Sudan University of Science and Technology
College of Graduate Studies

Determination of The Effects of Elapsed time Chemotherapy Treatment on Radio Nuclide Bone Scan Image Quality for patient on ca-breast

تحديد تأثير العلاج الكيميائي للوقت المنقضي علي النويدات المشعة لجودة صورة مسح العظام لمرضي سرطان الثدي

A thesis submitted for partial fulfillment of the Requirements of M.Sc. degree in Nuclear Medicine Technology

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الآيـــة

يقول الله عز وجل:

اقْرَأْ بِاسْمِ رَبِّكَ الَّذِي خَلَقَ (1) خَلَقَ الْإِنْسَانَ مِنْ عَلَقٍ (2) اقْرَأْ وَرَبُّكَ الْأَكْرَمُ (3) الَّذِي عَلَّمَ بِالْقَلَمِ (4) عَلَّمَ الْإِنْسَانَ مَا لَمْ يَعْلَمْ (5).

سوره العلق – الآية (1-5)

DEDICATION

*To my parents (**Mohamed&Salwa**)*

*To my brothers (**Saria&Albraa**)*

*To my colleagues especially (**Mr. Abdelbagi**)*

*To my all friends especially (**ZabiaTagEldeen**)*

To any one that help me in this research

ACKNOWLEDGEMENT

First of all, I would like to say Alhamdulillah for giving me the health and strength to finish this research.
Then I would like to thank my supervisor **Dr. Salah Ali Fadlalla**
his sincere supervision, advice and guidance from the very early stage of this research as well as giving me extraordinary experiences throughout the work, above all he provided by the encouragement.
I would like to express my gratitude to college of medical radiological science members and staff.
Finally , I would like to the staff of National Cancer Institute, especially the staff of Nuclear Medicine department for their help and cooperation to achieve my gall.

ABSTRACT

The bone scan is the accepted initial imaging modality for skeletal metastases. Some patients use chemotherapy in the initial stages before and after surgery for breast cancer patients according to the international protocol; this study aimed to evaluate the time elapsed between the bone scan and chemotherapy dose It is a prospective study designed and conducted in the Nuclear Medicine Department, National Cancer Institute- Wad Madani, which included 50 female breast cancer All patients were diagnosed with breast cancer according to the histopathology report and were received chemotherapy treatment patients with mean age 48.22 years, and their mean weight 74.7 kg, mean dose 25.4 mci ^{99}Tc-MDP, were investigated via bone scan with MEDISO gamma camera The duration of the study was from March 2019 to July 2019 .The results of this study showed that the direct linear relationship between the acquired counts and the elapse time after chemotherapy , the coefficient of this relationship indicates that the count will be increased by 26 kilo counts per day . their is a direct positive relationship between the patient weight (kg) and the administered dose (mci) ,when the weight of the patient increase must be increasing the doses. So the longest the interval time between last chemotherapy and bone scan the more image will be high optimal, where it was preferred to be more than three weeks.

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المستخلص

فحص العظام هو طريقه التصوير الاوليه المقبوله للانتشار الهيكل العظمي . يستخدم بعض المرضى العلاج الكيميائي في المراحل الاولية قل و بعد الجراحة لمرضى سرطان الثدي وفقا للبروتوكول الدولي , هدف هذه الدراسة الى تقييم الوقت المنقضي بين فحص العظام و جرعة العلاج الكيميائي وهي دراسة استباقية صممت و اجريت في قسم الطب النووي المعهد القومي للسرطان في ود مدني و الذي شمل 50 من سرطان الثدي للاناث تم تشخيص جميع المرضى بسرطان الثدي وفقا الى تقرير التشريح المرضى و تم استقبال مرضى العلاج الكيميائي الذين متوسط اعمارهم 48 عاما متوسط اوزانهم 74 كيلو جرام من متوسط جرعة 25ملي كوري تاكنيشيوم و تم فحصهم عن طريق فحص العظام باستخدام كاميرا جاما ميدسيو. كانت مدة الدراسة من مارس 2019–يوليو2019 , و اظهرت نتائج هذه الدراسة وجود علاقه خطيه بين العد المكتسب و الزمن المنقضي بعد العلاج الكيميائي , يشير معامل هذه العلاقه الي ان العدد سيزداد بمقدار 26 كيلو كاونت , هنالك علاقه ايجابيه مباشره بين وزن المريض(كيلو جرام) والجرعه المعطاة(ملي كوري) ,عندما يزيد وزن المريض يجب زياده الجرعه. لذا كلما طالت الفترة الزمنية بين العلاج الكيميائي الاخير و مسح العظام ستكون الصورة الاكثر مثالية حيث كان يفضل ان يكون اكثر من ثلاثة اسابيع .

List of Contents

Chapter one

Chapter two

Chapter three

Chapter four

Chapter five

List of Tables

List of figure

Abbreviations

ACS	**American Cancer Society**
ASCO	**the American Society of Clinical Oncology**
ASCO	**American Society of Clinical Oncology**
CIPN	**chemotherapy-induced peripheral neuropathy**
CT	**Computed tomography**
D C I S	**Ductal Carcinoma in Situ**
DICOM	**Digital imaging and communication in medicine**
L C I S	**Lobular carcinoma in situ**
LEHR	**Low energy high resolution**
MDP	**methylenediphosphate**
MRI	**Magnetic resonance image**
NCCN	**The National Comprehensive Cancer Network**
PACS	**picture archiving and communications systems**
PCT	**Patient care technician**
PHA	**a pulse height analyzer**
PMT	**Photomultiplier tubes**
Q.C	**Quality control**
QOL	**Quality of life**
RICK	**Radiation and Isotopes Center of Khartoum**
SPECT	**Single photon emission computed tomography**
TNM	**Tumor node metastases**

Chapter one
Introduction

1-1 Introduction:

Bone scintigraphy is one of the most frequently performed of all radionuclide procedures. Radionuclide bone imaging is quick, relatively inexpensive, widely available, and exquisitely , sensitive and is invaluable in the diagnostic evaluation of numerous pathologic conditions. The procedure is performed with technetium-99m–labeled bisphosphonates. These compounds accumulate rapidly in bone, and by 2–6 hours after injection, about 50% of the injected dose is in the skeletal system. The uptake mechanisms of bisphosphonates have not been completely elucidated. Presumably they are adsorbed to the mineral phase of bone, with relatively little binding to the organic phase. The degree of radiotracer uptake depends primarily on two factors: blood flow and, perhaps more importantly, the rate of new bone formation.(Genant*et al*.,1974; Galasko, 1975)

Important point to consider before diagnosing a flare reaction on bone scan is the period that has elapsed between the pretreatment scan and the beginning of therapy. If there is substantial delay, even as short as 3-6 weeks, between the firstscan and onset of treatment, interval progression of metastases could go unrecognized. For correct interpretation of serialscans, the pretreatment scan should be obtained as close to theonset of therapy as possible. The overall accuracy of the radionuclide bone scan for monitoring bony metastases fromcarcinoma of the prostate is excellent. In our review of scans obtained 3 months after initiation of treatment, this early scan provided misleading information in 6% of studies, showing apparent deterioration in the face of clinical

improvement. It isemphasized, however, that this phenomenon is exceptional(Pollen *et al*., 1981).

The phenomena of cancer metastasize due to some properties of the cancer cell, as cancer cells show uncontrolled mitotic divisions causing unorganized growth, amebic movement, and cancer cells do not undergo differentiation. The breast cancer is commonly affecting female with a percentage rate equal to 34.5% in Sudan, and scarcely among males 0.1%. Such high incidence of breast cancer among female in which they ascribed the high incidence of female breast cancer to estrogen hormone that promotes the development of breast cancer. Chemotherapy Treatment uses medicine to weaken and destroy cancer cells in the body, including cells at the original

cancer site and any cancer cells that may have spread to another part of the body. Chemotherapy, often shortened to just "chemo," is a systemic therapy, which means it affects the whole body by going through the bloodstream. Chemotherapy was used to treat the early stage, invasive breast to get rid of any cancer cells that may be left behind after surgery and to reduce the risk of the recurrence, advanced stage cancer to destroy or damage the cancer cells as much as possible and in some cases, chemotherapy is given before surgery to shrink the tumor size .

1-2 Problem of the study:

In the sudan, bone scintigraphy in usually requested for chemotherapy patient without knowing the suitable time between chemotherapy and bone scan to the beast of the researcher's knowledge.

1-3 Importance of the study:

The study Determines the interval time between chemotherapy cycle and bone scan, to get high quality image and minimum hazard to the patient.

1-4 Objectives

1-4-1 General Objective

The general objective of this study is to Determination The Effects of elapsed time Chemotherapy Treatment on Radio nuclide Bone Scan Image quality for patient on ca-breast .

1-4-2 Specific Objectives:

1. To determine the image quality in according to elapsed time between the bone scan and chemotherapy.
2. To establish a protocol for bone scan within chemotherapy patients.
3. To minimize the radiation hazard to chemotherapy patients.

Chapter two

Literature Review

2-1 Anatomy of breast:

The breast (mammary gland) is one of the accessory organs of the female reproductive system. The breast develops considerably after puberty but they only reach their full function state of development in the latter part of pregnancy .after puberty each female breast forms a rounded eminence on the anterior and lateral walls of the chest , on the surface of the pectoral is major muscle.

The breast is an endocrine gland placed on the front of the chest, consisting of glandular acini, also called alveoli, coated by cells that have the property of securing milk under the influence of hormones such as prolactin. In the adult woman, the breast is made up of glandular tissue, connective tissue, and adipose tissue that determine the size, shape and texture of the organ. At the apex of the breast is the mammary areola, a pigmented skin area whose surface is characterized by the presence of modified sebaceous glands that, with their secretion, have the function of making the nipple soft and elastic. At the surface of the nipple, the tubules from which the secretion product of the gland comes out. The whole of the acorns form the lobules that, clustering, form the lobes separated from the connective tissue. The milk produced from the acules of each lobule is harvested in a duct end or lobular excretor which is confluent with those from other lobules of the same lobe, giving rise to gallotomorphic ducts; the latter, below the nipple, dilate to form 5-8 mm wide galactoids, which function as small milk containers. Galactic sinuses result in so-called milking pores on the nipple apex.

Estrogen and progesterone induce changes in the glandular tissue depending on the period of the menstrual cycle, with sometimes painful swelling and nodular formations reaching the maximum size towards the end of the menstrual cycle and then regressing again. Most tumors develop at the terminal end of lobular units of the breast parenchyma. Glandular tissue is more abundant in the super-external portion of the breast; therefore about half of the tumors affect this area of the gland The thoracic wall includes ribs, intercostal muscles and toothed muscle front, but not the pectoral muscles Regional lymph nodes Lymphatic Drainage of the Breast is composed of three main routes. The axillary, transpectoral and internal mammary Staging intramammary lymph nodes are considered as axillary and supraclavicular lymph nodes such as regional lymph nodes. Metastases in other lymph nodes, including internal control cervical or breast cancels as remote metastases Regional lymph nodes are-axillary vein rotary interceptors and satellites of the vein vein axillary and collateral are subdivided into.-Level (lower achilles) lymph nodes laterally to the side margin of the small pectoral muscle-Level (mid axillary) lymph nodes between the lateral margin and the medial margin of the chest pectoral muscle and the interferential lymph nodes of Rotter-III level (apical axillary) lymph nodes placed medially at the medial margin of the small pectoral (**Virginia A. Cirolla**, 2017).

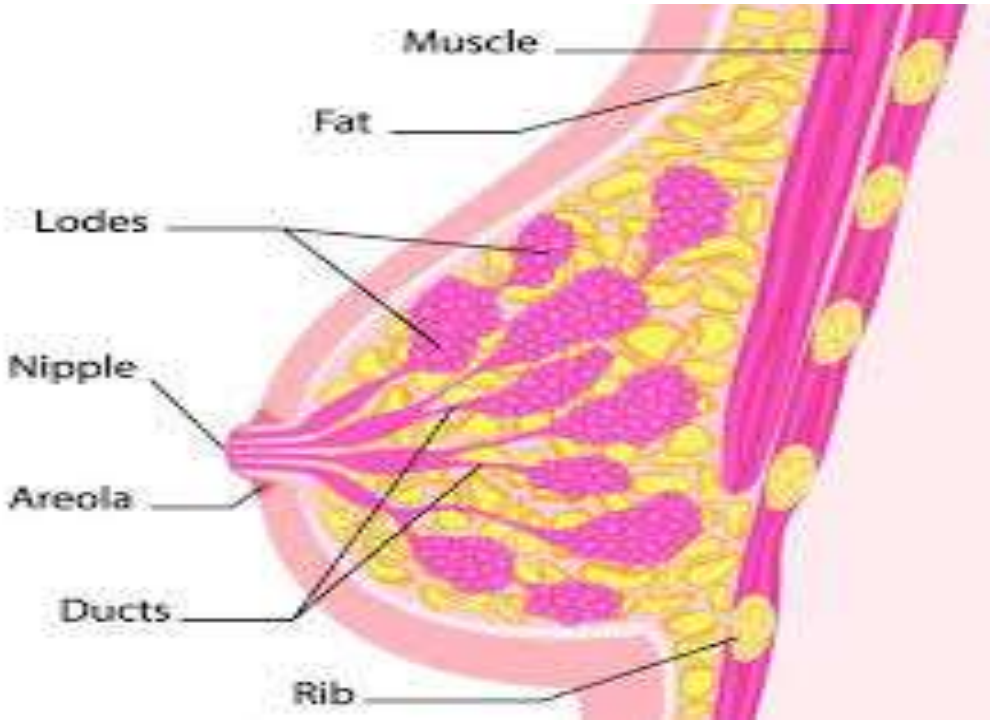

Figure 2-1 :the normal anatomy of breast, Breast Anatomy,2017. (Virginia A. Cirolla).

2-2 Physiology of breast:

The primary function of mammary gland is to nurture young by producing breast milk the production of milk is called lactation. Breast play an important part in human sexual behavior, they are one of the most visible or obvious female secondary sex characteristics .

At puberty the oestrogen secretion increased by the ovaries causes growth of the lactiferous ducts and progesterone stimulates alveolar growth. During pregnancy there is considerable duct proliferation and alveolar development under the influence of the greatly increased concentration of oestrogen , progesterone and placental lactogen . after the birth of the child , the concentration of these

hormones fall but prolactin secretion continues and increases if breast feeding is established (Dean and west, 1987).

2-3 pathology of breast:

The most common pathologic type for breast cancer includes the following:

2.3.1 Breast carcinoma

Carcinoma of the breast is divided into categories : non invasive and invasive . non invasive carcinoma is a distinct lesion of the breast that has the potential to became invasive cancer . these lesions are restricted to the glandular lumen and do not have access to the lymphatic system or blood vessels . non invasive cancer may also termed in situ. Ductal carcinoma in situ (D C I S) is isolated within the breast duct and has not spread to other areas of the breast the breast tumors generally includes: lobular carcinoma , fibro adenoma , cysts , gynecomastia , intraductal papilloma , and Paget's disease of the nipple .

Lobular carcinoma is situ (L C I S) is abnormal cells that have been detected in one or more of the breast lobes.

Cysts : cyst are fluid - filled sacs that are benign and appear as well circumscribed masses . their density is usually that of surrounding tissue . to positively diagnose a cyst , the ulatrasonography and needle biopsies have to be used.

Fibro adenoma : fibro adenomas are the most common benign tumors composed of fibrous and glandular tissue

Fibro cystic change: this common , benign condition is usually bilateral in pre menopausal woman . it includes a variety of conditions : the most obvious are fibrosis and cystic dilation of ducts.

Gynecomastia : this is benign condition of the male breast which there a benign glandular enlargement of the breast .

Intraductal papilloma ; this is small growth inside the duct of the breast near the nipple , it the mammographic appearance is shown typically normal , while ultra- sonography would be helpful.

Paget's disease of the nipple : paget's disease me be invasive or non invasive (Bontrager, 2001).

2-4 Introduction of cancer:

Cancer is a group of diseases characterized by the uncontrolled growth and spread of abnormal cells. If the spread is not controlled, it can result in death. Although the causes of cancer are not completely understood, numerous factors are known to increase the disease's occurrence, including many that are modifiable (e.g., tobacco use and excess body weight) and those that are not (e.g., inherited genetic mutations and immune conditions). These risk factors may act simultaneously or in sequence to initiate and or promote cancer growth. Cancer usually develops in older people; 80% of all cancers in the United States are diagnosed in people 55 years of age or older. Certain behaviors also increase risk, such as smoking, having excess body weight, and drinking alcohol. In the

US, approximately 39 out of 100 men and 38 out of 100 women will develop cancer during their lifetime. These probabilities are estimated based on cancer occurrence in the general population and may overestimate or underestimate individual risk because of differences in exposures (e.g., smoking), family history, and/or genetic susceptibility. For most types of cancer, risk is higher with a family history of the disease. This is thought to result primarily from the inheritance of genetic variations that confer low or moderate risk and/or similar exposures to lifestyle/ environmental risk factors among family members, as opposed to inheritance of genetic alterations that confer a very high risk, which occurs much more rarely. Relative risk is the strength of the relationship between exposure to a given risk factor and cancer. It is measured by comparing cancer occurrence in people with a certain exposure or trait to cancer occurrence in people without this characteristic.

Stage describes the extent or spread of cancer at the time of diagnosis. Proper staging is essential for optimizing therapy and assessing prognosis. For most cancers, stage is based on the size or extent of the primary tumor and whether the cancer has spread to nearby lymph nodes or other areas of the body. Several staging systems are used to classify cancer. A system of summary staging is used for descriptive and statistical analysis of population based tumor registry data and is particularly useful for looking at trends over time. According to this system, if cancer cells are present only in the layer of cells where they developed and have not spread, the stage is in situ. If cancer cells have penetrated beyond the original layer of tissue, the cancer has become invasive and is categorized as local, regional, or distant based on the extent of spread. Clinicians mainly use a different staging system, called TNM. The TNM

system assesses cancer growth and spread in 3 ways: size extent of the primary tumor (T), absence or presence of regional lymph node involvement (N), and absence or presence of distant metastases (M). Once the T, N, and M categories are determined, a stage of 0, I, II, III, or IV is assigned, with stage 0 being in situ, stage I being early, and stage IV being the most advanced disease. However, some cancers do not have a stage IV (e.g., testis) and others (e.g., lymphoma) have alternative staging systems. As the biology of cancer has become better understood, additional tumor-specific features have been incorporated into treatment plans and/or staging for some cancers.(Kimberly Miller, 2019).

2-4-1Breast cancer:

Breast cancer is the most common non-cutaneous malignancy among women, representing 4 in 10 female cancer survivors in the United States. Long-term survival is common after breast cancer treatment, with a 5-year survival rate of almost 90%; thus, addressing survivors' unique post-treatment needs is critical to providing quality health care.

Nearly a decade ago, two landmark publications from the Institute of Medicine highlighted the importance of surveillance, health promotion, and assessing and managing the myriad of physical, psychological, spiritual, social, and practical long-term and late effects faced by many cancer survivors after completing active treatment., Recent publications affirm the importance of addressing health, wellness, and quality of life (QoL) concerns of post-treatment cancer survivors. In recognition of the increasing need for information to support primary care clinicians who care for breast cancer survivors, this guideline was developed to provide recommendations to enhance the quality of clinical follow-up care for those who have completed initial treatment for female breast cancer (eg,

surgery, radiation, targeted therapy, and/or chemotherapy). Although many evidence-based clinical guidelines exist for diagnosis and treatment, there are few evidence-based clinical care guidelines addressing life-long follow-up care for survivors by cancer type. The National Comprehensive Cancer Network® (NCCN®) guidelines are evidence- and consensus-based for the treatment of patients with breast cancer that include information on recommended surveillance for cancer recurrence or new cancers. The NCCN also has symptom-specific survivorship care guidelines addressing anthracycline-induced cardiac toxicity, anxiety and depression, cognitive function, fatigue, pain, sexual function, sleep disorders, healthy lifestyles and immunizations and infections. In addition, the American Society of Clinical Oncology (ASCO) has guidelines for the follow-up and management of patients with breast cancer as well as symptom-based guidelines specific to fatigue, chemotherapy-induced peripheral neuropathy (CIPN), and anxiety and depressive symptoms; ASCO is also developing guidelines on the prevention and monitoring of cardiac dysfunction in survivors of adult cancers and on the management of chronic pain. Furthermore, ASCO recently endorsed the American Cancer Society (ACS) guideline on prostate cancer survivorship. The ACS/ASCO Breast Cancer Survivorship Care Guideline builds upon prior guidelines by providing comprehensive, holistic recommendations specific to post-treatment breast cancer clinical care to help primary care clinicians better manage potential long-term and late effects and to provide timely and appropriate screening and surveillance to improve the overall health and QoL of breast cancer survivors. Breast cancer treatment depends on the stage at diagnosis, the size and location of the tumor, and tumor characteristics. Those who have stage II or III disease at diagnosis may receive more involved cancer treatment, which can result in greater likelihood and

severity of the impact of treatment. Treatment generally includes two key components—treatment of the breast and local lymph nodes with surgery either with or without radiation therapy (“local therapy”) and drug treatments for cancer cells that may have spread (“adjuvant systemic therapy”) outside the breast. Surgical treatment for breast cancer includes breast-conserving surgery with radiation or mastectomy with or without radiation and with or without immediate/delayed reconstruction. In women with a very high risk of contralateral cancer from inherited susceptibility (eg, patients with mutations in the breast and ovarian cancer susceptibility genes *BRCA1*/*BRCA2*), contra-lateral prophylactic mastectomy may be performed. Systemic therapy may precede (“neoadjuvant”) or follow (“adjuvant”) local therapy and consists of combinations of hormonal therapy, chemotherapy, and biological agents.

There is no standardized follow-up model for patients with early stage breast cancer who have completed surgery, chemotherapy, and radiation. Most of these women will have endocrine-responsive tumors and will require endocrine therapy for a total of 5 to 10 years. Randomized trials have shown equivalent outcomes with follow-up by either the oncologist or a primary care physician. Shared follow-up care between one or more oncologists and the primary physician is an additional possibility. However, the great majority of these patients will eventually be discharged back to their primary clinician for ongoing follow-up. It should be noted that these patients remain at risk indefinitely for complications of their previous cancer treatment. Most also remain at risk indefinitely for local and/or systemic recurrence of their breast cancer(Carolyn D, 2016).

2-4-2Chemotherapy:

Cancer has been known as a deadly disease of mankind from prehistoric times. Research into cancer treatment began recently from a historical . One of the most common and fundamental forms of treatment is chemotherapy, which involves injecting into the body an agent designed to attack the cancer cells. Unfortunately, this agent also attacks normal cells causing common side effects such as hair loss. Much research into chemotherapy is involved with designing the agent so as to maximize the effect on cancer and minimize the side effects . Very recently, research has been initiated in modelling cancer treatment using mathematical and/or computer models . Some of these models deal with the treatment from an optimization , from a compartmental, and from a dynamical . We are interested in dynamical models which look at the interaction between normal and cancer cells at one or more given sites in the body, the cancer spreads from one site to another physiological organ via the blood stream or via the lymphatic system. This process is known as metastasis. It is sometimes the case where the secondary tumor, i.e., the cancer at the secondary site, is the one that is fatal. Hence, it. is important to consider a chemotherapy treatment model when metastasis occurs.. The most common metastatic sites are liver, lung, and brain . It is also known that the metastasis increases with increasing size of the primary tumor. A further consideration of the metastasis is that due to the processes involved, there is often a time delay (sometimes significant) for the metastasis to occur . Hence, it is reasonable to model the interaction between cancer and normal cells at two specific sites with metastasis between the primary and the secondary sites with a time delay (suani pinho 2002).

2-5 The Skeletal System:

The skeleton consists of over 200 individual bones which can be classified as belonging to either the axial or the appendicular skeleton. The axial skeleton includes the bones of the spine, ribs and sternum, skull and facial bones, while the pelvis, scapulae and limb bones comprise the appendicular skeleton. Microscopically bone consists of a fibrous matrix, composed mainly of collagen, and mineral matrixofinorganicsalts,includingcalcium,phosphate, and carbonate, with the principal component being crystals of hydroxyl-apatite. Bone is a highly vascular, living tissue with remarkable resilience and capacity for regeneration and remodeling. Two cell types in bone perform this remodeling process: the osteoclasts, which a relarge phagocytes responsible for bone resorption and removal, and the osteoblasts, which forsm new bone. It is the synthesis of bone by osteoblasts that accounts for the accumulation of radiolabeled phosphate on a bone scan, with the radiopharmaceutical being incorporated into newly formed crystals of hydroxyl-apatite. This system of bone resorption and synthesis is finely balanced and continues throughout life, with complete skeletal turnover approximately every 20 years. In normality the process occurs diffusely in the skeleton and uptake of radionuclide is uniform and of low intensity. In disease states causing increased bone turnover there is a greater accumulation of radionuclide with respect to normal(*Margaret E. Brooks2005)* .

2-5-1Nuclear Medicine Imaging:

In nuclear medicine clinical information is derived from observing the distribution of a pharmaceutical administered to the patient. By incorporating a radionuclide into the pharmaceutical ,measurements can be made of the distribution of this radiopharmaceutical by noting the

amount of radioactivity present. These measurements maybe carried out either in vivo or in vitro. In vivo imaging is the most common type of procedure in nuclear medicine, nearly all imaging being carried out with a gamma camera .Nuclear medicine is intrinsically an imaging technique showing the body's biochemistry, the particular aspect depending upon the choice of the radiopharmaceutical. This is in contrast to other commonly used imaging procedures whose main strengths are showing anatomy. Where a knowledge of the precise amount of activity present in an organ is required then positron emission tomography can provide this, although while its usage is increasing it still remains a specialized technique .If an image of the distribution is not essential, collimated scintillation probe detectors aligned with the organ of interest may be used . If the amount of radioactivity present is very low then high-sensitivity whole body counters, consisting of heavily shielded probe detectors, are necessary .In vitro measurements are made on samples of material taken from the patient, such as breath, blood, urine, and feces, to determine the amount of radiopharmaceutical present. Such measurements are made using the gamma- or beta-sample. The diagnostic information is provided by the action of the pharmaceutical; the role of the radioactivity is purely a passive one, enabling the radiopharmaceutical to be localized. For this reason it is possible to use low levels of radioactivity and so the potential hazard to the patient can be kept small (Peter F. Sharp, 2005).

2-5-2The Gamma Camera System:

The gamma camera is the principal instrument for imaging in nuclear medicine and it consists of a large detector in front of which the patient is positioned. Gamma cameras with more than one detector are now common, allowing a higher throughput of patients by acquiring two or more views simultaneously. Every aspect of the modern gamma camera

is under computer control, allowing the operator to select the study acquisition time, or the number of counts to be acquired, to set the pulse height analyzers to reject scattered radiation, control the detector and patient bed positions for SPECT and whole body procedures, and display the image. All gamma camera manufactures sell associated computers and software to process and display the acquired images. The type of computer and the operating system upon which the software functions have, in the past, varied between manufacturers. This has led to a number of problems, which has hindered the transfer of data between systems. However, in recent years, driven by the demand for onscreen reporting of images by clinicians and the need to transfer data to picture archiving and communications systems (PACS), these problems have, in part, been overcome. The solution has been to develop an industry standard data format (DICOM) which, when used with the correct software, will allow the free movement of data between imaging systems. Although all manufacturers will promote their products as being fully DICOM compliant, unfortunately a number of specific problems remain (Peter F. Sharp, 2005).

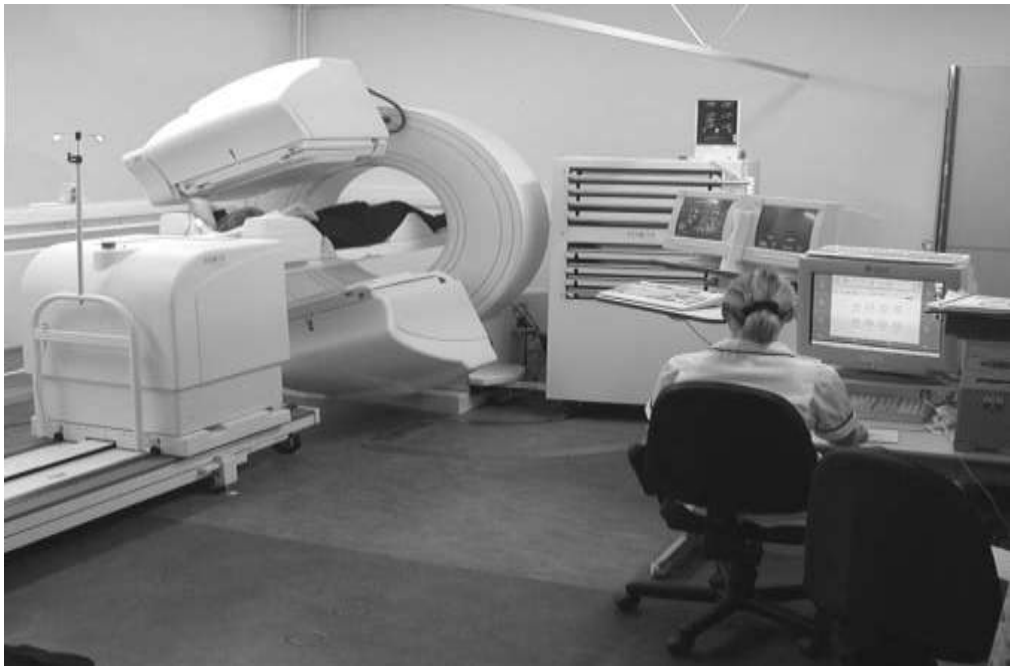

Figure 2.2: The gamma camera in Practical nuclear medicine (Peter F. Sharp).

The patient is lying between the detectors of this double-headed system. To the right of the camera is a rack containing extra collimators. The technician is seated at the computer controlling data acquisition and image display.

2-5-3 Mode of Operation of the Gamma Camera:

The image of the distribution of the gamma-ray-emitting radiopharmaceuticalis produced in the scintillation crystal by a collimator. The gamma rays, which are not visible to the eye, are converted into flashes of light by the scintillation crystal. This light is, in turn, transformed into electronic signals by an array of photomultiplier tubes (PMT) viewing the rear face of the crystal. After processing, the outputs from the PMTs are converted into three signals, two of which (X and Y) give the spatial location of the scintillation while the third (Z) represents the energy deposited in the crystal by the gamma ray. To improve their quality these signals then pass through correction circuits. The Z signal goes to a pulse height analyzer (PHA), which tests whether the energy of the gamma ray is within the range of values expected for the particular radionuclide being imaged. If the Z signal has an acceptable value, then a signal is sent instructing the display to record that there has been a gamma ray detected, the position being determined by the X and Y signals (Peter F. Sharp, 2005).

2-5-4Bone scan:

Bone scintigraphy is one of the most frequently performed of all radionuclide procedures. Radionuclide bone imaging is quick, relatively inexpensive, widely available, and exquisitely sensitive and is invaluable in the diagnostic evaluation of numerous pathologic conditions. The

procedure is performed with technetium-99m–labeled diphosphonates. These compounds accumulate rapidly in bone, and by 2–6 hours after injection, about 50% of the injected dose is in the skeletal system. The uptake mechanisms of diphosphonates have not been completely elucidated. Presumably they are adsorbed to the mineral phase of bone, with relatively little binding to the organic phase. The degree of radiotracer uptake depends primarily on two factors: blood flow and, perhaps more importantly, the rate of new bone formation (1–3). Although protocols vary among institutions, imaging is typically performed 2–6 hours after intravenous administration of 740–925 MBq (20–25 mCi) of Tc-99m–labeled diphosphonates. The delay between injection and imaging allows clearance of the radiotracer from the soft tissues, resulting in a higher target-to-background ratio and improved visualization of bone. Skeletal detail can be further enhanced by encouraging patients to drink copious amounts of fluid after radiotracer injection. A gamma camera equipped with a low-energy, high-resolution collimator will yield the highest-resolution images. Additional anterior and posterior whole-body images are often obtained as needed (Charito Love .,2003).

2-5-5Normal Appearances and Interpretation:

In the normal adult skeleton individual bones are visualized, and uptake is symmetrical about the midline There may be some background soft tissue uptake, particularly in an obese patient. Both kidneys and the urinary bladder

should be readily identifiable. Knowledge of skeletal and urinary tract normal variants is necessary to avoid misinterpretation.

In the normal immature skeleton the greatest uptake of MDP occurs at the epiphyseal plates, the sites of active bone growth. Uptake fades when the

epiphyses fuse and growth ceases. This phenomenon can be useful when early or delayed epiphyseal closure is suspected. Interpretation needs to take account of the age of the patient and findings which may be considered incidental at that age. Full and accurate clinical information is vital, including any history of trauma or surgery. Current medication may also be relevant. With this knowledge the bone scan appearances can be placed in clinical context. Previous bone scan should be available for comparison, at the time of reporting as their contribution can be pivotal. If there is any doubt about the significance of an abnormality, the availability of other imaging can be invaluable, and these studies should be viewed alongside the bone scan to gain most benefit from the exercise. If further imaging of an area is deemed necessary, plain films are still the best first-line investigation. These may demonstrate and even characterize a lesion to account for the bone scan uptake. In view of the increased sensitivity of the bone scan over plain film, if the radiographs are normal, CT or MRI should be considered. The choice of modality will depend on the area of the body in question, and the suspected pathology (Margaret E, 2005)

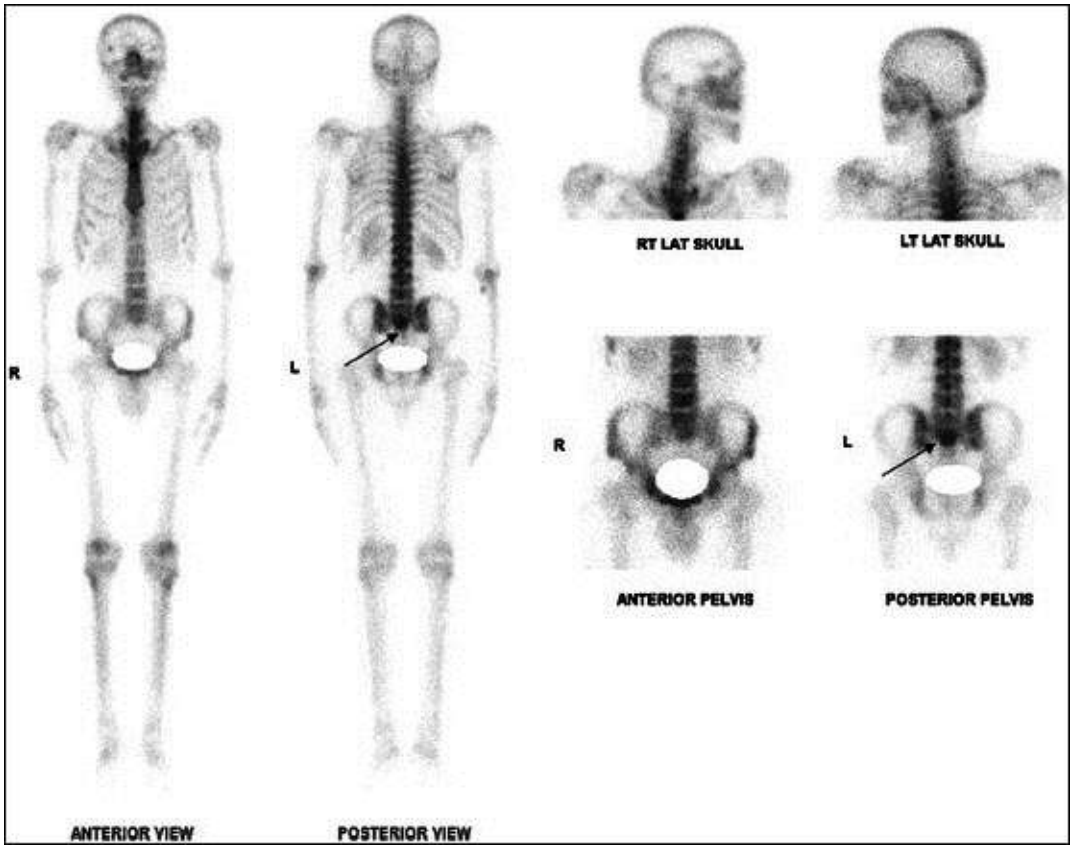

Figure 2.2:The 99mTC –MDP- whole body bone scan skeletal phase image in Practical nuclear medicine

2-5-6Non-skeletal Uptake:

While a radionuclide bone scan is performed primarily to assess the skeleton, there can be findings in other systems. These may be incidental or relevant to the bone pathology. It is important therefore not to overlook the urinary tract and the soft tissues when evaluating the examination.

By virtue of the renal excretion of MDP, normal variants in the urinary tract are exposed. They should be recognized as such and documented, as this may be their first demonstration. Uptake in only a single kidney implies absence or impaired function of the other. Ectopia, malrotation, ptosis, and fusion abnormalities (e.g. horseshoe kidney) are all well visualized if renal function is adequate In bladder or prostatic malignancy the bone scan ,executed primarily for identification of skeletal metastases, can also highlight urinary obstruction, though this is likely to have been

detailed on a prior ultrasound examination. In other clinical circumstances the referrer may not be aware of, or expecting, this finding and its detection may prompt further investigation. Urine leaking from a ruptured collecting system can have a bizarre appearance . In renal malignancy the primary mass lesion, if large enough, can be appreciated as a photopenic defect. Occasionally this will be noted unexpectedly, and while it is not specific for a neoplasm, further investigation is mandatory to exclude renal carcinoma. Some soft tissue MDP uptake is normal and the amount varies with body mass and renal function. Once again, demonstration of abnormal soft tissue uptake may be incidental or of significance, depending on the clinical setting. This uptake occurs when there is soft tissue calcification or ossification , or when MDP accumulates for other reasons, such as in a pleural effusion. This latter example can have a subtle appearance, particularly if bilateral, and is best appreciated on the posterior view . The more common causes of extra-osseous uptake are listed .

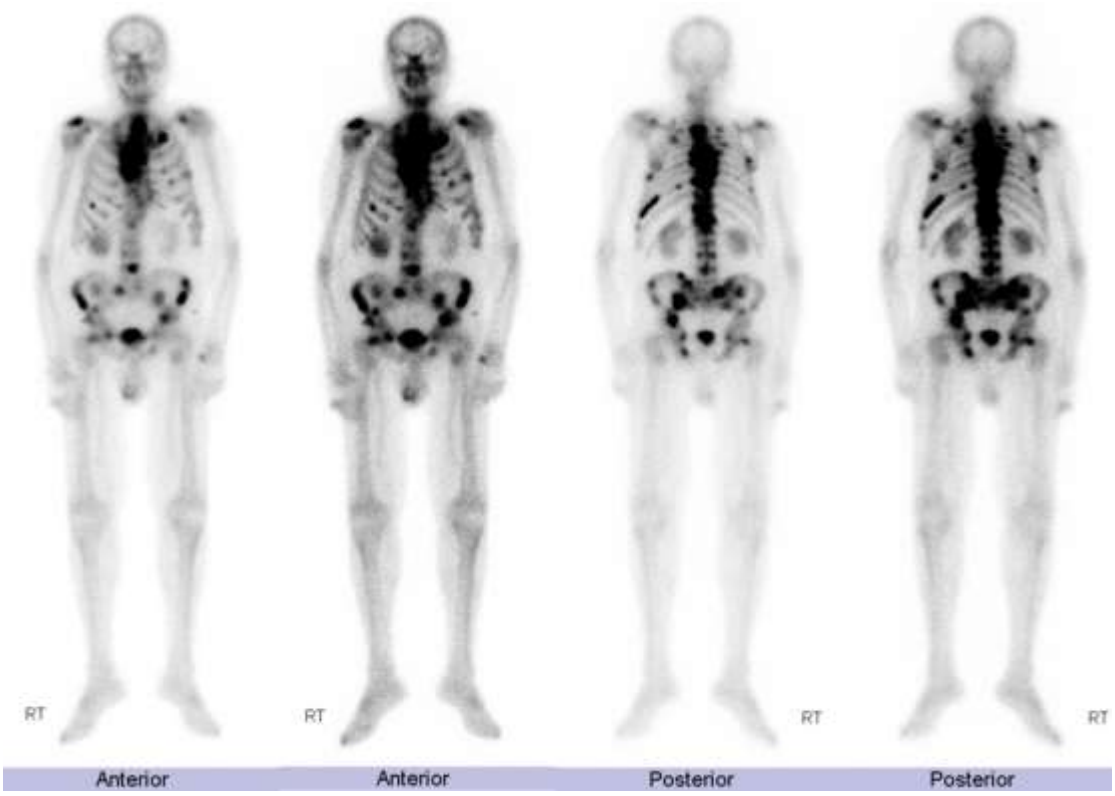

Figure 2.3: The 99mTC –MDP- whole body bone metastasis in Practical nuclear medicine

2-6 Previous studies:

-In study done by(**Gihad et al.** 2017) in Assessment Of The Time Elapsed Between Bone Scan And Chemotherapy Dosefor Breast Cancer, Bone scan is the accepted initial imaging modality for skeletal metastases. Some patients use chemotherapy in the initial stages before and after surgery for breast cancer patients according to the international protocol, this study aimed to evaluate the time elapsed between bone scan and chemotherapy dose. It is a retrospective study designed and conducted in the Nuclear Medicine Department, Radiation and Isotopes Center of Khartoum. (RICK) which included 50male and female cancer patients with age ranged between 25-90 years, weighing 40-90kg were used in the study. All patients were diagnosed as breast cancer according to the histopathology report and were received all chemotherapy treatment. The results of this study revealed that the most common drugs used for adjuvant and nanadjuvant chemotherapy and there are a direct linear relationship between the acquired counts and the elapse time after chemotherapy , the coefficient of this relationship indicates that the count will be increased by 0.018 mega counts per day starting from 0.81 mega counts. there is a direct positive relationship between the patient weight (kg) and the administered dose (mci) ,when the weight of the patient increase must be increasing the doses. This study concluded that the suitable time of bone scan post chemotherapy is one month and chemotherapy would lead to more influence on the bone scan.

In study done by(Knop M.D et,al 1990) Scintigraphic evaluation of tumor regression during preoperative chemotherapy of osteosarcoma , The effect of preoperative chemotherapy (PCT) on the uptake of ^{99m}Tc-

labeled diphosphonates into tumor bone was quantitatively assessed from serial scan studies of 30 osteosarcomas and correlated with the histomorphological changes determined from the surgical specimens. The parametric images of the tumor blood pool and labeled methylene diphosphonate (^{99m}Tc-MDP) plasma clearance by the tumor bone enabled a sensitive distinction to be made preoperatively between a good (>90% tumor cell destruction) and a poor (<90% tumor cell destruction) tumor response. Overall accuracy in presurgical prediction of tumor regression was found to be 88% and 96% for the blood pool and ^{99m}Tc-MDP clearance measurements, respectively ($P \leq 0.0004$). In addition, it proved possible to localize resisting areas of viable tumor up to 1.0 cm in diameter. Even at the half-way stage of PCT, a poor response could be reliably predicted (overall accuracy 91% and 100%, respectively; $p \leq 0.011$). Therefore, ^{99m}Tc-MDP parametric imaging is a highly sensitive and specific modality for an objective and accurate assessment of tumor regression during PCT of osteosarcoma.

In the study carried by (Jemianne Bautista Jia, 2015) about Chemotherapy-related complications in the kidneys and collecting system: an imaging perspective. The agents most commonly associated with chemotherapy-associated nephrotoxicity are methotrexate, semustine, streptozocin, mithramycin, and cisplatin. Certain chemotherapeutic agents have adverse effects on the kidneys and urothelium that can be visualized radiographically, including cystic change, interstitial nephritis, papillary necrosis, urothelial changes, haemorrhagic cystitis, acute tubular necrosis, and infarction. This review focuses on imaging features identifying complications of chemotherapy in the kidneys and collecting system and provides didactic cases to alert referring clinicians.

Chapter three

Materials and Methods

3.1 Materials

3.1.1 Machines used:

The material used to collect the data were categorized into, nuclear medicine an instrument which is MEDISO SPECT Gamma Camera(2005). Collimator used low energy high resolution parallel collimator (LEHR), and the radiopharmaceutical used the Tc-99m MDP injected intravenously,30 mci of TC-99mMDP , (+, - depending on extremes of body weight).

3.1.2 Radionuclide used:

bone scan metastases and structure can be evaluated using uptake and scintigraphy studies. methylenediphosphate (MDP) with technetium 99mTCformed, which show an affinity to hydroxyapatite of the bone tissue, in the chemical form of pertechnetate (^{99m} TcO4-),. Under sterile condition 5ml of sodium pertechnetate solution with maximum activity of 100-500mCi was added to the MDP vial content through the stopper. The vial Content was mixed for 20 minute. The pH value of the prepared radiopharmaceutical has 5-7. The 99mTc-MDP preparation is administered within 6 hours of the preparation time (shelf life).

3.2 Study Population

This study including patient that attending to nuclear medicine department for bone scan, in thenational national institute of cancer in Wad Madani ,and The duration of the study was from March 2019 to July 2019.

3.3Sample size:

fifty patients were included in this study and the sample selected prospective.

3.4 Data analysis

The data were analyzed using the Statistical Package for the Social Science software (SPSS), and personal computer version acer (2005).

3.5 Technique and method

3.5.1 1Patient preparations:

The patient was prepared according to the following points: The request form should be completed with all patient details and sufficient clinical details to justify the patient's exposure to radiation. An information sheet about the test should be explained to the patient. **t**he patient should be adequately hydrated prior to the study. Bone scan is influenced by normal variations in the degree of hydration, because of auto regulation mechanisms. Specific hydration is usually required, a steady intake of fluids over the duration of the study is recommended (approximately 500 ml/h) , The patient was encouraged to avoid immediately before imaging if the catheter is present the back should be emptied before imagine.

3.5.2 Technique of uptake:

Before the injection of the radioactive dose was measured accurately in the dose calibrator. The dose should be minimizing in case of children or low weight patient using different calculation methods. (it is also can be used to maximize the dose in case of high weight patients).bone uptake was performed2-3hours after an intravenous injection of 740-1110MBq (20-30mCi) of ^{99m}Tc-pertechnetate for bone scan.

SPECT gamma camera was equipped with a low-energy, high resoulation, parallel collimator. Images was obtained on a matrix size of (512 x 1024 x16) and scan speed was (13cm/min). At least one image

was obtained for the anterior and posterior bone for800,000 counts, (45^{o} anterior and posterior oblique, lateral view images may be obtained If needed).

Distribution of radiation in bone determined visually and during the process we need the background subtraction of bladder and side of injection.

Interview XP programmed was used to display the bone scan ,while color and contrast were manipulated to enhance the bone image resolution during this study.

Ethical confederation :

Ethical approval had been granted before examination from the hospital nuclear medicine department and consent from the patient .

Chapter four
Results

Table 4-1: Frequencies statistic of patient data

	Age	weight	Height	dose
Mean	48.22	74.7	165.12	25.4
SD	12.3	9.8	6.39	2.6
Max	70	91	183	29
Min	22	58	151	19

Table 4-2: show the frequency of patient age

Patient age	Frequency
22-34	4
35-46	21
47-58	11
59-70	14

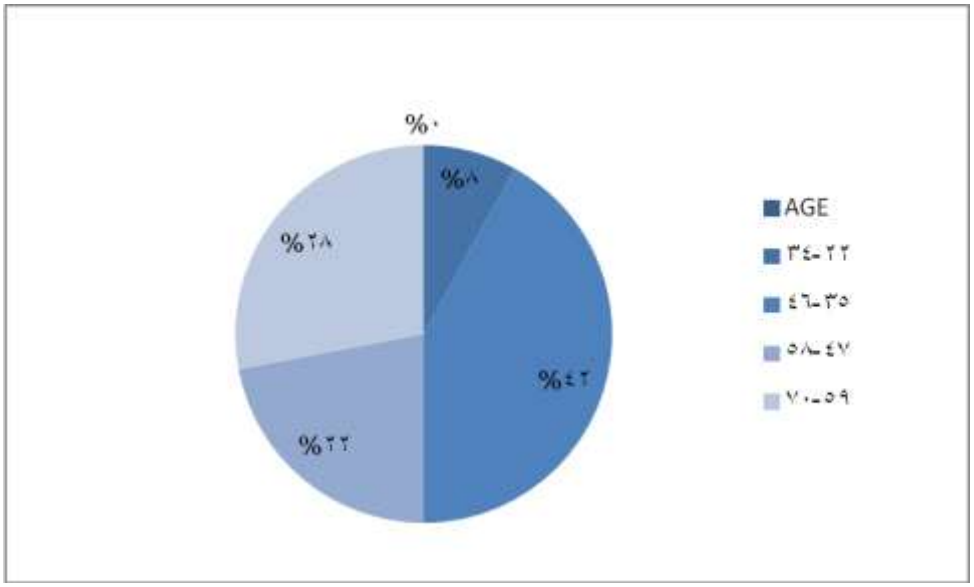

Figure 4-1: show the distribution of age.

Table 4-3: show the frequency of patient's weight in (Kg)

Patient Weight	Frequency
58-67	16
68-76	11
77-85	14
86-95	9

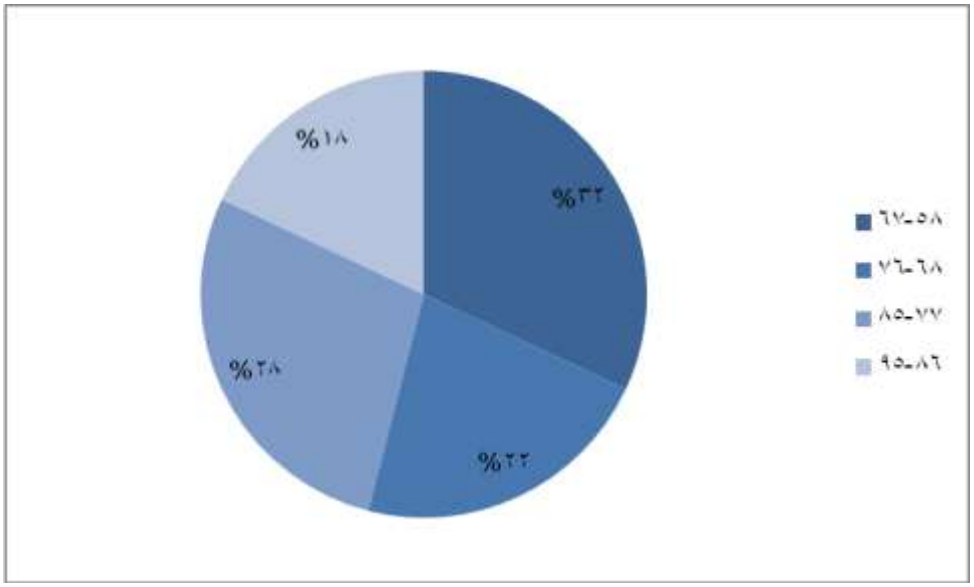

Figure 4-2: show the distribution of weight in (kg).

Table 4-4: show the frequency of patient height in (cm).

Patient Height	Frequency
151-157	6
158-163	9
164-169	28
170-175	4
176-181	2
182-187	1

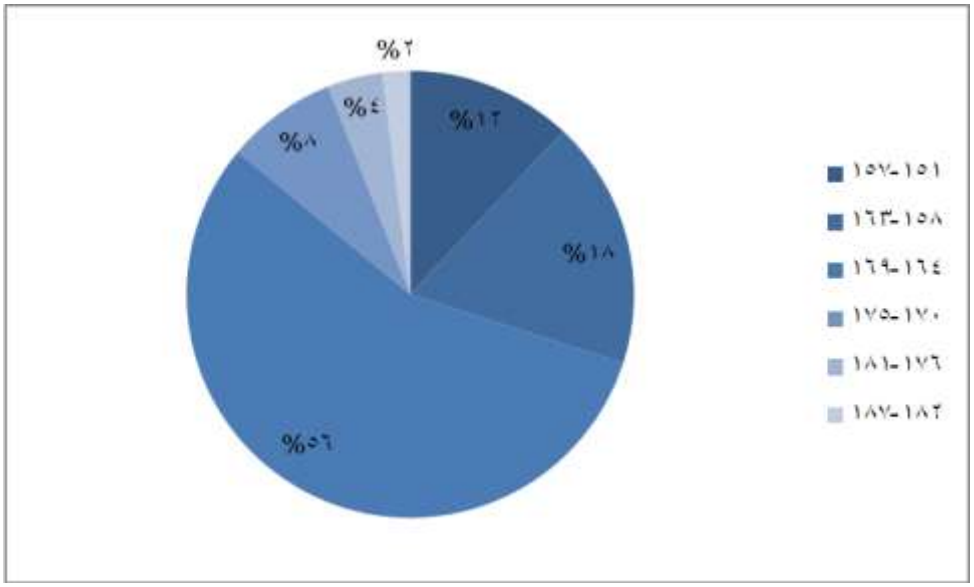

Figure 4-3: show the distribution of patient height in (cm).

Table 4-5: show the frequency of patient dose in (mci)

Dose	Frequency
15-20	3
21-25	20
26-30	27

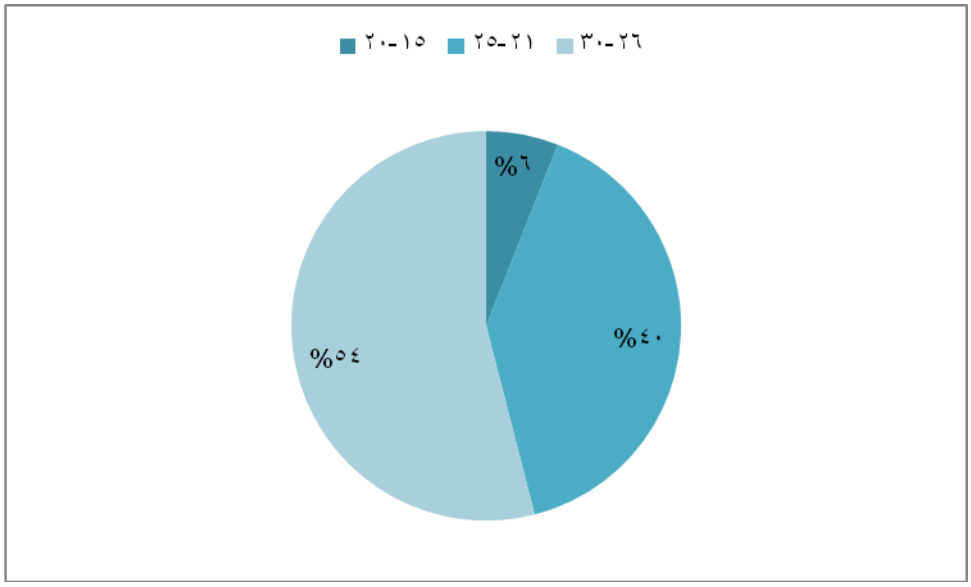

Figure 4-4: show the distribution of patient dose in (mci).

Table 4-6:show the frequency of patient sample, interval time .

Interval time	Frequency
1 -10	18
11- 20	24
21- 30	8

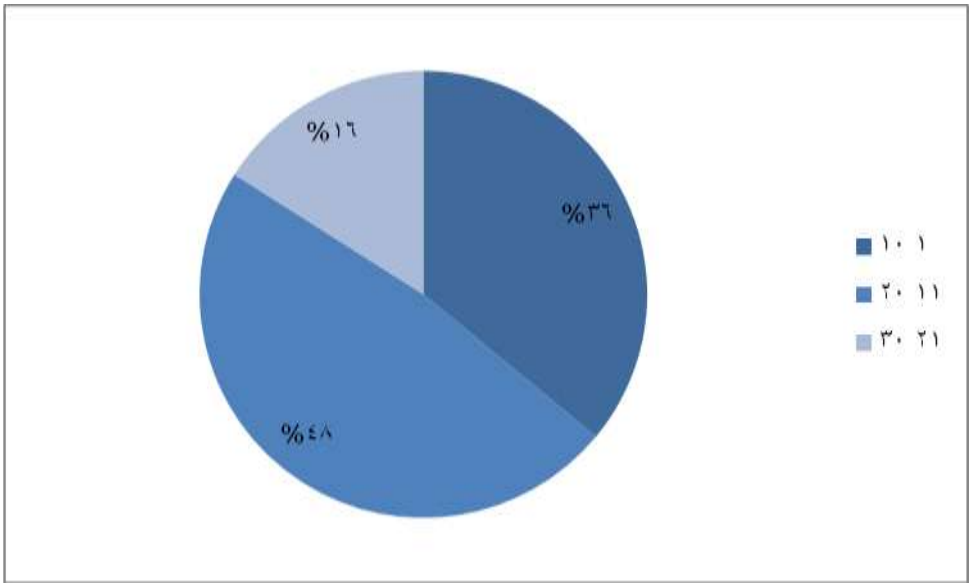

Figure 4-5: show the distribution of interval time of patient sample.

Table 4-7:show the frequency of patient count and days after chemotherapy.

COUNT	DAYS
800	5 DAYS
1000	15 DAYD
1200	20 DAYS

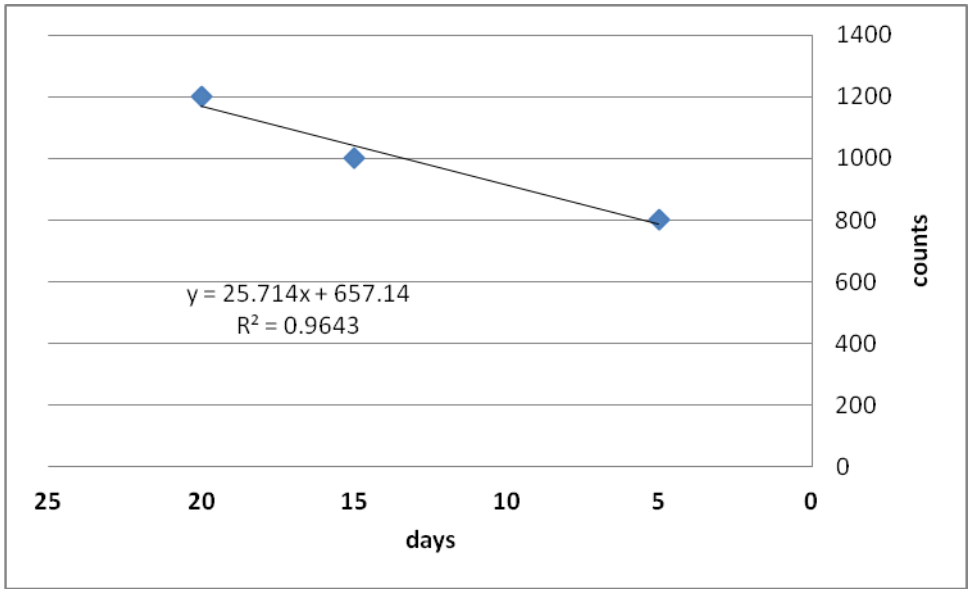

Figure 4-6: show the distribution of patient count and days after chemotherapy.

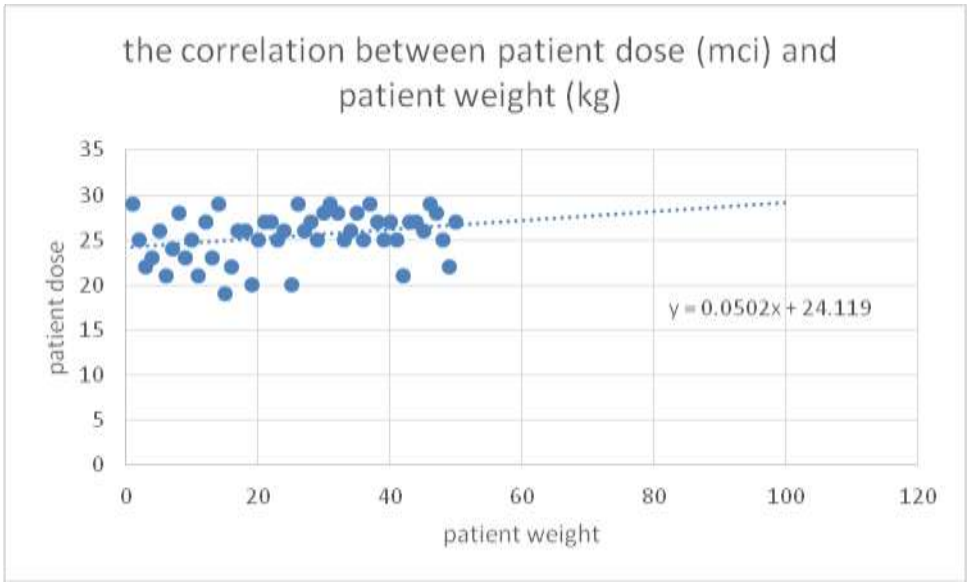

Figure 4-7: show the correlation relationship between patient's dose (mCi) and their weight (kg)

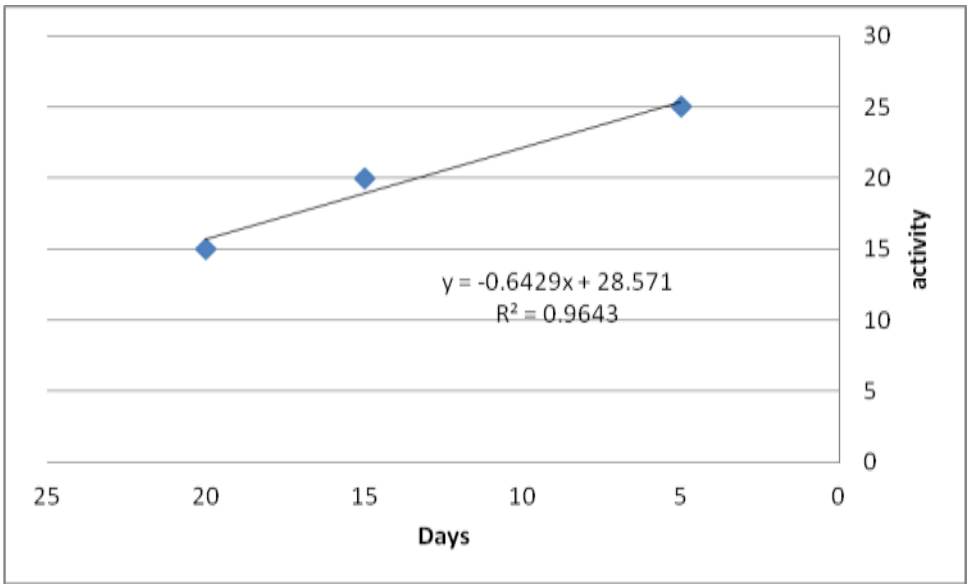

Figure 4-8 : show the correlation relationship between injected activity and days after chemotherapy.

Chapter Five

Discussion, Conclusion and Recommendations

5.1 Discussion:

The aim of this study was to determine the interval time between chemotherapy cycle and bone scan, to get high quality image and minimum hazard to the patient, and to find the accurate time for bone scan. The result showed the frequency distribution of patient's age within the sample of study, that the high incidence of breast cancer was among the mean ages 48.22 year (42% of all patients under study)Figure 1 .

Also showed the distribution of patient weight, as shown that about 32% of patients sample under study were in mean weight 74.7 Kg. Figure 2. also showed the height of patients under study, as shown that about 56% of patient sample were in mean height between 165.12 cm Figure 3.

the frequency distribution of patient dose within the sample of study, as shown that about 54% of patient sample were given a mean dose 25.4 mci , (according to the patient weight)Figure 4 .

the count increase linearly by 26 kilo count per days after chemotherapy and activity delivered to patient receive chemotherapy were more than normal which is 25 mci for chemotherapy patient activity decrease by 0.6 mci per days after chemotherapy Figure 8.

5.2 Conclusion:

The bone scan image is usually affected by the time when image was obtained, the hydration process, the amount of injected dose , the sensitivity and resolution of gamma camera., The results of this study showed that the direct linear relationship between the acquired counts and the elapse time after chemotherapy Counts(kilo) = (26 × days after chemotherapy) + 657 , the coefficient of this relationship indicates that the count will be increased by 26 kilo counts per day after their is a direct positive relationship between the patient weight (kg) and the administered dose (mci) Counts = (0.0502 × days after chemotherapy) + 24.119 ,when the weight of the patient increase must be increasing the doses. So the longest the interval time between last chemotherapy and bone scan the more image will be high optimal, where it was preferred to be more than three weeks.

5-3 Recommendations:

This study would like to highlight some points in a form of recommendations as follows:

Activity will be increase in respect to days after chemotherapy higher dose with first five days.

Scan should be usually done at least after three weeks or more.

Scan image should be done after injected dose at least three hours.

Further study can be done correlated amount and type of chemotherapy with count.

Another research can be done concerned other type of cancer.

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