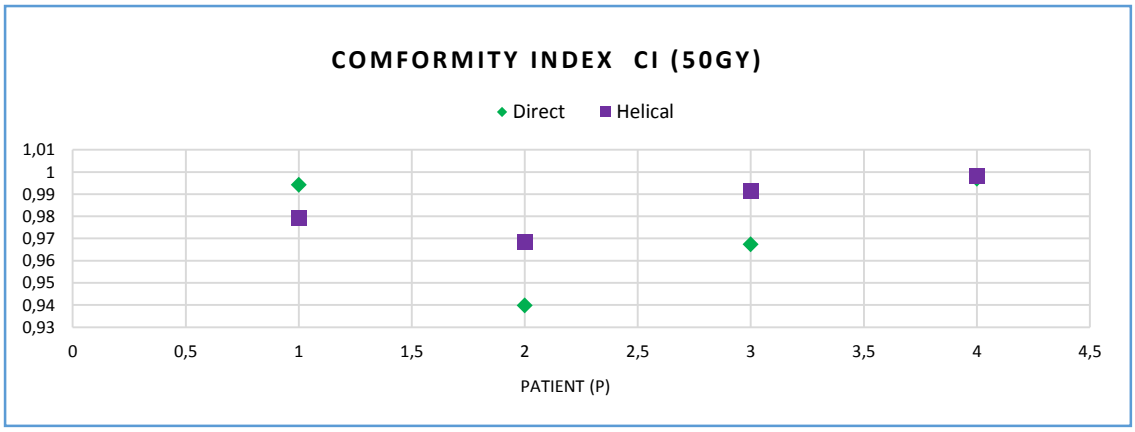

Figure IV-11 Conformity index calculated in PTV 1 for each patient in the two modes of delivery.

IV.7.2.2 PTV 2: Boost (Prescribed dose: 60Gy, 2.4Gy per fraction)

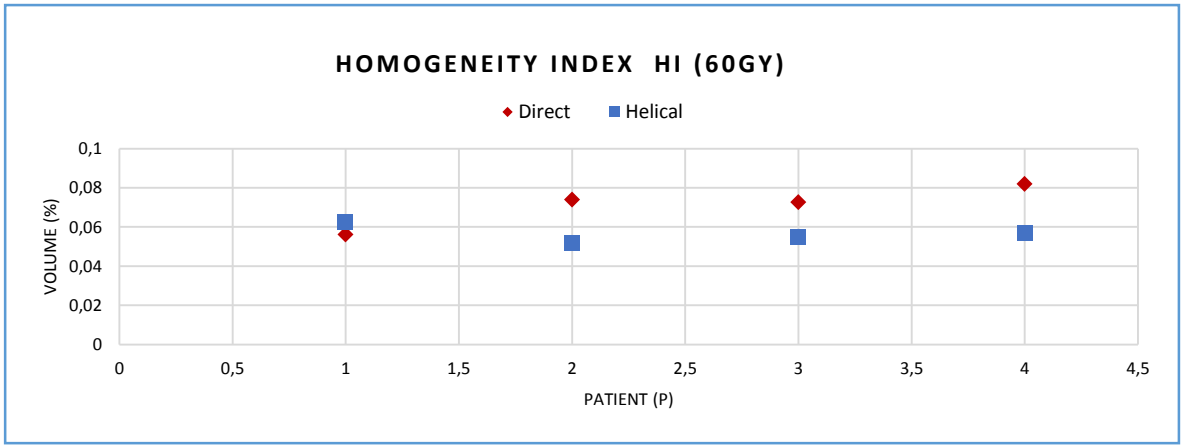

Figure IV-12 Homogeneity index calculated in PTV 2 for each patient in the two modes of delivery.

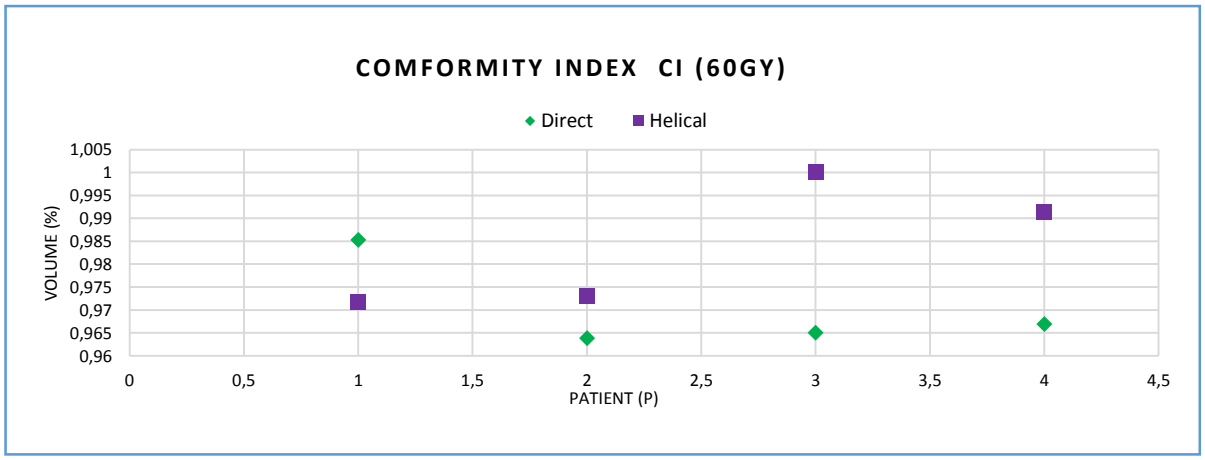

Figure IV-13 Conformity index calculated in PTV 2 for each patient in the two modes of delivery.

IV.7.2.3 Organs at Risk

In this category we have tow PTVs, so the OARs are infected by the dose covering of these targets. Figures below show the different doses received by each organ at risk in the two modes of delivery.

Heart

The average dose received by Heart for each patient (the first 3 patients have left-side breast target and the 4th have a right-side breast target), shown in Figure IV-14 and Figure IV-15, in which the dose constraint is: Ave D<5Gy.

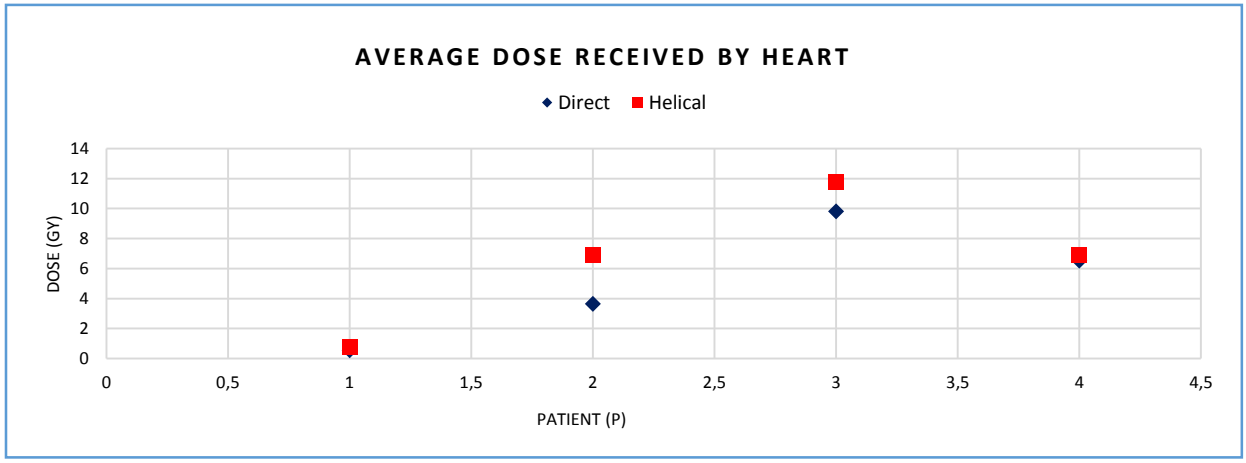

Figure IV-14 The average dose received by heart for the two breast sides with the tow modes of delivery.

Contralateral Breast

Volumes received 5Gy of dose by the Contralateral Breast with the two modes of delivery shown in Figure IV-15, in which the dose constraint is: V5<50%.

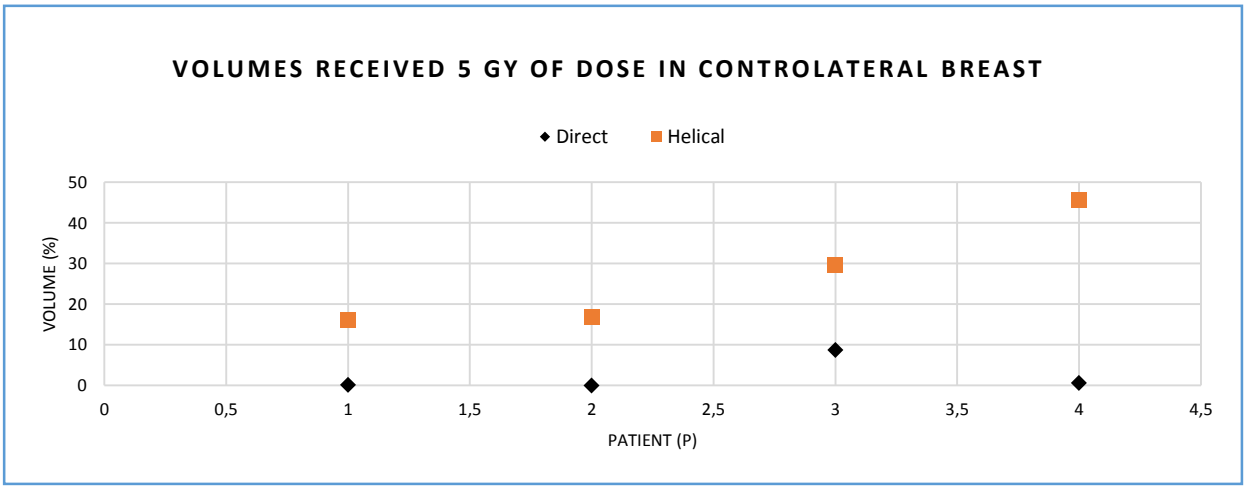

Figure IV-15 Volumes received 5Gy of dose by the Contralateral Breast in tow modes of delivery.

Contralateral Lung

Volumes received 10Gy of dose by the Contralateral Lung with the two modes of delivery shown in Figure IV-16, in which the dose constraint is: V10<50%.

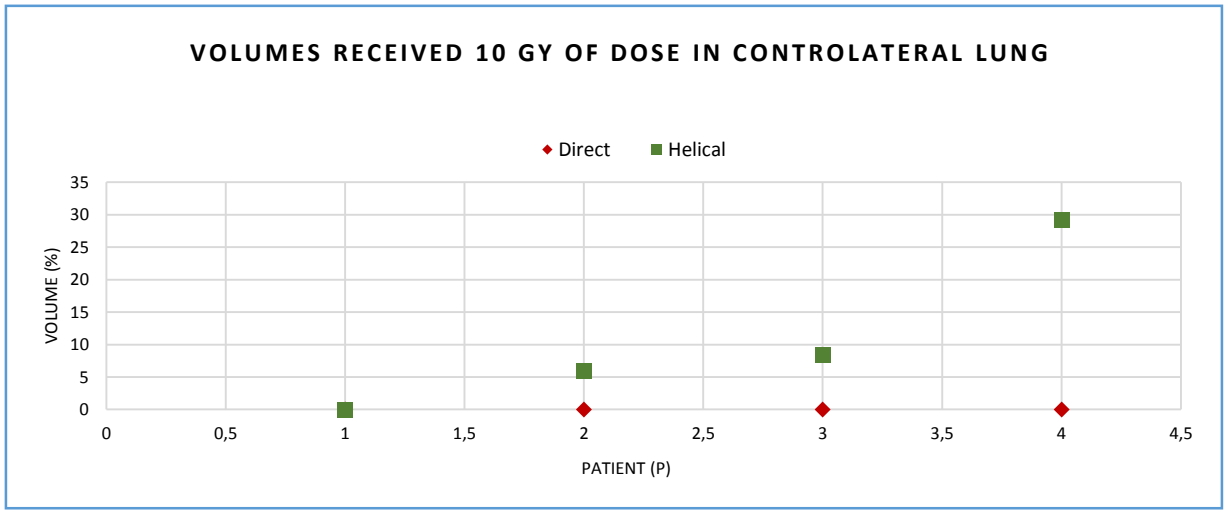

Figure IV-16 Volumes received 10Gy of dose by the Contralateral Breast in tow modes of delivery.

Ipsilateral Lung

Volumes received 15Gy of dose by the Ipsilateral Lung with the two modes of delivery shown in Figure IV-17, in which the dose constraint is: V15<50%.

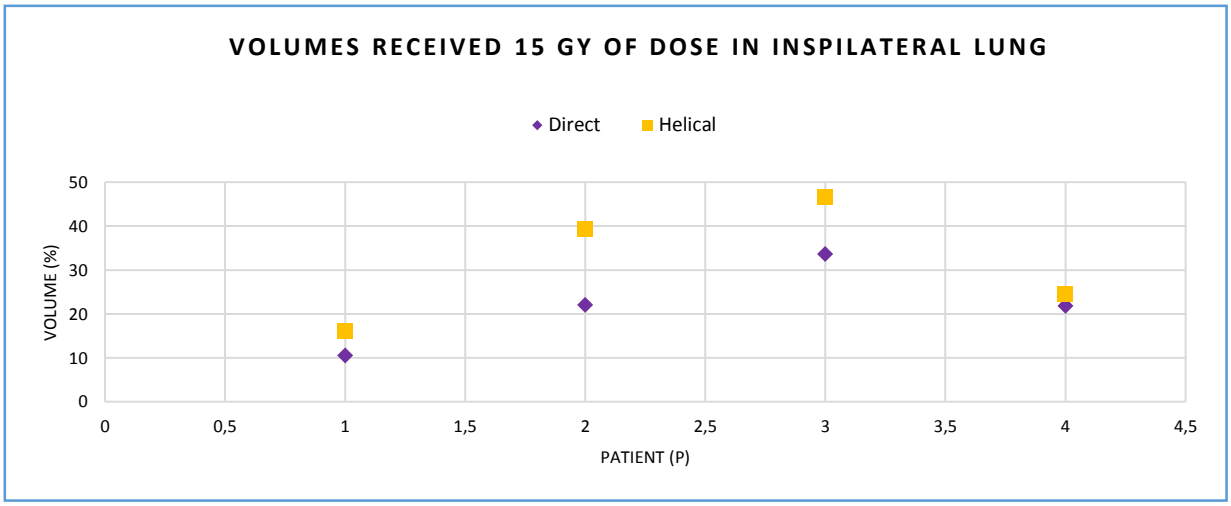

Figure IV-17 Volumes received 15Gy of dose by the Ipsilateral Lung in tow modes of delivery.

IV.7.2.4 Discussion

Given to the previous statistics data we noted that in this category of patients include a breast and a contained boost (target volume in the breast or chest wall takes more of dose, 60Gy), the homogeneity index values of the two PTVs are lower in TomoHelical mode than the TomoDirect

mode, while the conformity index values are higher in TomoHelical than the TomoDirect, that leads us to say that the volume covered by the reference dose in TomoHelical mode is better than the TomoDirect.

In the other side we have found about the organs at risk (heart, contralateral breast, contralateral lung and ipsilateral lung), the TomoDirect provides the lower value of dose than the TomoHelical, where it protects better the surrounding tissues around the PTVs.

TomoHelical cover better the PTVs and the TomoDirect protect better the OARs. The visual illustration of dose distribution can guide us to the preferable mode of radiation which will be delivered. For the patient 1 shown in Figure IV-18, the patient 2 shown in Figure IV-19 and the patient 4 shown in Figure IV-.20, the target volume Boost is located either in internal edge or in external edge of the breast that allows the good incidence for beam angles (TomoDirect) that gives good cover to the two PTVs (breast and boost), and protect better the organs at risk in the same time.

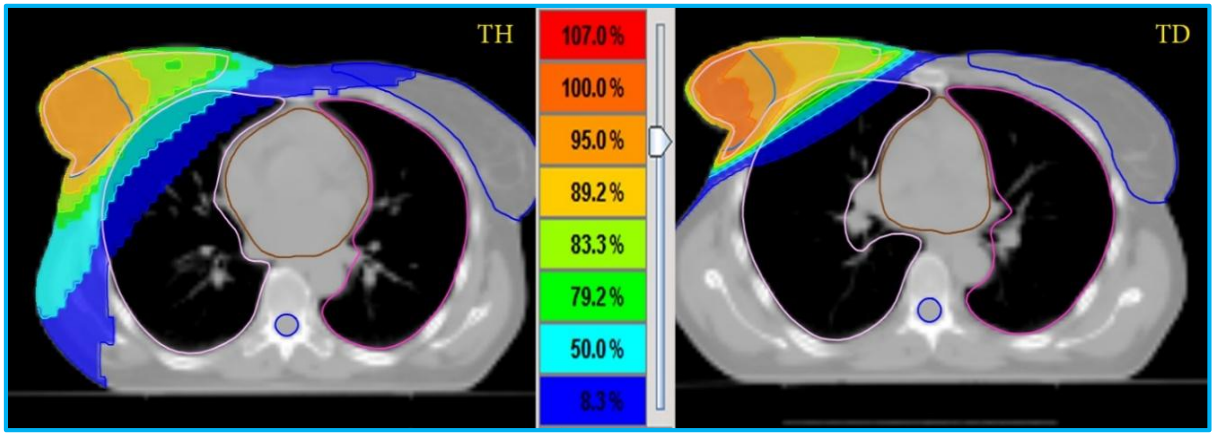

Figure IV-18 Dosimetric illustration of the two modes of delivery for the patient 1.

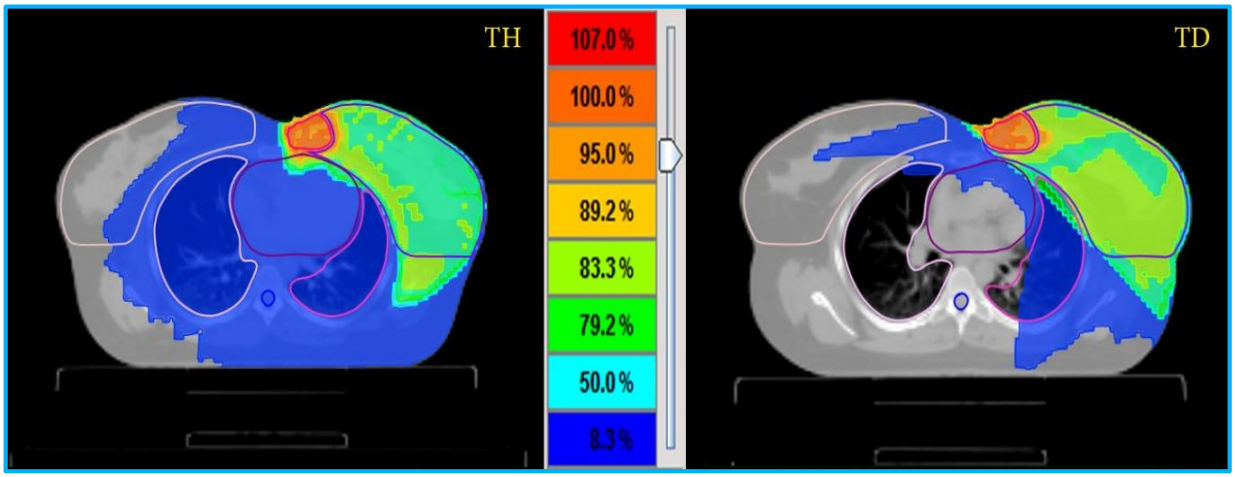

Figure IV-19 Dosimetric illustration of the two modes of delivery for the patient 3.

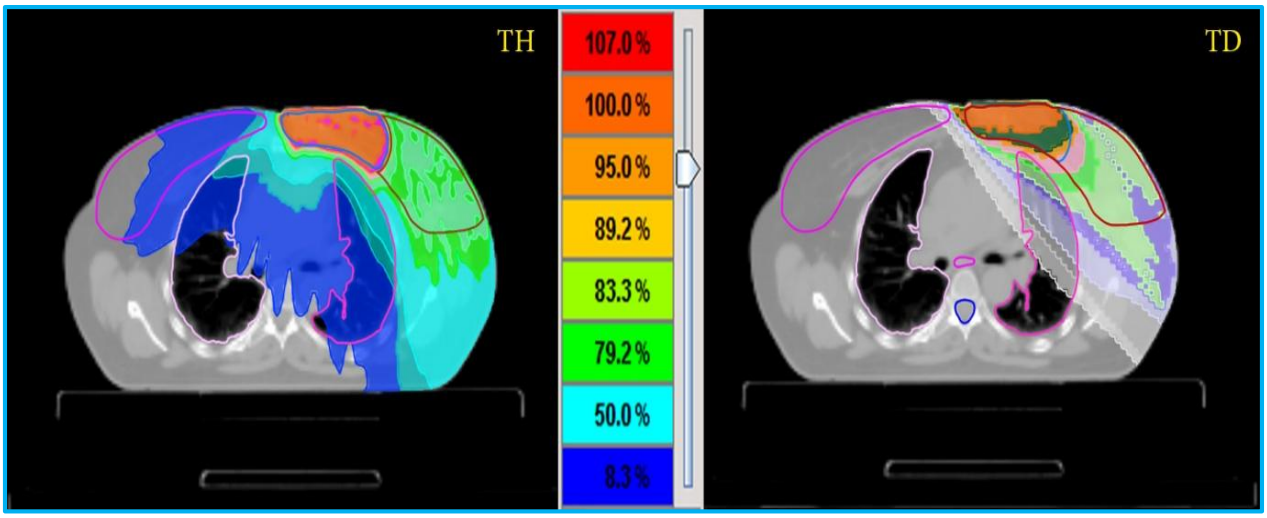

Figure IV-20 Dosimetric illustration of the two modes of delivery for the patient 4.

However about the patient 2 shown in Figure IV-21 the Boost target is located inside the PTV breast consist of three small volumes, in which by choosing the TomoDirect as a mode of delivery the diffusion of high dose outside of the PTV is too large which may cause an over dose contamination in the breast volume for the patient even that here we have better protection for OARs. But for the TomoHelical we have better covering of Boost target with lower dose contamination outside of the three volumes, and because we still in the allowed international constraints for the organs at risk according to ICRU, we chose in this case to treat by TomoHelical.

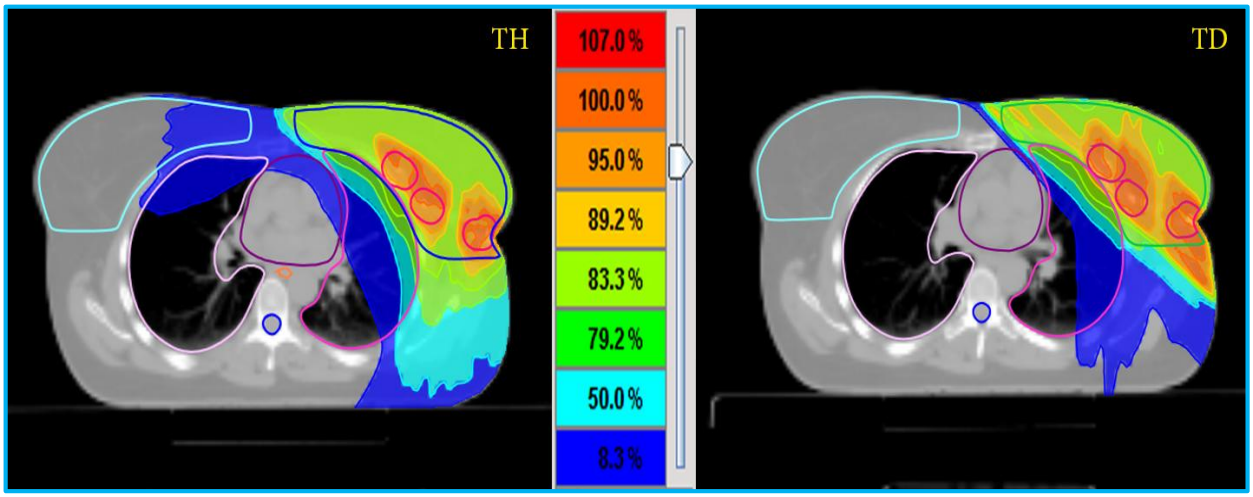

Figure IV-21 Dosimetric illustration of the two modes of delivery for the patient 2.

IV.7.2.5 Conclusion

For the pathological case include breast and boot as a PTVs, there is no recommended mode of delivery to the patient, but our choosing depends on the characteristics of boost target, whether it is located in edges of the breast or inside, and whether it consists by one volume or multiples.

IV.7.3 Third category

IV.7.3.1 PTV 1: Breast or Chest Wall (Prescribed dose: 50Gy, 2Gy per fraction)

To control the Homogeneity and the conformity of the dose in PTV 1, PTV 2, PTV 3, and PTV 4 we calculate the indexes of these two parameters for each patient in the two modes of delivery (Direct and Helical), results shown in Figure IV-22, Figure IV-23, Figure IV-24, Figure IV-25, Figure IV-26, Figure IV-27, Figure IV-28 and Figure IV-29.

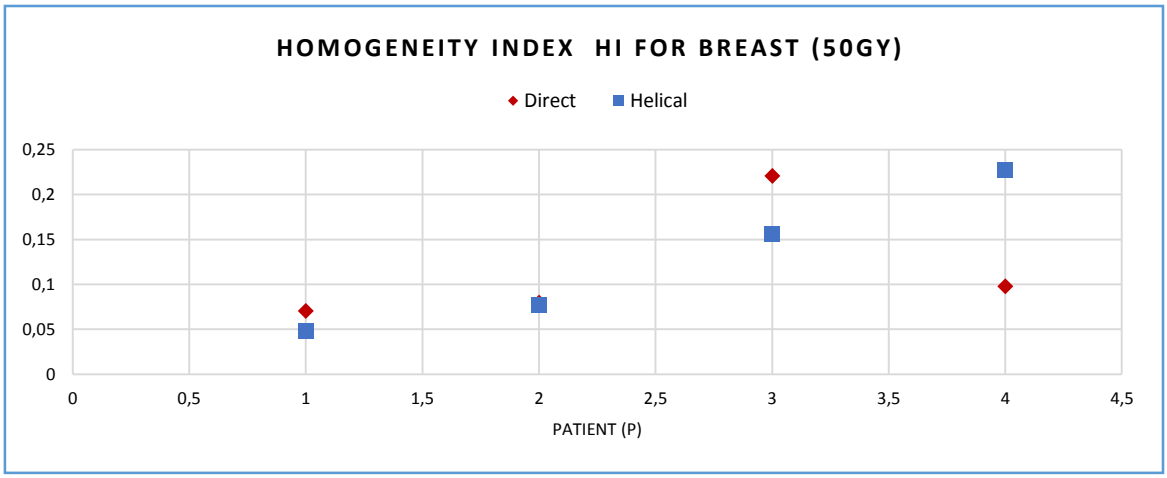

Figure IV-22 Homogeneity index calculated in PTV 1 for each patient in the two modes of delivery.

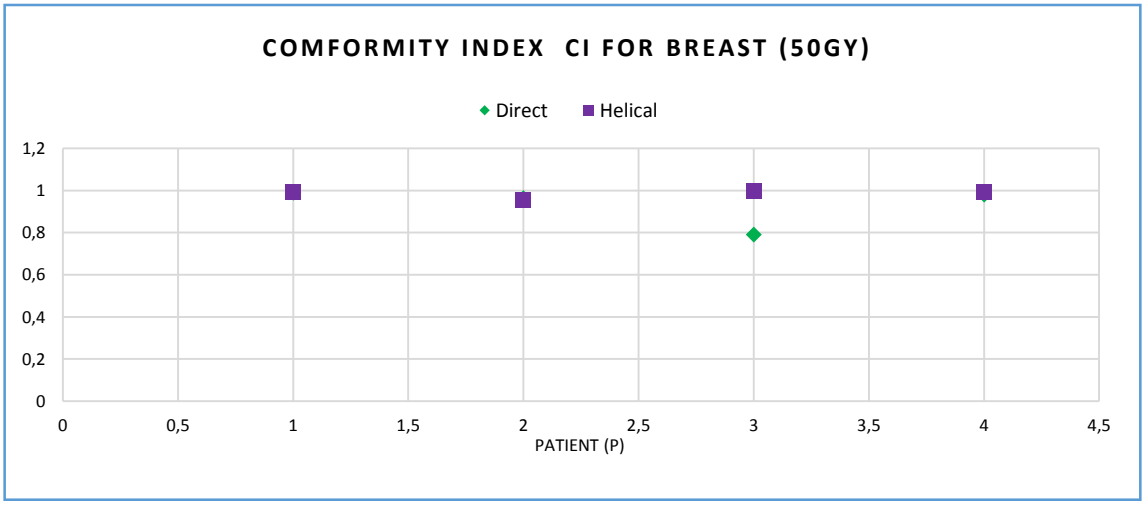

Figure IV-23 Conformity index calculated in PTV 1 for each patient in the two modes of delivery.

IV.7.3.2 PTV 2: Clavicle (Prescribed dose: 45 Gy, 1.8 Gy per fraction)

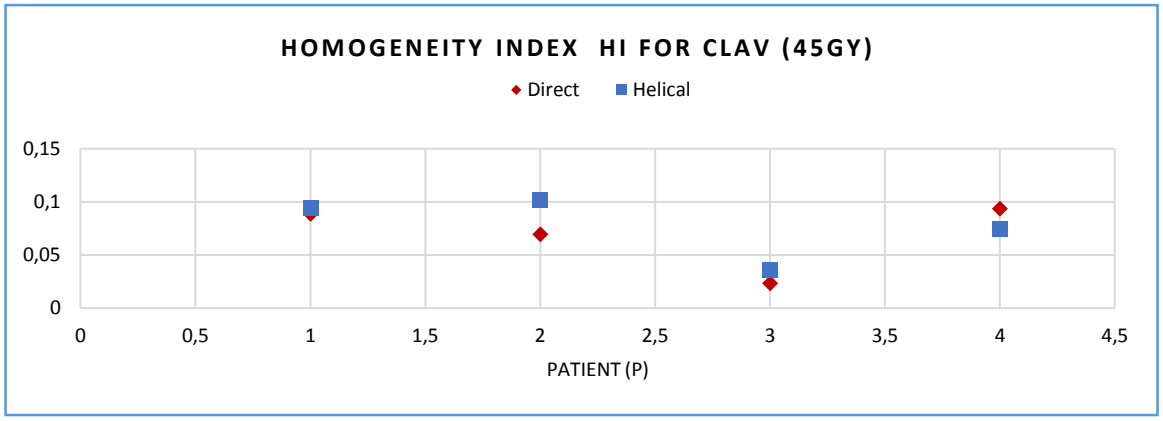

Figure IV-24 Homogeneity index calculated in PTV 2 for each patient in the two modes of delivery.

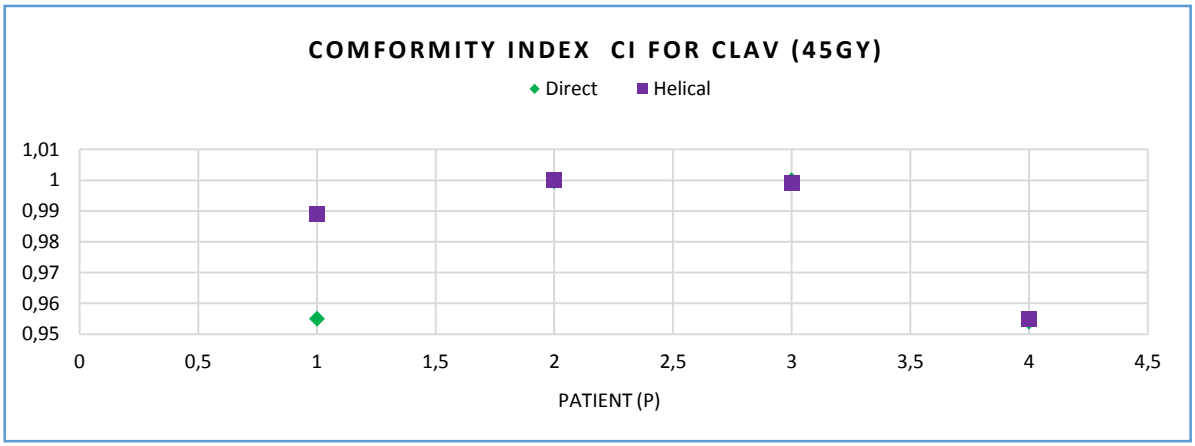

Figure IV-25 Conformity index calculated in PTV 2 for each patient in the two modes of delivery.

IV.7.3.3 PTV 3: Internal Mammary Chanel (Prescribed dose: 50 Gy, 2 Gy per fraction)

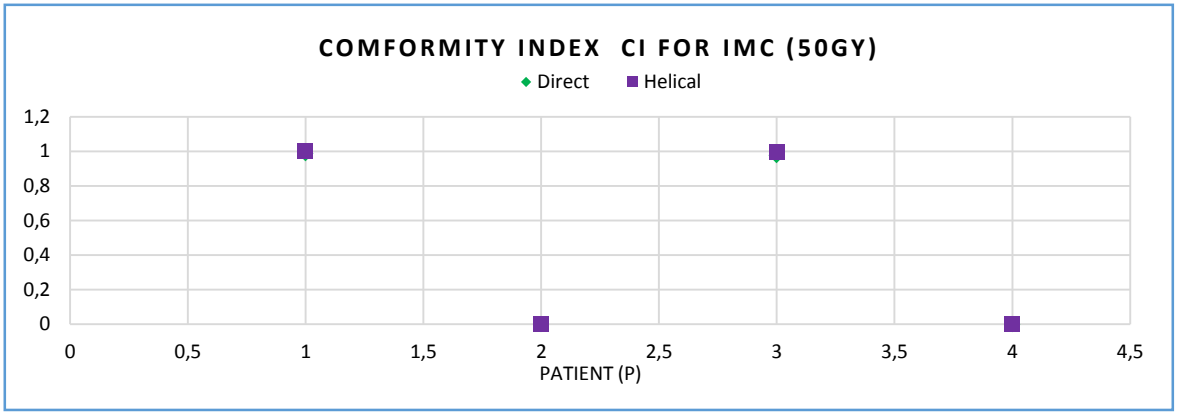

Figure IV-26 Homogeneity index calculated in PTV 3 for each patient in the two modes of delivery.

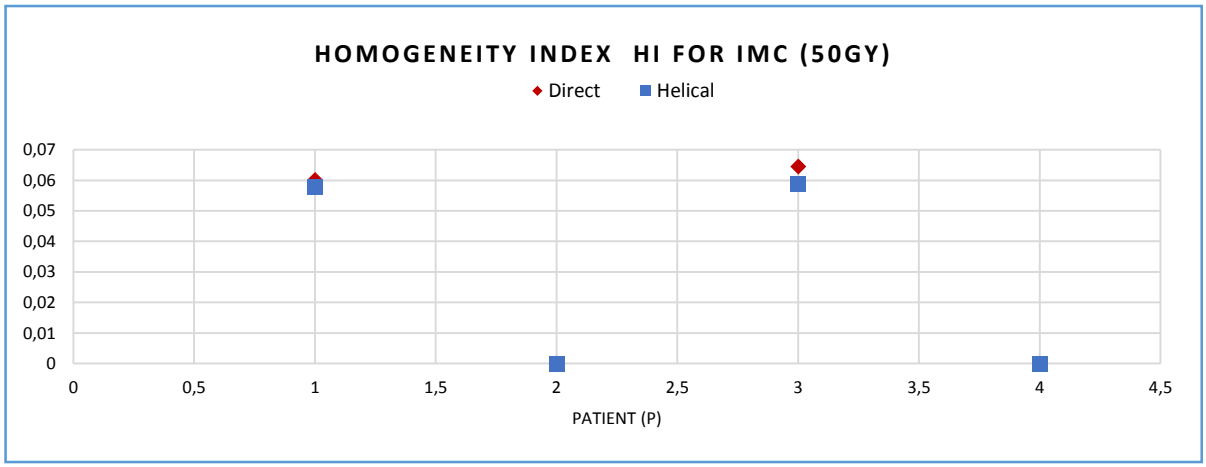

Figure IV-27 Conformity index calculated in PTV 3 for each patient in the two modes of delivery.

IV.7.3.4 PTV 4: Boost (Prescribed dose: 60 Gy, 2.4 Gy per fraction)

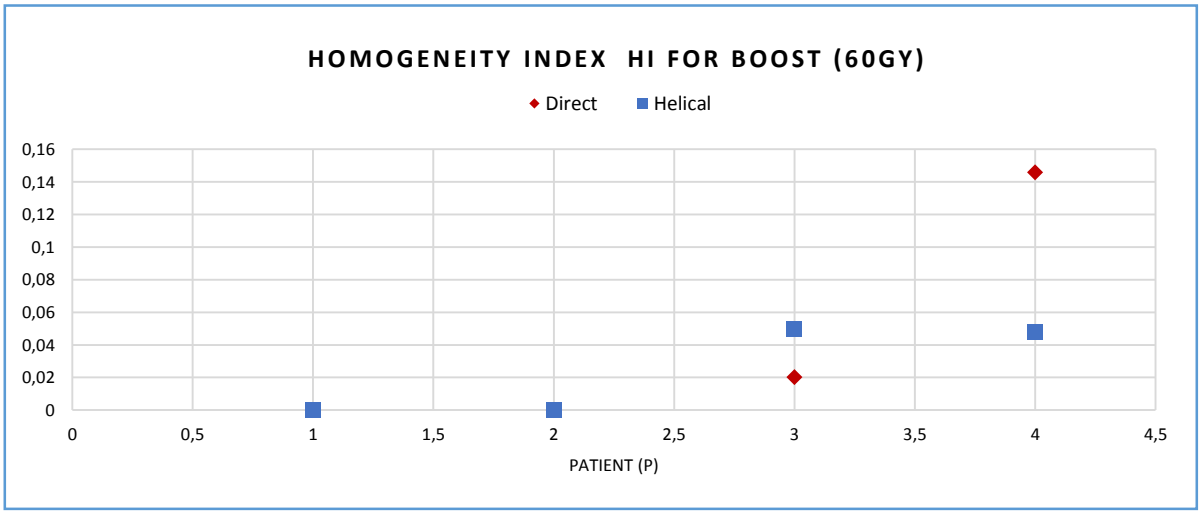

Figure IV-28 Homogeneity index calculated in PTV 4 for each patient in the two modes of delivery.

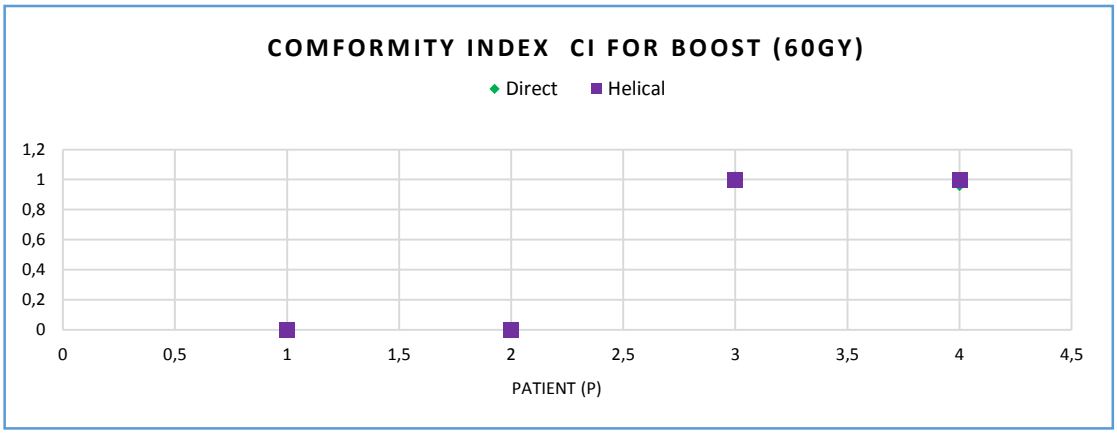

Figure IV-29 Conformity index calculated in PTV 4 for each patient in the two modes of delivery.

Organs at Risk

In this category we have four PTVs. The OARs here are infected by the high dose which delivered to cover all the targets, we chose a high dose constraint (20 Gy or more), to compare between the two modes of delivery. Figures below show the different doses received by each organ at risk.

Heart

The Volumes received 20 Gy of dose in Heart for each patient (the third patient have left-side breast target and the three others have a right-side breast target), shown in Figure IV-30, in which the dose constraint is: V20<15%.

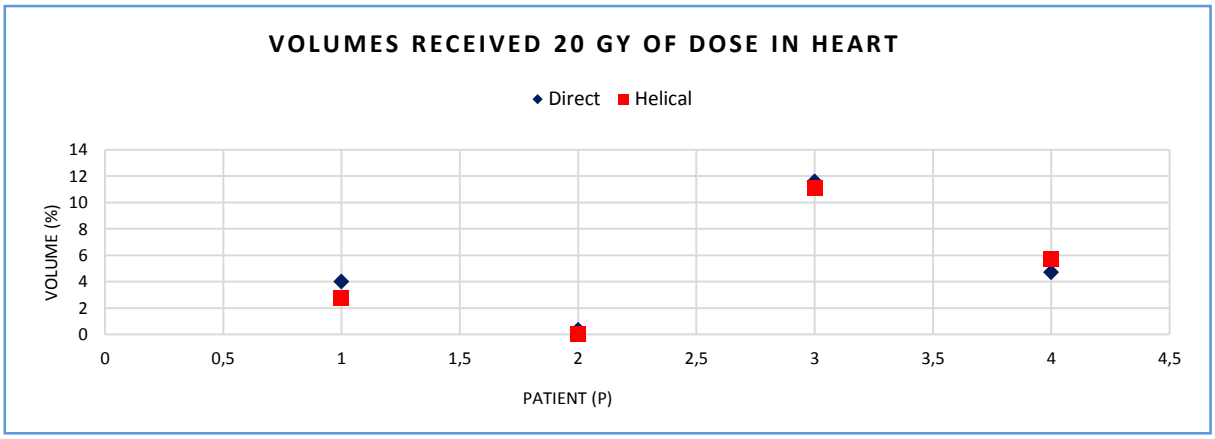

Figure IV-30 Volumes received 20 Gy of dose in heart for the two breast sides with the tow modes of delivery.

Contralateral Breast

Volumes received 20 Gy of dose in the Contralateral Breast with the two mode of delivery shown in Figure IV-31, in which the dose constraint is: V20<15%.

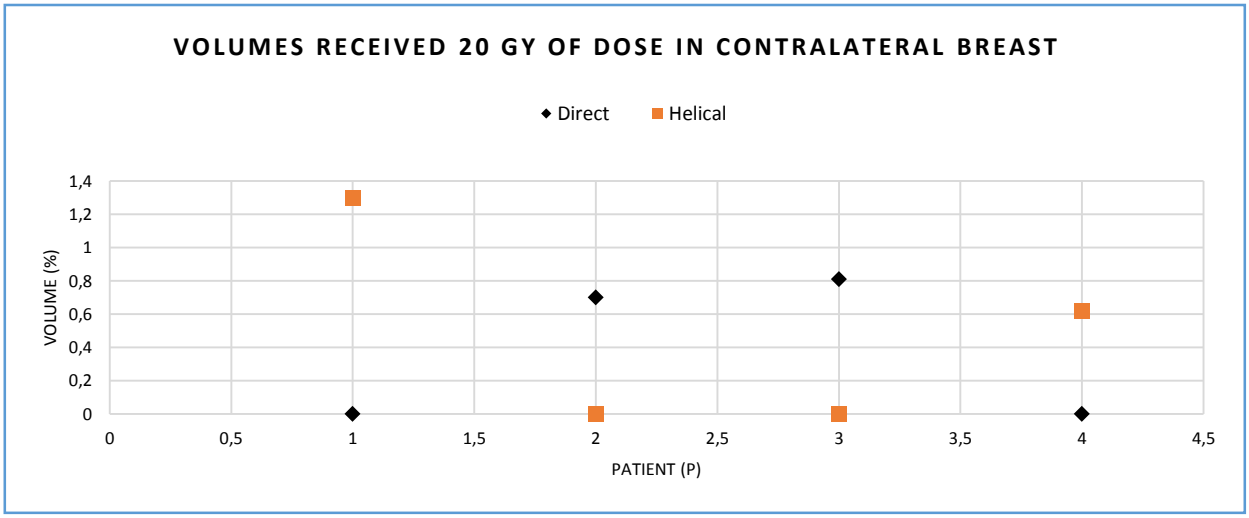

Figure IV-31 Volumes received 20 Gy of dose by the Contralateral Breast in tow modes of delivery.

Ipsilateral Lung

Volumes received 35 Gy of dose in the Ipsilateral Lung with the two modes of delivery shown in Figure IV-32, in which the dose constraint is: V35<15%.

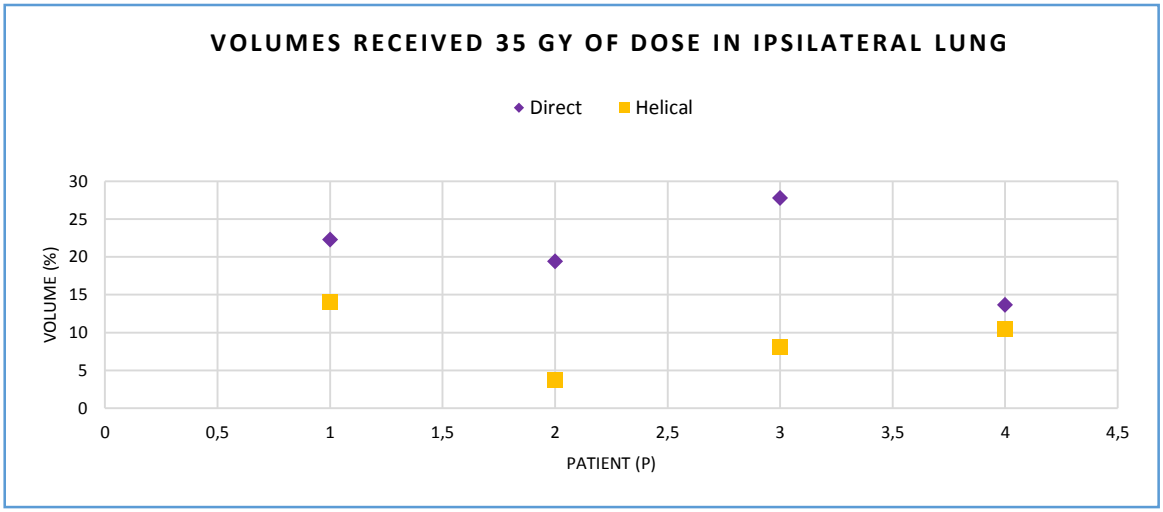

Figure IV-32 Volumes received 35Gy of dose in the Ipsilateral Lung in tow modes of delivery.

IV.7.3.5 Discussion

According to the previous statistics data about the PTVs and OARs for complicated pathological cases include two PTVs or more which are the breast, clavicle, IMC and boost, we observed that the homogeneity index values are lower in general in TomoHelical than in TomoDirect, and the conformity index values are equal in general, that leads to say that the TomoHelical cover the target volumes by the references dose better.

About the OARs we should first mention that in this case the low dose constraints are less important because of the existing of high doses coming from the irradiation of large zone (4 PTVs), that's why we have followed the constraints of high doses (20 Gy and more), that's because the high dose are more dangerous for the patient and may cause some determinist effects as heart attack.

We noted that for all the organs heart, contralateral breast, and ipsilateral lung the TomoHelical provides better protection than the TomoDirect. The contralateral lung is not included here because its maximum dose constraint according to ICRU is V15<20%, belongs to low doses, and we are dealing in this category just with high doses.

The visual illustration of dose distribution can confirm these dose indexes, as shown below with the patient 1 in Figure IV-33, the patient 2 in Figure IV-34, the patient 3 in Figure IV-35 and the patient 4 in Figure IV-36 with TomoHelical mode we have better covering of all PTVs and better protection of OARs in the same time, while in TomoDirect mode the targets are less covered by the

references dose with low protection of OARs, and with the existing of hot spots and the large diffusion of the high dose outside of PTVs.

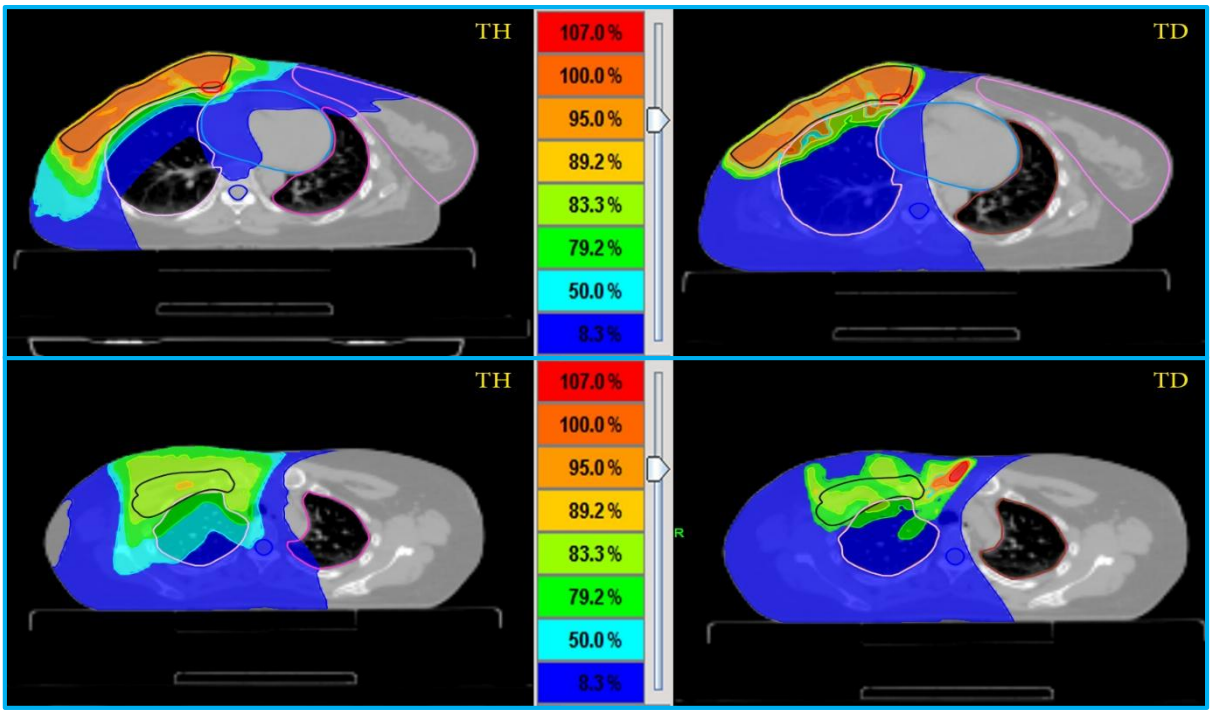

Figure IV-33 Dosimetric illustration of the two modes of delivery for the patient 1.

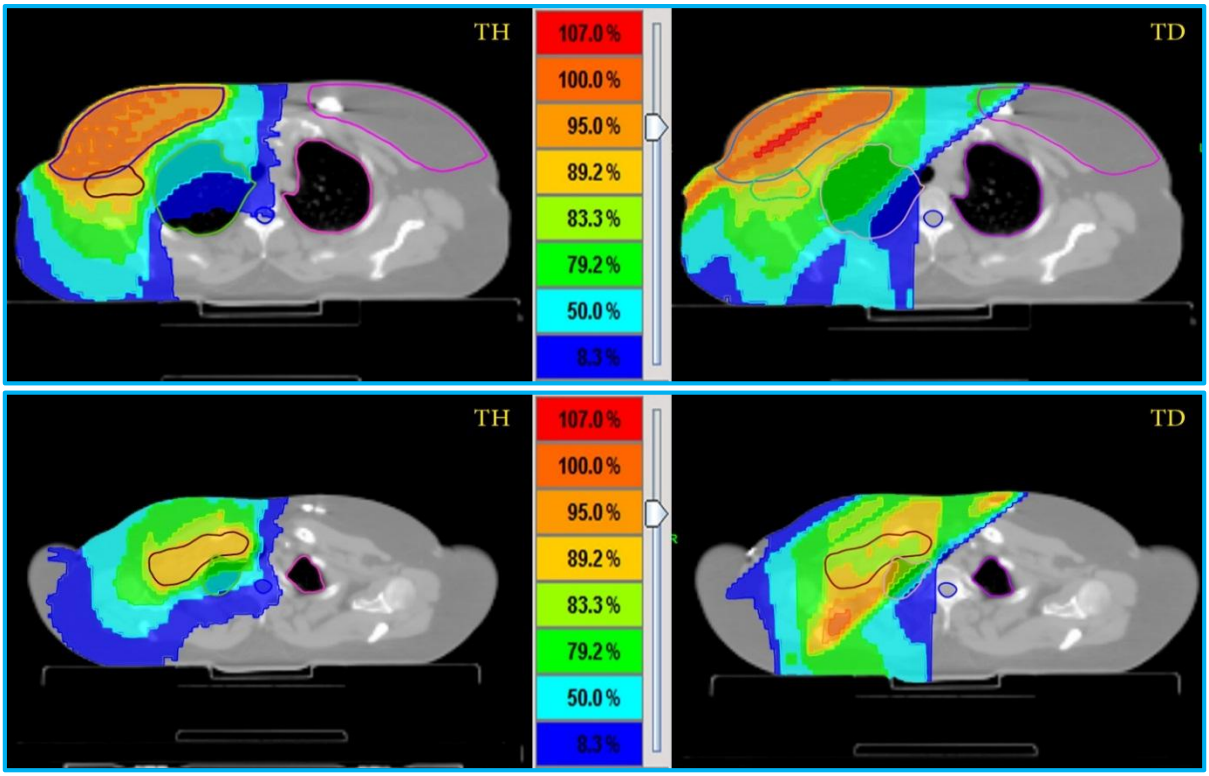

Figure IV-34 Dosimetric illustration of the two modes of delivery for the patient 2.

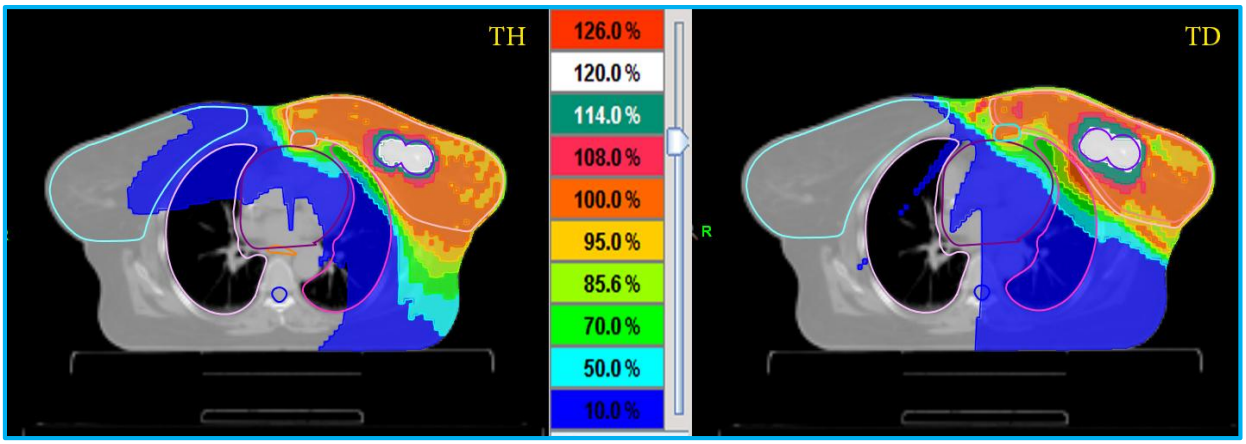

Figure IV-35 Dosimetric illustration of the two modes of delivery for the patient 3.

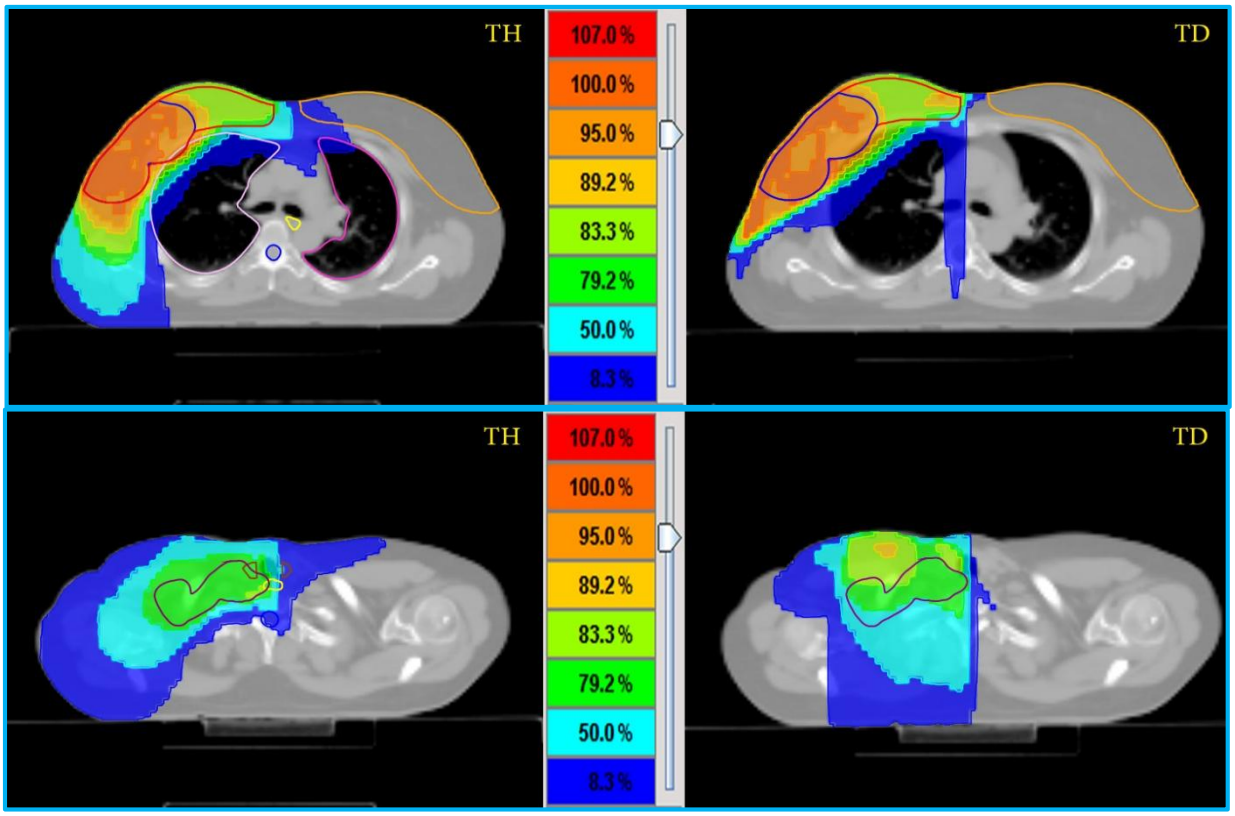

Figure IV-36 Dosimetric illustration of the two modes of delivery for the patient 4.

IV.7.3.6 Conclusion

For the complicated breast cancer cases and the advanced stages include as a PTVs breast or a chest wall and clavicle and IMC and boost it is preferable and recommended to choose the TomoHelical as a delivery mode in treatment to cover better the PTVs by the references dose and to preserve better the OARs without having hot spots or high dose contamination outside the target volumes.

IV.8 Conclusion

The main feature of Tomotherapy system is that it provides two modes of radiation delivery TomoDirect and TomoHelical, in which the physicist will have the full choice to choose the better mode according to the clinic data and pathological case, where it is recommended according to our results to treat by TomoDirect for the simples case include a Breast or a Chest wall alone as PTV, and treating by TomoHelical for the complicated cases include Breast or Chest wall, Boost, Clavicle, and IMC as PTVs, while for the cases include Breast or Chest wall and Boost as targets the choosing between the two modes it depends on the Boost characteristics like its localization in the breast and whether it is consisted by one volume or multiples, in which it is recommended to treat by TomoDirect mode when the boost is located in the edges of the breast and by TomoHelical mode when it is located inside the breast especially if it is formed by multiples volumes.

General Conclusion

Tomotherapy systems becomes today a necessity in treatment cancer filed because of the important features and advantages it collects technologies such as IMRT, IGRT, ART, TomoEDGE and the TomoDirect and the TomoHelical which can make a difference in treatment quality and patient's life, beside that Tomotherapy system can also treat cancers that have returned, even if the patient already had radiation therapy and have been told by others that he is not a candidate for more radiation.

The two modes of radiation delivery which we have studied in this memoir provide a wide range of treatment solutions which adapt with all pathological cases of breast cancer, where the covering of the target volumes by the references doses and protecting the OARs are much more better than the conventional treatment techniques which has generally only one mode of radiation delivery, in which the side effects of not suitable delivery mode may cause other problems for the patient in the time where he is looking to be treated, whereas the side effect may threat the patient's life and may lead to death.

Choosing TomoDirect or TomoHelical as a treatment delivery mode is not free from side effects and disadvantages as all treatment techniques in radiotherapy, but because that the advantages of the Tomotherapy system are so important until the actual moment in front of other treatment techniques we prefer to talk generally about the Brightside of this system. The main side effects of these tow mode of delivery is that the TomoHelical mode has a problem of delivering the low doses to organs at risk especially when we are in simple pathological case, that can cause a stochastic effects on the body appear in later time, while the TomoDirect mode has the invers, means the delivering of high doses to organs at risk and contamination by these high doses outside the region of interest especially in the complicated cases of breast cancer which include multiple target volumes, in which high doses can cause stochastics and determinist effects as well. While the actual limitation of Tomotherapy system itself that make it not available in all centers in Algeria and even in the world is the cost of the machine which is about six million dollars for full options Tomotherapy machine.

The Radixact treatment delivery System is the next generation of Tomotherapy platform from Accuray, designed to enable doctors and physicists to more efficiently and effectively deliver precise radiation treatments to more patients. The development of radiotherapy field is going on to the same goal which is giving a precise radiation treatment that eliminate cancer and protect the healthy organs with comfort situation of the patient and less treatment time. The thing that can make cancer easier to be full treated without any scares.

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Annex

Internships, Seminars and Formations in Medical Physics

CLINIQUE DES OASIS DE DIAGNOSTIQUE ET DE SOINS

EL MOUSTAJAB BOUHRAOUA, BP 150, 47032,
GHARDAIA, ALGÉRIE
Tél. 213-(0)-29-23-99-99
Fax. 213-(0)-29-23-99-98

ATTESTATION DE STAGE

Je soussigné Dr. BABZIZ AHMED, agissant en qualité de médecin radiologue de Clinique Des Oasis GHARDAIA , certifie que Monsieur *BENABDELLAH Ilyas*, a effectué un stage au sein de notre clinique du *10/09/2016* au *24/09/2016*.

Au cours de cette période, il a intégré le service d'imagerie médicale où il a participé dans la modalité suivante :

- IRM (imagerie par résonance magnétique)

Fait à *GHARDAIA*
Le *30/04/2017*

Signature
Dr. BABZIZ

SARL CLINIQUE DES OASIS EL MOUSTADJEB GHARDAIA Tél:029 88.99.99 de Diagnostic et de Soins

B HAMMOUDA ALLAH GERANT

Dr BABZIZ A.
Médecin Radiologue

CLINIQUE DES OASIS DE DIAGNOSTIQUE ET DE SOINS

EL MOUSTAJAB BOUHRAOUA, BP 150, 47032,
GHARDAIA, ALGÉRIE
Tél. 213-(0)-29-23-99-99
Fax. 213-(0)-29-23-99-98

ATTESTATION DE STAGE

Je soussigné Dr. BABZIZ AHMED, agissant en qualité de médecin radiologue de Clinique Des Oasis GHARDAIA , certifie que Monsieur *BENABDELLAH Ilyas*, a effectué un stage au sein de notre clinique du *24/09/2016* au *08/10/2016*.

Au cours de cette période, il a intégré le service d'imagerie médicale où il a participé dans les modalités suivantes :

- L'ultrason
- La radiologie conventionnelle RX

Fait à *GHARDAIA*
Le *30/04/2017*

Signature
Dr. BABZIZ

B. HAMMOUABDELLAH
GERANT

SARL CLINIQUE DES OASIS
EL MOUSTADJEB
GHARDAIA
Tél:029 88.99.99
de Diagnostic et de Soins

Dr BABZIZ A.
Médecin Radiologue

REPUBLIQUE ALGERIENNE DEMOCRATIQUE ET POPULAIRE
MINISTERE DE LA SANTE, DE LA POPULATION ET DE LA REFORME HOSPITALIERE
ETABLISSEMENT HOSPITALIER SPECIALISE EN ONCOLOGIE EMIR ABDELKADER D'ORAN

SERVICE DE RADIOTHERAPIE
Pr.A.BOUKERCHE.
Tel/Fax : 041 13 40 13.
Email : boukercheahtr@yahoo.fr.

Oran le : 10/06/2018

ATTESTATION

Durant Son stage au service de Radiothérapie de l'EHSO Emir Abdelkader d'Oran (du 24/04/2018 au 01/05/2018), Mr **BENABDELLAH Ilyes** a assisté et participé aux différentes étapes du déroulement du traitement en Radiothérapie (partie Physique Médicale), Simulation (GE), traitement sur LINAC (DHX2100), ainsi qu'à la validation des plans de traitement, et les différents contrôles de qualité des appareils (Simulation et Traitement).

Pr A. BOUKERCHE
RADIOTHERAPIE
Chef de Service HU
EHSO Emir Abdelkader d'Oran

Internship in chamids Mahmoodi Hospital – HCM - Tiziouzou

From 18 to 29 september 2018

About Radiotherapy and Stereotactic radiosurgery

CSA
CENTRE SIDI ABDELLAH
CANCEROLOGIE

Attestation de stage

Je soussigné, Monsieur Brahim Hocini, agissant en qualité de coordinateur du service de Radiothérapie au Centre Sidi Abdellah de Cancérologie CSAC, certifie que Monsieur ***Ilyas Ben Abdallah***, Etudiant à l'Université de Laghouat, a effectué un stage au sein de notre Centre du **04 au 11 Septembre 2018** et du **27 au 03 Mars 2019**.

Au cours de cette période, il a intégré le Centre, où il a effectué une étude dosimétrique comparative entre deux techniques de traitement du sein en Tomothérapie (TomoHelical vs TomoDirect).

Cette attestation lui est délivrée pour servir et valoir ce que de droit.

Fait à Alger

Le *10/06/2019*

SARL CROMASA
Ville nouvelle de Sidi Abdellah
route de Sidi Bennour
16093 Mahelma - ALGER
R.C : 16/00-0990452 B 12
NIF : 001216099045235 9

National Seminars

Attendance in the first medical physics day in December 2017 – Oran
Organized by: USTO and CAC of Oran.

Attendance in the third medical physics day in October 2018 – setif
Organized by: Setif University and CAC of setif

Attendance in the fourth medical physics day in October 2019 – setif
Organized by: Setif University and CAC of setif

international Seminars

participation in the international workshop in diagnosis imaging and radiotherapy from 01 to 04 December 2018 – Beirut – Lebanon

Getting the 15 points of CME (counting medical education) international medical physicists' credit.

Formations

Webinar about Stereotactic Radiosurgery

Organized by: American Brain Tumor Association

CERTIFICATE

PROUDLY PRESENTED TO

BENABDALLAH Ilyas

The ABTA presents: Whole Brain Radiation Vs Stereotactic Radiosurgery - July 10, 2018

Jul 10, 2018

Date of Completion

American Brain Tumor Association

Organizer

American Brain Tumor Association®

Providing and pursuing answers®

ملخص _____ أصبح نظام التوموتيرابي حاجة ضرورية في ميدان العلاج الاشعاعي للسرطان، خاصة مع الحلات المرضية التي لا تتطابق مع خصائص العلاج الاشعاعي التقليدي كسرطان الثدي المتقدم، نظام التوموتيرابي باحتوائه على نوعي إطلاق الأشعة نحو الورم السرطاني الموجه والدوراني وإضافة إلى المميزات العديدة التي يشملها هذ النظام كتوفره على تقنية التحكم في شدة الاشعاع، تقنية التصوير المرافق للعلاج الاشعاعي، تقنية العلاج الاشعاعي التوافقي، ونظام التحكم في التعريض الاشعاعي لحواف الورم السرطاني، يجعله يوفر جودة عالية من العلاج، بما يضمن الإزالة الكاملة للورم وحماية قصوى للأعضاء السليمة المحيطة به، وهذا يمثل الهدف الرئيسي من علاج السرطان بالأشعة.
الكلمات المفتاحية: التوموتيرابي، العلاج الاشعاعي الموجه، العلاج الاشعاعي الدوراني، التحكم في شدة الاشعاع، العلاج الاشعاعي التوافقي، التصوير المرافق للعلاج الاشعاعي، التحكم في التعريض الاشعاعي للحواف، سرطان الثدي.

Abstract ____Tomotherapy system becomes a necessity for some pathological cases of cancer which doesn't adapt to the conventional techniques of treatment such us the advanced stages of breast cancer, Tomotherapy by consisting of the tow modes of radiation delivery TomoDirect and TomoHelical in addition to other features and new technologies like the intensity modulated radiotherapy (IMRT), the imaging guided radiotherapy (IGRT), the adaptative radiotherapy techniques (ART) and the TomoEDGE system, provides a high good treatment quality by radiation, in which the radiation treatment will eliminate all the tumor and protect as possible the organs at risk, and that represent the main two goals of treatment by radiation.
Key words: Tomotherapy, TomoDirect, TomoHelical, IMRT, IGRT, ART, TomoEDGE, Breast cancer.

Résumé ___Le système de tomothérapie devient une nécessité pour certains cas pathologiques de cancer qui ne s'adapte pas aux techniques de traitement classiques, telles que les stades avancés du cancer du sein, Tomothérapie qui comprend les deux modes de délivrance du rayonnement TomoDirect et TomoHelical, en plus d'autres options et de nouvelles technologies comme la radiothérapie par modulation d'intensité (IMRT), la radiothérapie guidée par imagerie (IGRT), la radiothérapie adaptative (ART) et le système TomoEDGE, fournissent une qualité de traitement de haute qualité par des rayonnement, dans laquelle le trématent par des radiations élimine toute la tumeur et protège que possible les organes à risque, et qui représentent les deux objectifs principaux du radiothérapie.
Mots clés : Tomothérapie, TomoDirect, TomoHelical, la radiothérapie par modulation d'intensité, la radiothérapie guidée par imagerie, la radiothérapie adaptative, TomoEDGE, cancer du sein.