Sudan University of Science and Technology
College of Graduate Studies

Determination of Effects Induced by Bone Scintigraphy Dose in Blood Components

تحديد تأثيرات جرعة الأشعاع الوميضي لتصوير العظام على مكونات الدم

A thesis Submitted to the Senate of Sudan University of Science & Technology in fulfilment of requirement for the degree of Doctor of Philosophy in Nuclear Medicine

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DEDICATION

To my beloved parents and family

To those who seek for knowledge

To those who fund of sciences

To those who accept others

Abstract

The aim of this study was to present the main factor influencing the high request of bone scintigraphy in Sudan with its relative parameters and to quantify the effects induced by bone scintigraphy radioactive dose in blood components (WBCs, RBCs, Hemoglobin, Platelets) relative to biographic factors (age, gender and body mass index BMI) in addition to morphological changes in RBCs. The adapted method was the retrospective and minimum invasive experimental work in NM department at RICK during 2014 – 2018. The sample size was 350 patient who underwent bone scintigraphy and blood component measurement after getting the signature of informed consent.

The analyzed data by using SPSS showed that: the predominant cancer cases referred to bone scintigraphy were form Om-durman state (45.6%), Khartoum state (18.8%) and North state (14.6%) with the majority of these cases were breast cancer representing (52.1%) and most of them were female (70%). The left breast was the most one stroked by cancer (64%) with the upper outer quadrant being stroke by (44%) compared with other quadrants and the right breast involvement by cancer represents (33%). And the common involved age groups were 40-50 years old. The right and left breasts cancer commonly gives metastases to lumbar vertebrae (26.7%, 22%), then dorsal vertebrae (14%, 19%), the pelvic bone (10%, 12.7%), the ribs (5%, 11.3%), the cervical vertebrae (8.7%, 10.7%), the skull (7.3%, 9.2%) and the femur bone with percentage of (6.7%, 10%) respectively and the right breast cancer showed relatively high metastatic percent to skeletal system segments than the left breast cancer, with specific preference to lumbar vertebrae.

In general WBC count increases eventually following the increment of age grouping and BMI then decreased after 61 years old and among obese (30 –

39.9) but got rapid peaking among Morbidly obese (≥ 40 Kg) however the general trend remains in normal range. The RBCs count increases following ageing and BMI, up to 50 years old and normal BMI (18.5 – 24.9) then got decreases within normal fluctuation respectively. While hemoglobin in g/dl doesn't influenced significantly (P-value = 0.21) by aging and BMI increment. Lymphocytes count decreased continuously following ageing; but increased following the increment of BMI insignificantly (P-value = 0.3) in both cases and remains within normal level in both cases.

Then after the interval time of bone scintigraphy (3.0 - 3.5 hours) with an average radioactive dose of 15±2.9 mCi; the WBCs count decreased significantly by 3.8% at P-value = 0.00 and 0.05 relative to age and BMI respectively. The RBCs reduced but insignificantly (P value = 0.31) by an average of 3.6% relative to initial count.

The RBCs% appeared less than normal among underweight patients (BMI < 18), but increases and fluctuating normally as BMI increased and got abnormal increment among morbidly obese patients (BMI ≥ 40).

The reduction of RBCs% increased following the ageing through 18-39 years old and by 73-83 years old became prominent with an average reduction of 3.6%. The reduction also seen in HGB level by 3.1% and the Lymphocytes decreased insignificantly (P-value = 0.42) by 10.3% relative to normal average level. The analysis also, revealed that: the PLT count does not influenced by aging but decreased significantly (P-value = 0.04) as the BMI increases. However, after interval time of bone scan; it decreases significantly (P-value = 0.01) by 12.5% following aging, and significantly (P-value = 0.02) by 12.0% following the increment of BMI relative to the initial count.

The radioactive scintigraphy dose also induced morphological deformities in RBCs such as: loss of biconcavity and increased in diameter (10 ±0.4 µm) at

15 mCi. And at 20 mCi; the RBCs developed spikes mimicking Tribulus terrestrial (zygophyllaceae) fruit like which known as anisocytosis and poikilocytosis shape. And at 25 mCi; RBCs appeared with intensive anisocytosis and poikilocytosis with shrinking size

الخلاصة

الهدف من هذه الدراسة هو عرض العامل الاساسي لزيادة طلب فحوصات الطب النووي لفحص العظام بالنويدات المشعة و من ثم تحديد التاثيرات الناجمة من الجرعة الإشعاعية المستخدمة في مسح العظام بالنظائر المشعة لمكونات الدم (كريات الدم الحمراء، كريات الدم البيضاء، الهيموغلبين والصفائح الدموية) باعتبار العوامل الحيوية (العمر، الجنس ومؤشر كتلة الجسم) اضافتة للتغيرات الشكلية لكريات الدم الاحمر . المنهجية المتبعة هي جمع البيانات الطبية التاريخية للمرضى والعمل المخبري ذوالحد الأدنى من التداخل السريري وذلك بقسم الطب النووي بمستشفى العلاج بالأشعة والطب النووي (مستشفى الذرة) في الفترة من 2014 – 2018. عدد حالات العينة المدروسة 350 مريضا وبعد الحصول على موافقة وتوقيع المريض لاجراء فحص قبل وبعد المسح الاشعاعي لمكونات الدم، تم اجراء المسح الاشعاعي للمرضى ومن ثم اخضعت البيانات للتحليل الاحصائي بإستخدام برنامج المجموعة الاحصاية للعلوم الاجتماعية SPSS.

اوضحت النتائج الاتي: ان اغلبية الحالات السرطانية تم تحويلها من محافظة أم درمان (45.6%) و الخرطوم (18.8%) و الولاية الشمالية (14.6%) حيث يمثل سرطان الثدي نسبة (52.1%) من الحالات و من بينهم نسبة النساء كانت (70%) و نسبة اصابة الثدي الايسر كانت الأعلى وتمثل (64%) . بتقسيم الثدي الى اربعة ارباع وجد ان الربع العلوي الخارجي للثدي الايسر اكثر اصابة بسرطان الثدي بنسبة (44%) و الفئة العمرية الأكثر اصابة بين النساء هي (50-40 سنة)

اوجدت الدراسة ان الثدي الأيمن و الأيسر يعطي ثانويات منتشرة في كل من الفقارات القطنية (22%, 26.7%) ، الفقارات الظهرية (14%, 19%) ، عظم الحوض (12.7%, 10%) ، الأضلع (11.3%, 5%) ، الفقارات الرقبية (10.7%, 8.7%) ، عظم الجمجمة (9.2%, 7.3%) ، و عظم الفخذ (10%, 6.7%) على التوالي. حيث ان سرطان الثدي الايسر يعطي ثانويات للجهاز العظمي اكثر من الأيسر . و لاجراء فحص الطب النووي للعظام تم تقييم مكونات الدم . وبشكل عام وجد ان عدد كريات الدم البيضاء يزداد بزيادة الفئة العمرية ومؤشر كتلة الجسم ثم ينخفض بعد عمر 61 عاما ومؤشر كتلة الجسم (39.9 – 30) ولكنه يزداد سريعا ويصل الذروة عند البدانة الممرضة (≥ 40 Kg) بينما تصل كل هذه التغيرات ضمن المعدل الطبيعي. ايضا تزداد عدد كريات الدم بزيادة كل من العمر ومؤشر كتلة الجسم حتى عمر 50 سنة ومؤشر كتلة الجسم الطبيعي (24.9 – 18.5) ثم تأخذ في النقصان بتذبذب ضمن المعدل الطبيعي تباعا للعمر ومؤشر كتلة الجسم. والهيموقلوبين يبدو غير متأثرا بزيادة

العمر ومؤشر كتلة الجسم. ايضا انخفض عدد الخلايا الليمفاوية بإستمرار تباعا لزيادة العمر و زادت غير معنويا (P-value = 0.3) بزيادة مؤشر كتلة الجسم، مع بقاء التغيرات ضمن المعدل الطبيعي.

بعد الفترة الفاصلة بين التصوير والمسح الاشعاعي للعظام (3.5 - 3.0 ساعة) و اعطاء المرضى متوسط جرعة مقدارها (5±2.9 ملي كوري) انخفض عدد كريات الدم البيضاء معنويا (P-value = 0.00 and 0.05) بنسبة (3.8%) مقرونا بالعمر و مؤشر كتلة الجسم على التوالي. و انخفضت كرات الدم الحمراء غير معنويا (P value = 0.31) بمتوسط (3.6%) بالنسبة الى المعدل الطبيعي ، كما ظهرت كرات الدم الحمراء اقل من المعدل الطبيعي في المرضى ذوي النقص في مؤشر كتلة الجسم الاقل من الطبيعي (BMI < 18) و لكنها زادت متذبذة في المعدل الطبيعي بزيادة مؤشر كتلة الجسم و من ثم زادت بصورةغير طبيعية في المرضى ذوي البدانة الممرضة (.(BMI ≥ 40) . كما اظهرت الدراسة انخفاض نسبة كريات الدم الحمراء% بدى مستمرا خلال الاعمار 18-39 سنة وبحلول 73-83 سنة اصبح بارزا بمتوسط انخفاض (3.6%) ولوحظ ايضا انخفاض مستوى الهيموغلبين بنسبة (3.6%) وانخفاض الخلايا الليمفاوية غير معنويا (P-value = 0.42) بنسبة (10.3%) مقارنة بالمعدل الطبيعي . ايضا اوضح التحليل ان الصفائح الدموية لا تتأثر بتقدم العمرو لكنها تتاثر معنويا (P-value = 0.04) بزيادة مؤشر كتلة الجسم. وبعد الفترة الفاصلة بين التصوير والمسح الاشعاعي للعظام انخفض معدل الصفائح الدموية معنويا (**P-value = 0.01**) بنسبة (**12.5%**) تباعا لتقدم العمر وممعنويا (**P-value = 0.02**) بنسبة (**12.0%**) تباعا لمؤشر كتلة الجسم مقارنة بالمعدل الطبيعي.

كما تسببت جرعة مسح العظام الاشعائية في حدوث تشوهات شكلية في كرات الدم الحمراء مثل فقدان التقعر الثنائي وزيادة في القطر (0.4 ± 10 مليميتر) عند الجرعة (15 ملي كيوري) و ظهور نتوءات على سطح كريات الدم الحمراء مشابهة لنبتة (الدريصة) تشير الى تباين الخواص و الاتزان (anisocytosis and poikilocytosis) عند الجرعة (20 ملي كيوري) ثم ازدادت كثافة النتوءات و التشوهات و صغر الحجم عند الجرعة (25 ملي كيوري)

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Thanks, are expressed to the RICK – NM department for allowing me to select and interact with the sample of research.

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LIST OF ABBREVIATIONS

Abbreviation	**Meaning**
ACR	American College of Radiology
Gy	Gray
ICRP	International Commission on Radiation Protection
MBq	Mega Becquerel
NMI	Nuclear medicine imaging
PET	Positron Emission Tomography
RBCs	Red blood cells
TLD	Thermoluminescent Dosimeter
WBCs	White blood cells

Chapter One
Introduction

Nuclear medicine imaging (NMI) as one of indispensable technology has been used for diagnosis of different pathologies, staging of cancerous diseases and researches, as it provides morphological anatomy, physiological information and even metabolic process (Rau´l et al, 2014; Eisenhauer et al, 2009). Despite its valuable benefits and low exposure dose; there have been potential radiation exposure hazards for both staff and patients which should be considered under radiation protection guides and rules to limit the stochastic effects (ICRP, 2010). And the variation of reference doses for bone scintigraphy among different radiation health institutions as well as the method used to calculate and determine the optimum or ideal radioactive dose for specific scanning are still persisting as a matter of challenge for radiation practitioners; as still there is potential radiation hazards to patient and staff. Such potential radiation hazards striking the blood components and sensitive anatomical organs that would be worth to study and researched by scholars.

The previous studies in this realm revealed that: the effects of ionizing irradiation accompanied by symptoms and signs (*diarrhea, nausea, vomiting, fatigue, infection and internal hemorrhage*) within few minutes after exposure then followed by considerable reduction in blood components with immediate response in white blood cells (WBCs) and severe drop within 24 hours; which is dependent on quality of radiation, dose, dose rate, fractionation and the status of the object (Jenine et al, 2013; Paul et al, 2014); while platelets decrease gradually by time (Maks et al, 2011).

The trend of this study; focus on the quantitative effects of radioactive dose of bone scan in NMI induced in blood components; bearing in our mind that: the applied radioactive doses for bone, renal, cardiac and thyroid scintigraphy are: 740-1110, 111–740, 296– 1110, 74 – 370 MBq respectively as indexed by Shackett, (2009), and in general; the nuclear medicine dose ranged from 10 – 30 mCi (ACR, 2012; Donohoe et al, 2003).

The normal count of blood components that may response to irradiation representing the WBCs which are ranged from 4,000 to 10,000 counts\mm^3 (lymphocyte (20-40%), monocyte (6-10%), neutrophils (40-60%), eosinophils (0.5-1) and basophils (0.5-1%)), RBCs are 4.8-5.8 million cells\mm^3 in males and 4.2-5.2 million cells\mm^3 in the females in addition to Plates counts from 100,000 to 400,000 platelets\mm^3 (average 250,000). And the normal sizes of blood components RBCs = 6 to 8 micrometers, while the shape could be as round, biconcave and disc-shaped (Diez-Silva et al, 2010). All these characteristics of blood components could be influenced by ionizing irradiation and may show variable response as quantitative and morphological changes.

The effects of radiation dose in blood components have been highlighted by Eastlind & Charlonneau, (1988), and they found that there were no significant differences in the dose response between isolated lymphocytes and granulocytes, whereas these cells had significantly more damage seen in whole blood lucokocytes and the neutrophils and they could tolerate a dose up to 175 Gy i.e. showed no change of aggregation while the granulocytes were appeared more radio-resistance than lymphocytes. In the same scope, Van et al, (1974) have revealed that a dose of 25-50 Gy would result in a reduction of monocytes growth and survival in isolated culture while the RBCs were shown to be most radio-resistance to γ-radiation relative to whole blood components.

The estimation of Blood components in human body could be carried out by different means, such as ^{51}Cr (Na_2CrO_4)-labeled red blood cells (RBCs) and ^{125}I-human serum albumin to measure (RBCs) and plasma volume. ^{111}In-oxine (oxyquinoline) and ^{99m}Tc /HMPAO (D, L-hexamethyl propylene amine oxime) Ceretec, exametazime are used to measure WBCs, while the induced morphological changes could be carried out from hematological and histological sections to reveal the induced changes relative to normal ones.

Since the Nuclear Medicine (NM) may accompanied with considerable side effects, particularly in the blood components, the aim of this research is to estimate the effects of radiation dose received by blood components (WBCs and RBCs) due to bone scintigraphy using ^{99m}Tc-MDP (Methylene Di-Phosphate).

The standard radioactivity dose of radiopharmaceuticals in adults is based on the ideal standard weight of a patient, 70 kg (Hansen et al, 2006), and the parameters such as pregnancy and sometimes renal function are considered limiting factors in the radiation dose delivered to the patient. Obtaining acceptable image quality in an obese patient frequently requires use of an activity higher than used in a patient of ideal weight. However, the radiation dose to the patient recommended by the International Commission on Radiological Protection limits the increase in activity, and hence the dose may not be high enough to produce an adequate study for proper interpretation due to a reduced signal-to-noise ratio and increased scatter in the acquired image. In positron emission tomography (PET), for example, an increase in the injected dose according to patient weight can be used to overcome poor image quality due to scatter, but the dose cannot exceed 925 MBq (25 mCi) (Everaert et al, 2003). A common procedure used in myocardial perfusion imaging is to calculate the activity on the basis of patient weight and adjust upward for heavier patients by using a fixed formula dose such as 11.47 MBq (0.31 mCi)/kg for ^{99m}Tc agents or 1.48 MBq (0.04 mCi)/kg for ^{201}Tl or the general equation:

$$Patient\ dose = \frac{Standard\ Dose\ \times Patient\ weight\ (Kg)}{Standard\ weight\ (70\ Kg)}$$

Another option to overcome this limitation and improve image quality is to prolong the acquisition time or use a multidetector system for higher statistical counts (Karesh et al,2006; Hansen et al, 2006).

2. The problem of the study:

The predominance of diseases that required bone scintigraphy has been increased recently in Sudan with consideration that: Bone Scintigraphy dose ranged between 10-30 mCi of Tc-99m (Shackett, 2009) that mixed with pharmaceutical (meythalen-di phosphonate) and the differences in applied methods to determine the ideal scanning dose as well as the variation in protocol of bone scan, all have been as factors to induce radiation effects in blood components (reduction and morphological changes).

3. Objectives of the study

- To determine the states from which the patients are referred for bone scintigraphy
- To determine the common cancer type referred to bone scintigraphy
- To determine the gender frequency% of bone scintigraphy
- To show the common breast and its quadrant involved by cancer
- To determine the common age involved by cancer and the common anatomical sites stroked by cancer secondaries relative to right/left breast.
- To determine the common cancer histological types involving the breast.
- To correlate between blood components (WBCs, RBCs, HgB, Lymph, Platelets) with biographic data (Age and BMI)
- To quantify the effects of blood components (RBCs, WBCs, lymph and platelets) due to exposure by bone scintigraphy dose.
- To determine the significance effect of bone scintigraphy dose in blood components
- To determine the morphological effects (histological damage) of RBCs induced by bone scintigraphy dose

4. Significance of the study:

The current study presenting the highly request of bone scintigraphy examinations in Sudan together with the main factor that influencing this highly requests. And furtherly the study will highlight the relative parameters related to the factor that influencing the increasing requests for bone scintigraphy. Then it will present the impact of utilizing radioactive dose of bone scintigraphy in the blood components.

5. Outline of the study

The following study falls in five chapters. Chapter one presents the introduction about blood (definition, component. function, nuclear medicine and bone scan definition. Chapter two highlighting the literature review that related to general radiation effects in blood components. Chapter three concerns with the methodology of the study. Chapter four presenting the results and discussion. Chapter five imply the conclusion, recommendation and references.

Chapter Two
Literature Review

Chapter Two
Literature Review

The following section will highlight the ionizing radiation that applied in medical fields and their relevant impact in the blood components as general and specifically the white blood cells (WBCs) and red blood cells (RBCs). In this regard; the common ionizing radiation applicable in medical field imply x-ray for diagnostic purposes and therapeutic tasks, g-radiation for diagnostic nuclear medicine imaging (NMI) and radiotherapy in addition to particles (Neutrons, protons, electron) therapy.

Despite the limited exposure to radiation as low dose irradiation (LDI) (≤100 mSv) or low dose rate irradiation (LDRI) (< 6 mSv/H) in diagnostic radiology, however it may precede by certain radiation thickening (Feng & Konstantin, 2018). And based on the available studies that ascertained LDI or LDRI may induce cancer (Shah et al, 2012; Busby et al, 2009; Cardis et al, 2005), cataract (Ainsbury et al, 2009), cardiovascular diseases (Sumner, 2007) and long-term psychological consequences (Pastel, 2002); therefore, more efforts should be consider to prevent non-stochastic and limiting stochastic radiation effects. These radiations thickening could be dependent on many factors such as: gender, genetic background, age, nature of radiation exposure, and human epidemiological experimental designs. As it has been approved by Richard

& Richard, (1981) that: about 0.5% of cancer mortalities were ascribed to diagnostic x-rays in the USA for 30 years before 1981. The common highlighted committed dose by radiation workers was for western countries which was 5 mSv/year for interventional fluoroscopists (cardiologists and radiologists) that leading to cancer risk probability as 1/100 after incubation period of 20-30 years of work (Marazziti et al, 2012). Parallel to this fact, Chen et al, (2010) stated that: the radiology and nuclear medicine examinations account for mean effective dose of 3.0 mSv, while the patients underwent cardiac radiologic examination in USA received mean cumulative effective dose of 23.1 mSv over three years (range 1.5–543.7 mSv). A recent study of almost 1,000,000 non-elderly adults in healthcare markets across the United States showed that a considerable number of patients received up to 0.05 Sv/year; such considerable value, given as reference levels that provided by International Commission on Radiation Protection (ICRP) as: 0.02-0.05 Sv/year (Fazel et al, 2009; Squillaro et al, 2018). Accordingly, Nassef and Kinsara, (2017) showed that: the annual average effective doses for diagnostic radiology, nuclear medicine, and radiotherapy workers were 0.66, 1.56, and 0.28 mSv, respectively at King Abdul-Aziz University hospital in KSA. And furthermore, Abdulrahman, (2016), had assessed the dose received by personnel and patients in fluoroscopic urology in selected Saudi Arabia hospitals using thermoluminescent dosimeter (TLD). He found that: the dose received by the patient’s head (eyes) was 3.2, 3.1 mSv, waist was 5, 4.3 mSv and the legs were 3.5, 3.3 mSv per month for the right and left side of the patient respectively, by the assistant urologist and radiation technologist was 0.3 mSv, by the operation preparer, nurse, and anaesthetists was 0.27, while the urologist received 0.28 mSv. In general, fluoroscopic examinations (*operations that need real-time image*) blamed for considerable exposure doses to patients and staff in comparison to that caused by conventional radiography as assumed by Martin et al, (2016). The efforts of technologies and imaging techniques to minimize radiation exposure dose in clinical radiography is still suffering of shortage as many scholars and ICRP thoughts so (ICRP, 2010; Hellawell, 2005). The well-established recommendation and techniques applied to reduce exposure dose in fluoroscopy is the usage of pulsed fluoroscopy instead of continuous one. Also, radiation protections officers at level of ICRP and International Atomic Energy Agency (IAEA) have subjected the radiology departments under scrutiny and periodic exposure dose assessment in order to keep the effective dose limit within 20 mSv/year for workers and 1 mSv/year for public (Covens et al, 2007). In addition to application of As Low As Reasonable Achievable (ALARA) principle, time and distance factor, and shielding where applicable. Therefore, by applying these recommendations; protecting the workers and community against biological damage and the consequence diseases could be achieved (Malone et al, 2012; Mettler et al, 2008).

The previous studies in this realm revealed that: the effects of ionizing irradiation greater than (LDI) (≤100 mSv) or (LDRI) (< 6 mSv/H) in diagnostic radiology; accompanied by certain symptoms and signs (*diarrhea, nausea, vomiting, fatigue, infection and internal hemorrhage*) within few minutes after exposure then followed by considerable reduction in blood components with immediate response in white blood cells (WBCs) and severe drop within 24 hours; which is dependent on quality of radiation, dose, dose rate, fractionation and the status of the object (Jenine et al, 2013; Paul et al, 2014). While platelets decrease gradually by time (Maks et al, 2011). Also, El-Shanshoury et al, (2016) presented the significant reduction effects of blood components due to total body irradiation of Rats by Gamma radiation with doses of 0.1, 0.2, 0.3, 0.4, 0.5, 0.75 and 1.0 Gy. From general review, there is numerous literatures related to quantitative effects of radiation in the blood components while the qualitative (morphology) effects are so limited and almost so scarce.

Also, Abojassim et al, (2015) studied the effect of gamma ray (Cesium-137 source with 5 μCi) at doses of 0.055 Gy, 0.11 Gy and 0.165 Gy on some hematological parameters of albino female rats (4 groups each 3 rats). The First group was control (R1), (R2) received 0.055Gy, (R3) received 0.11Gy and (R4) received 0.165Gy. the Blood components subjected to investigations were the red blood cells (RBC), white blood cells (WBC) counts, hemoglobin (Hb), packed cell volume (PCV), Mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH) and mean corpuscular hemoglobin concentration (MCHC). The results showed that: there was significant ($p \leq 0.05$) decrease in the RBCs, Hb and Ht%, Platelets, WBCs count, lymphocytes count, monocytic, neutrophils, esinophiles and basophiles while MCV and MCH was increased and MCHC% did not change significantly. These impact of irradiation on blood components have been shown in Figures (2.1-2.13)

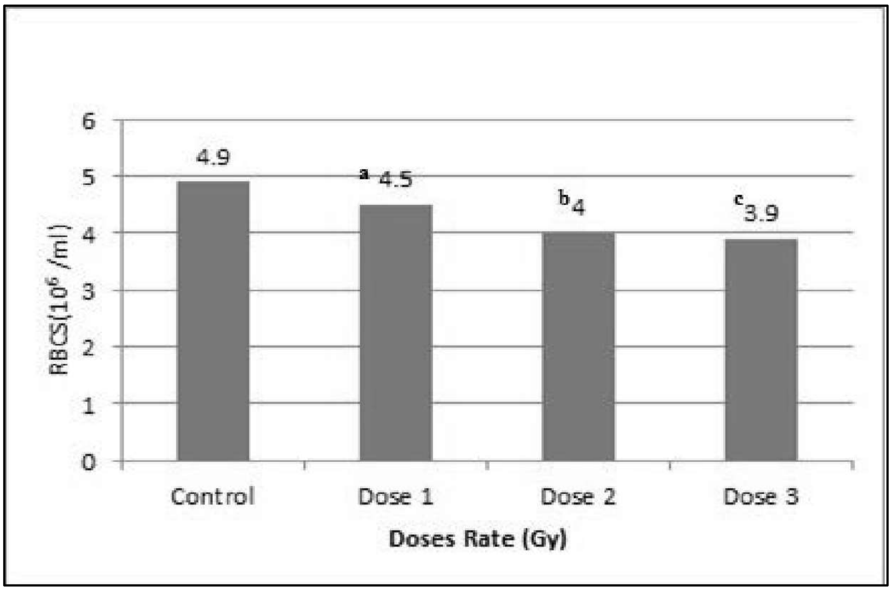


Figure (2.1): Effect of low doses of gamma ray on RBCS counts in female rats (a, d and c: means significant difference at P≤0.05) (Abojassim et al, (2015).

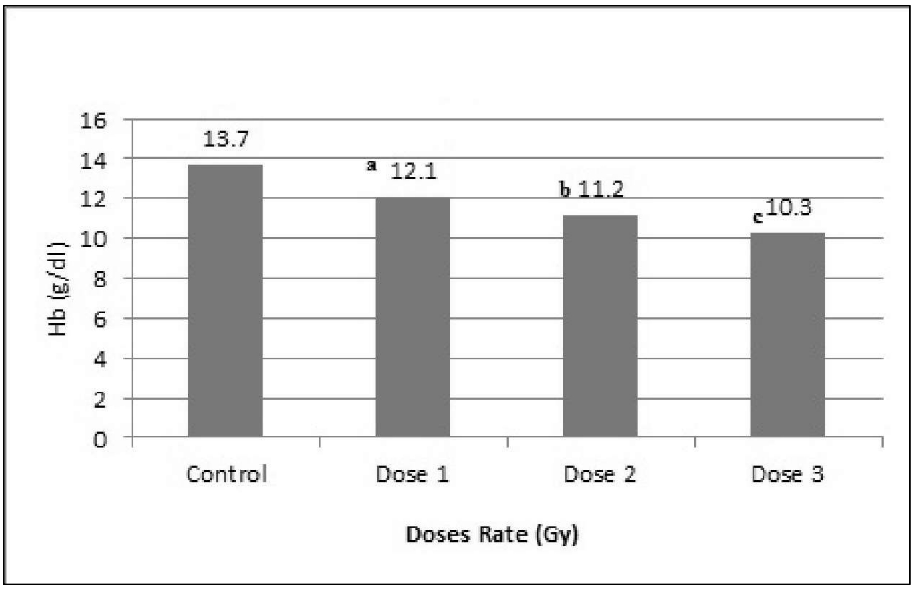


Figure (2.2): Effect of low doses of gamma ray on Hb(g/dl) counts in female rats. (a, b and c: means significant difference at $P \leq 0.05$) (Abojassim et al, (2015).

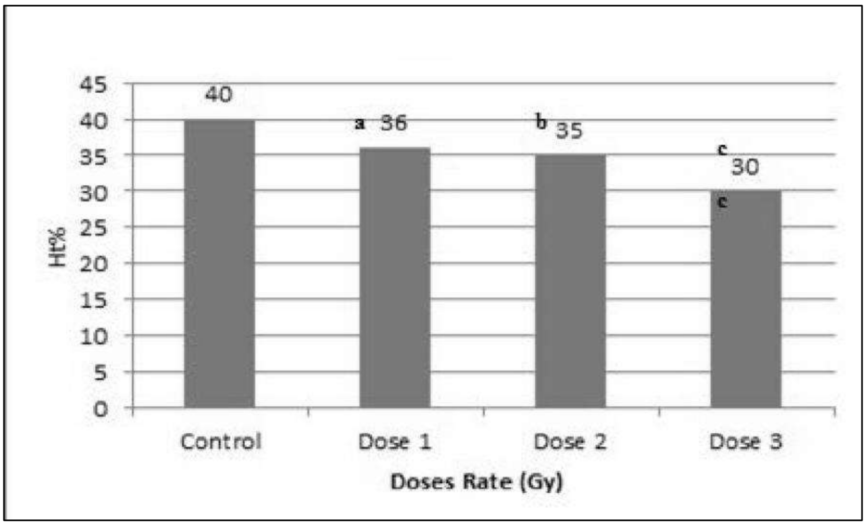


Figure (2.3): Effect of low doses of gamma ray on Ht% counts in female rats. (a, d and c: means significant difference at $P \leq 0.05$) (Abojassim et al, (2015).

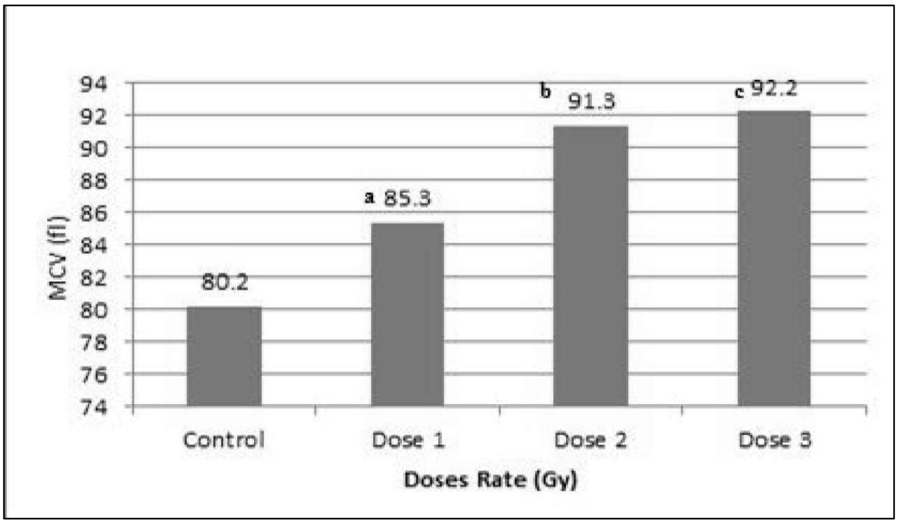


Figure (2.4): Effect of low doses of gamma ray on MCV (fl) counts in female rats. (a, b and c: means significant difference at $P \leq 0.05$) (Abojassim et al, (2015).

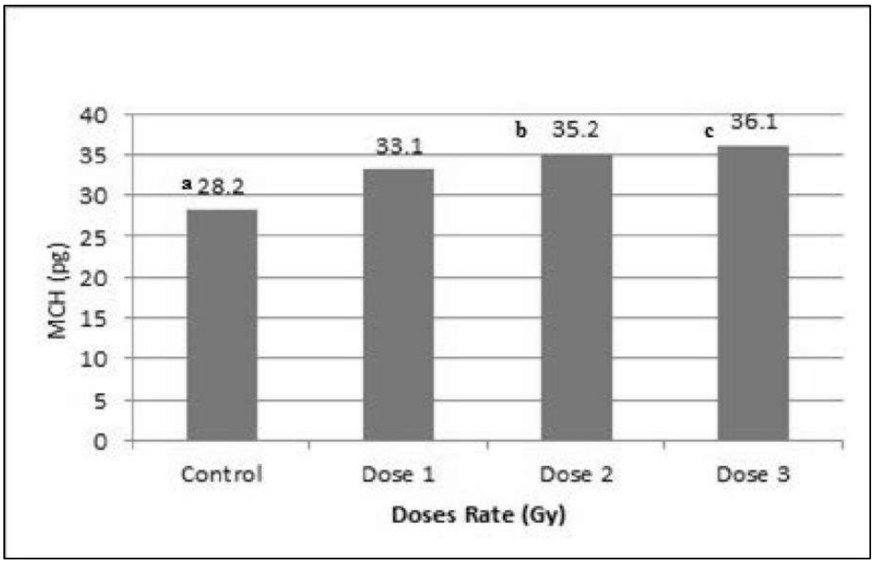


Figure (2.5): Effect of low doses of gamma ray on MCH (Pgl) counts in female rats. (a, b and c: means significant difference at $P \leq 0.05$) (Abojassim et al, 2015).

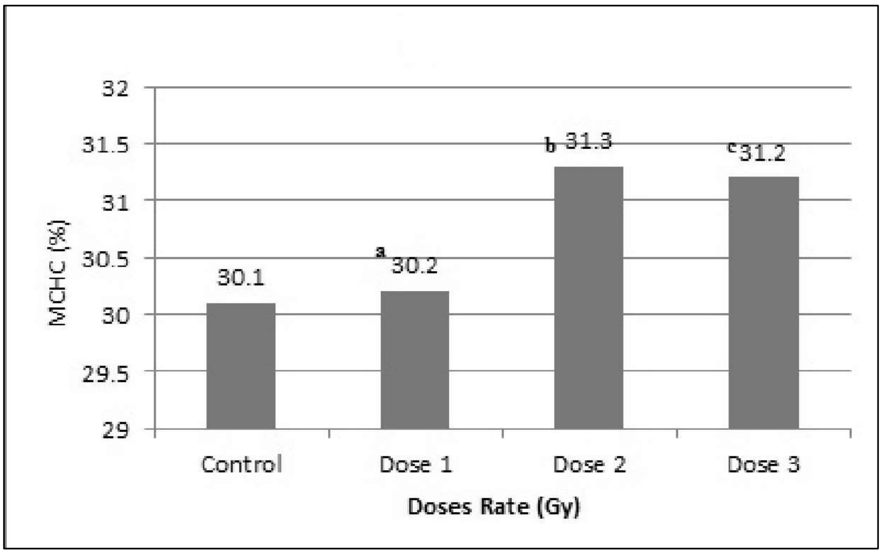


Figure (2.6): Effect of low doses of gamma ray on MCHC (%) counts in female rats. (a, b and c: means no change in significant) (Abojassim et al, 2015).

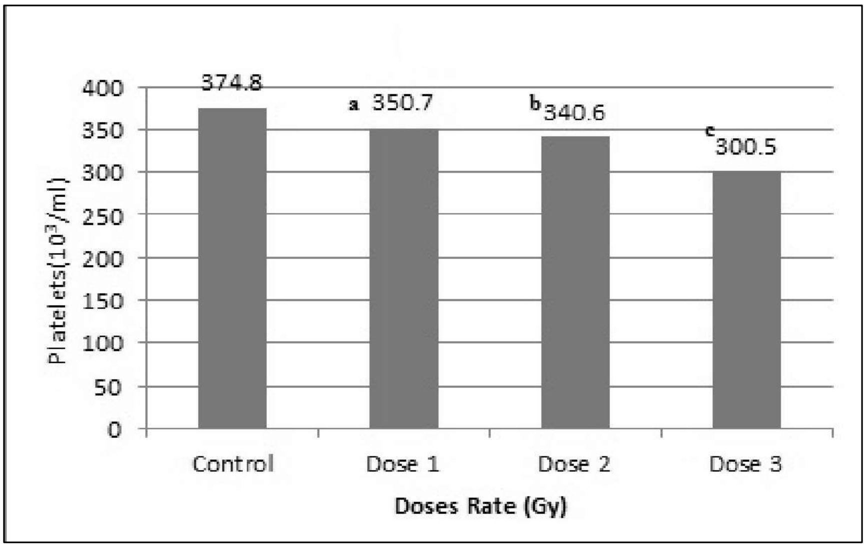


Figure (2.7): Effect of low doses of gamma ray on Platelets counts in female rats. (a, b and c: means significant difference at $P \leq 0.05$) (Abojassim et al, 2015).

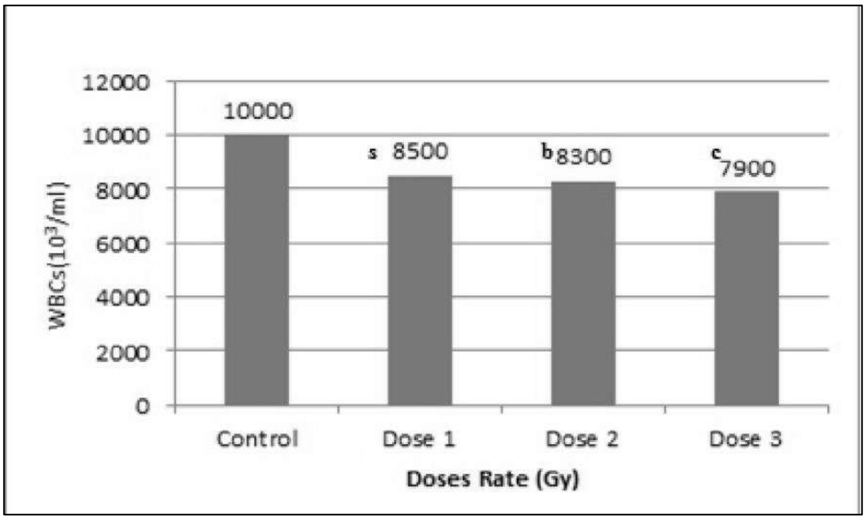


Figure (2.8): Effect of low doses of gamma ray on WBCs counts in female rats. (a, b and c: means significant difference at $P<0.05$) (Abojassim et al, 2015).

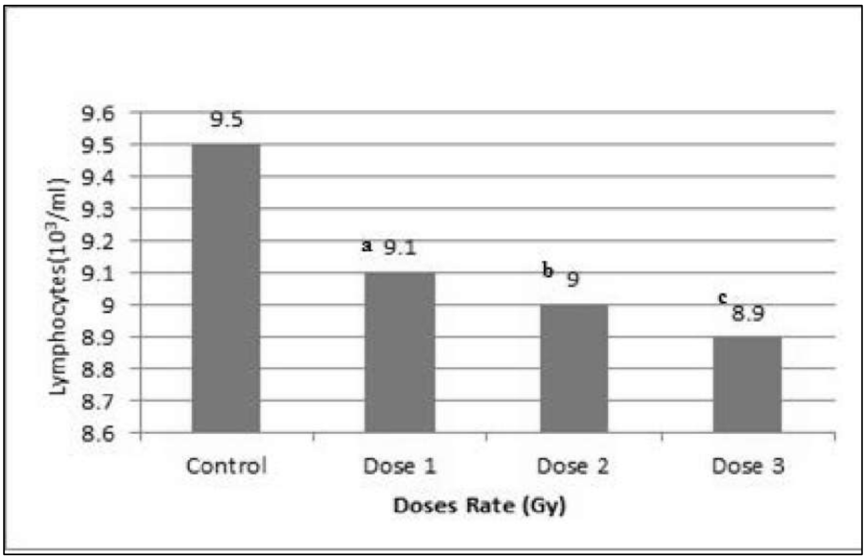


Figure (2.9): Effect of low doses of gamma ray on Lymphocytes counts in female rats. (a, b and c: means significant difference at $P \leq 0.05$) (Abojassim et al, 2015).

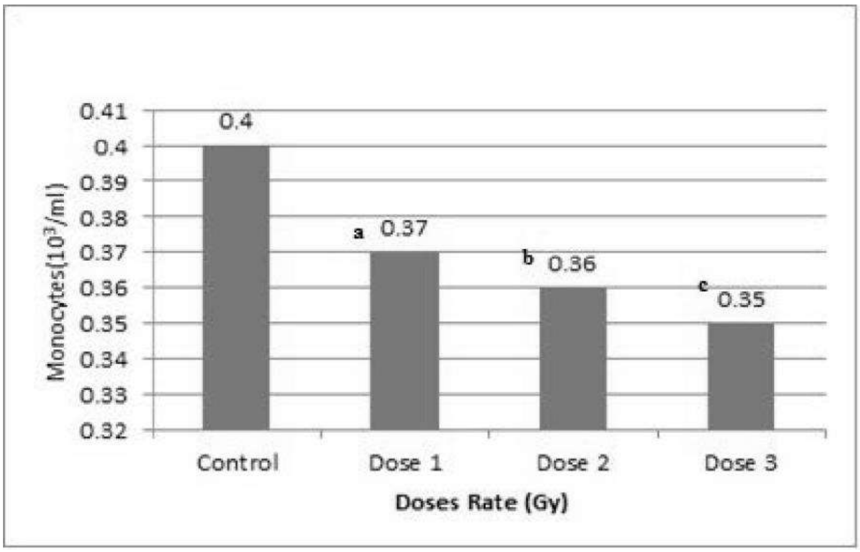


Figure (2.10): Effect of low doses of gamma ray on Monocytic counts in female rats. (a, b and c: means significant difference at $P \leq 0.05$) (Abojassim et al, 2015).

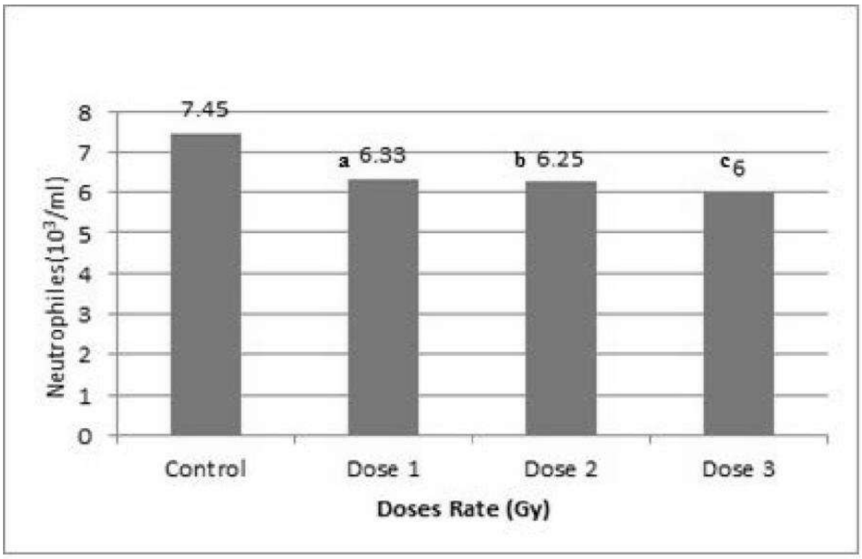


Figure (2.11): Effect of low doses of gamma ray on Neutrophils counts in female rats. (a, b and c: means significant difference at $P \leq 0.05$) (Abojassim et al, 2015).

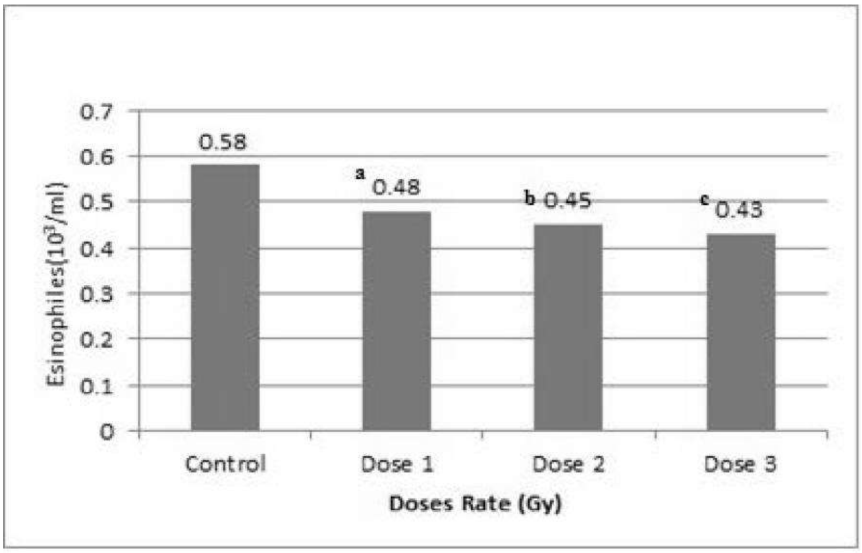


Figure (2.12): Effect of low doses of gamma ray on Eosinophil counts in female rats. (a, b and c: means significant difference at $P \le 0.05$) (Abojassim et al, 2015).

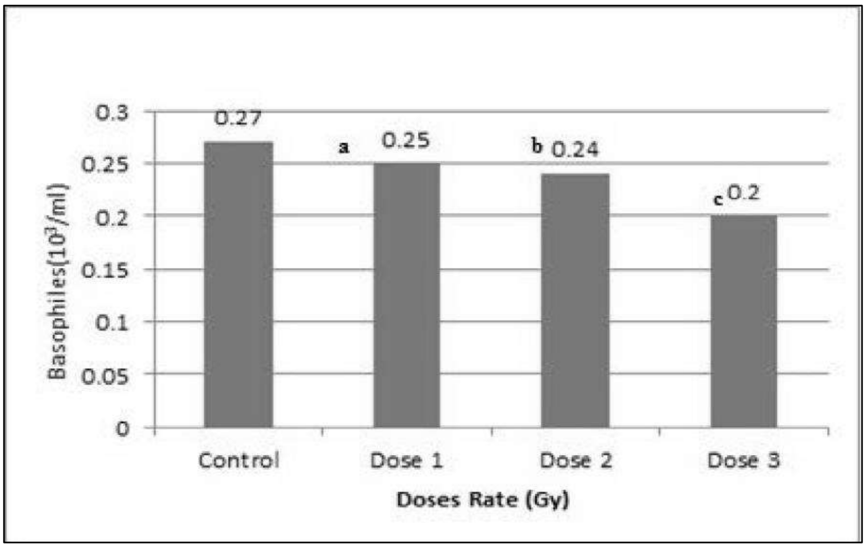
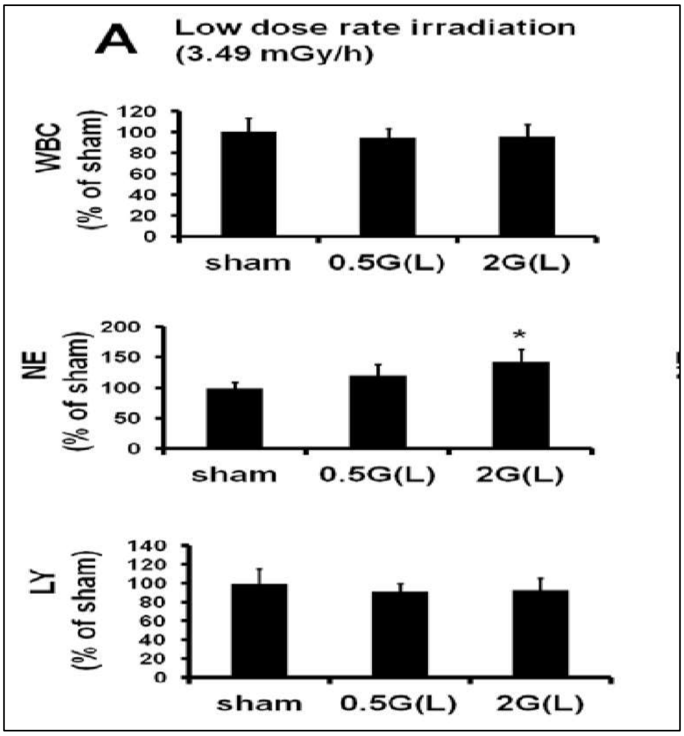
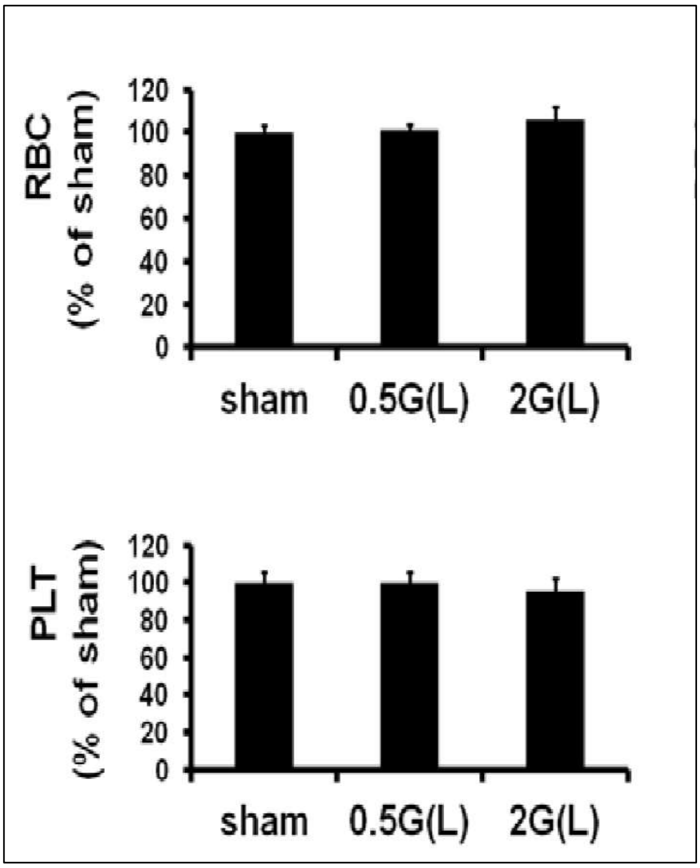


Figure (2.13): Effect of low doses of gamma ray on Basophiles counts in female rats. (a, b and c: means significant difference at $P \leq 0.05$) (Abojassim et al, 2015).

Yeonghoon et al, (2013) studied, effects of dose and dose rate using whole body radiation on plasma cytokines and blood count from male BALB/c mice were evaluated. They examined the blood and cytokine changes in mice exposed to a low (3.49 mGy h^{-1}) and high (2.6 Gy min^{-1}) dose rate of radiation at a total dose of 0.5 and 2 Gy, respectively. Blood from mice exposed to radiation were evaluated using cytokine assays and complete blood count. Their results showed that: the peripheral lymphocytes and neutrophils decreased in a dose dependent manner following high dose rate radiation. The peripheral lymphocytes population remained unchanged following low dose rate radiation; however, the neutrophils population increased after radiation as shown in Fig. (2.14).


A
Low dose rate irradiation
(3.49 mGy/h)
WBC
(% of sham)
120
100
80
60
40
20
0
sham
0.5G(L)
2G(L)
NE
(% of sham)
200
150
100
50
0
*
sham
0.5G(L)
2G(L)
LY
(% of sham)
140
120
100
80
60
40
20
0
sham
0.5G(L)
2G(L)


RBC
(% of sham)
120
100
80
60
40
20
0
sham
0.5G(L)
2G(L)
PLT
(% of sham)
120
100
80
60
40
20
0
sham
0.5G(L)
2G(L)

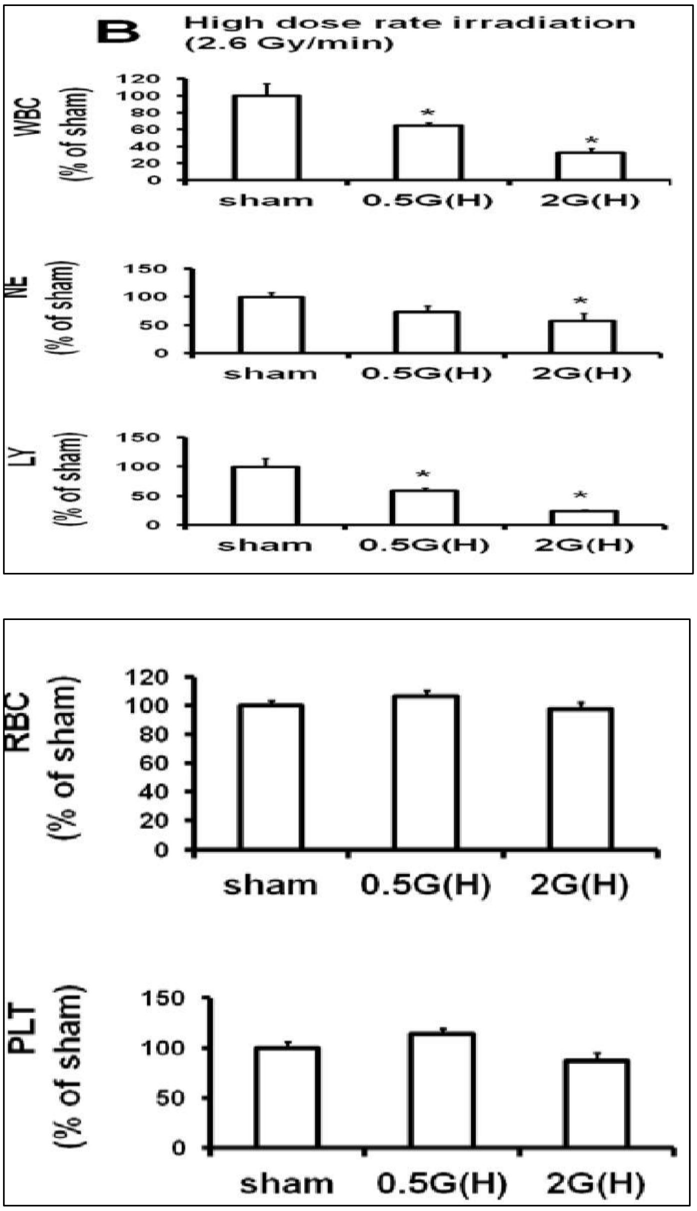


Figure 2.14: Effects of low-dose-rate and high-dose-rate of irradiation on the number of white blood cell (WBC), Neutrophil (NE), Lymphocyte (LY), Red blood cell (RBC), and Platelet (PLT) in mice peripheral blood. A low-dose-rate of radiation increased in the number of NE in a dose dependent manner; however, there were no changes in the WBC, LY, RBC and PLT populations (A). The high-dose-rate of radiation decreased the number of WBC, NE and LY in a dose dependent manner (B). Data are presented as the mean ± standard error of the mean (n=7). *P < 0.05 as compared to sham Yeonghoon et al, (2013).

The impact of ionizing radiation in medical field imaging exceeds the quantitative effects in blood components and furtherly involving the morphological changes.

In this regard the worth to be highlighted before the morphological changes occur, is the normal morphology of RBCs. The mature erythrocyte (RBC, normocyte, discocyte) has a remarkable structure in that it lacks a nucleus and organelles, and yet all components necessary for survival and function are present. It is described as a biconcave disc with a survival time of approximately 120 days. On a Romanowsky (i.e., Wright's, Giemsa) stained blood smear, this mature red cell has a reddish-orange appearance. The RBC has an average diameter of 7-8 and an average volume of 90 fL (femtolitre). The area of central pallor is approximately 2-3 μm in diameter (Fig. 2.15). The primary function of the red cell is the transportation of O_2 to the tissues of the body and transportation of CO_2 back to the lungs for expulsion. Fundamental to the red cell is the formation of hemoglobin, which is ultimately responsible for binding the oxygen molecule for transport (Jones, 2009).

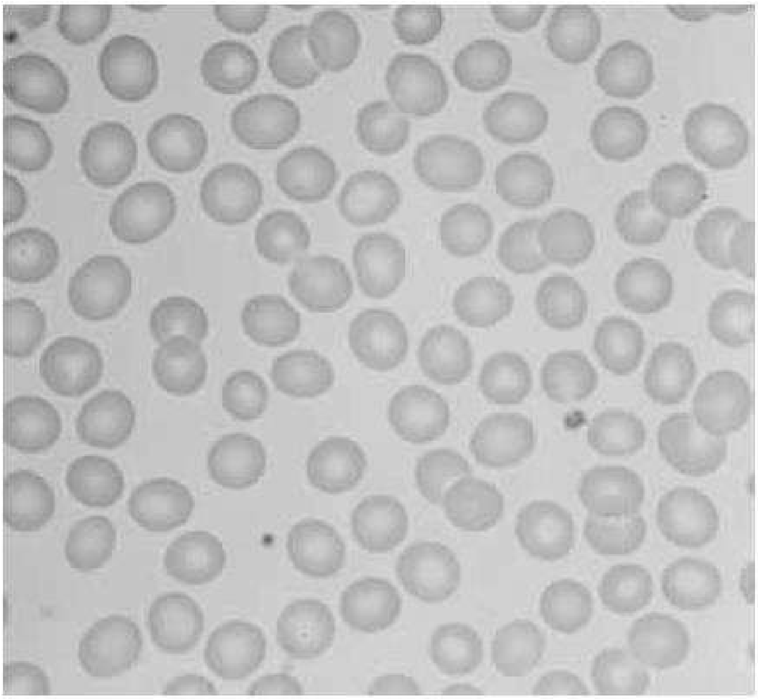


Figure 2.15: shows the morphology of a normal Red Blood Cells (RNCs) (Jones, 2009)

The induced morphological changes expressed in terms of Red Cell Distribution Width (RDW) which indicates a size change (**Anisocytosis**) or shape change (**Poikilocytosis**) of red blood cells (RBCs) and the Mean Corpuscular Volume (MCV) showed the susceptibility and indicative for appearance of **cytomegaly** (MCV > 100 fL) or **atrophocytes** (MCV< 100 fL) due to impact factor (Jones, 2009). The presented morphological changes of RBCs in literature are so limited and the mentioned ones were related to pathologies such as: **Burr Cells** due to liver disease, renal disease, severe burns, and bleeding gastric ulcers. **Helmet Cells** due to **glucose-6-phosphate dehydrogenase (**G6PD) deficiency and pulmonary emboli, **Schistocytes** due to disseminated intravascular coagulopathy (DIC), thrombotic thrombocytopenic purpura (TTP) and hemolytic uremic syndrome. **Teardrop Cells** due to severe anemias, myeloproliferative disorders and pernicious anemia. **Sickle Cells** due to sickle cell anemias, and sickle thalassemia. **Microcytes** due to iron-deficiency anemias, thalassemia, lead poisoning, and sideroblastic anemia. **Macrocytes** due to megaloblastic anemias, high reticulocyte count, liver disease, and myelodysplatic syndromes. **Target Cells** due to liver disease, hemoglobinopathies, thalassemia, and sideroblastic anemias. **Spherocytes** due to hemolytic anemias, post transfusion and hereditary spherocytosis. **Elliptocytes** due to hereditary elliptocytosis, iron-deficiency anemias, and thalassemia. **Stomatocyte** due to acute alcoholism and malignancies. And finally, **Acanthocytes** due to congenital abetalipoproteinemia, vitamin E deficiency, alcohol intoxication and post splenectomy (Fig. 2.16) (Jones, 2009). However, some studies suggested that low-dose-rate radiation does not induce blood damage, which was unlike high-dose-rate radiation treatment; low-dose-rate radiation exposure activated the hematopoiesis through the increase of flt3 ligand and G-CSF. Radiation reduces the number of stem and progenitor cells, which in turn reduces the turnover of circulating cells (Fliedne et al, 1996). As a result, leucopenia may appear, with an increased risk of opportunistic infections. These effects are dependent on both the radiation dose and the heterogeneity of the irradiation (Eric, 2019).

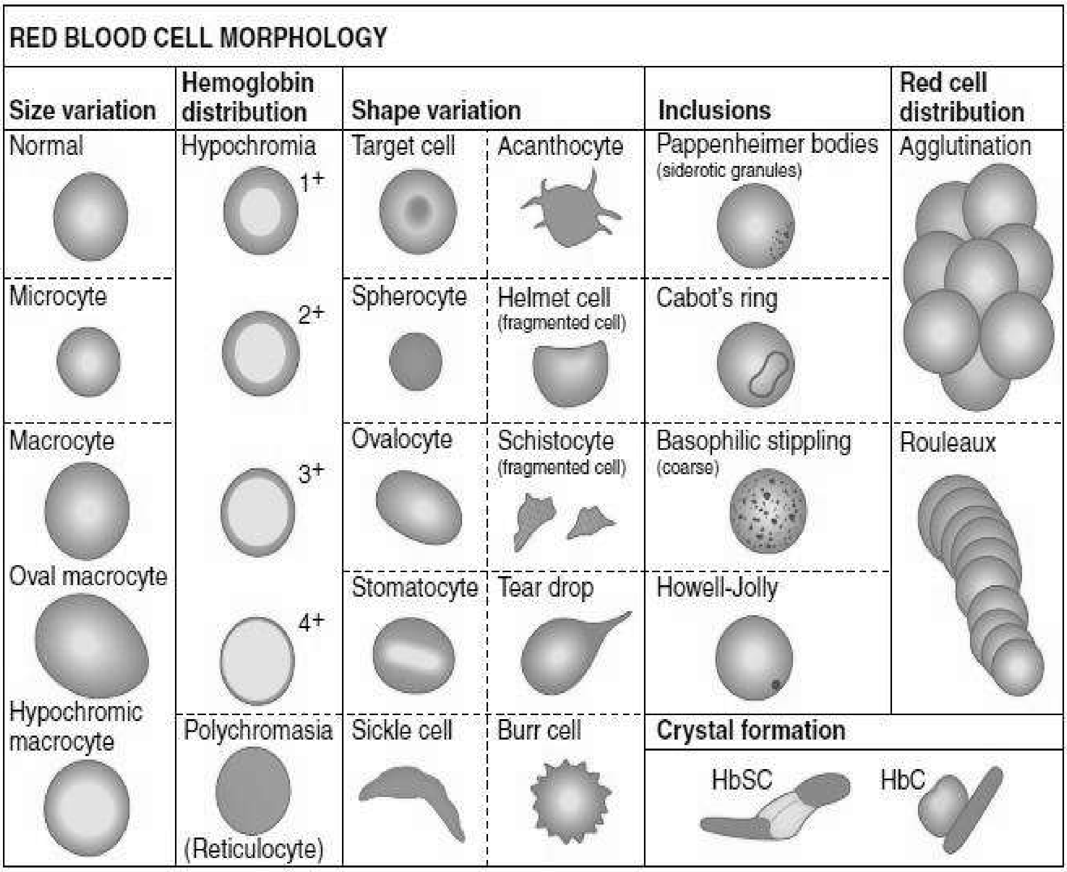


Figure 2.16: shows the composite chart of normal and abnormal red cell morphology (Jones, 2009).

Mary, (2004) showed many types of RBCs morphologies changes but rather than as radiation impact. And the common highlighted changes presented in the following microscopic images: Poikilocytes (RBCs appeared as variety of shapes as seen in (Fig. 2.17), including teardrop-shaped cells, oval-shaped cells, smaller and larger RBCs than usual.

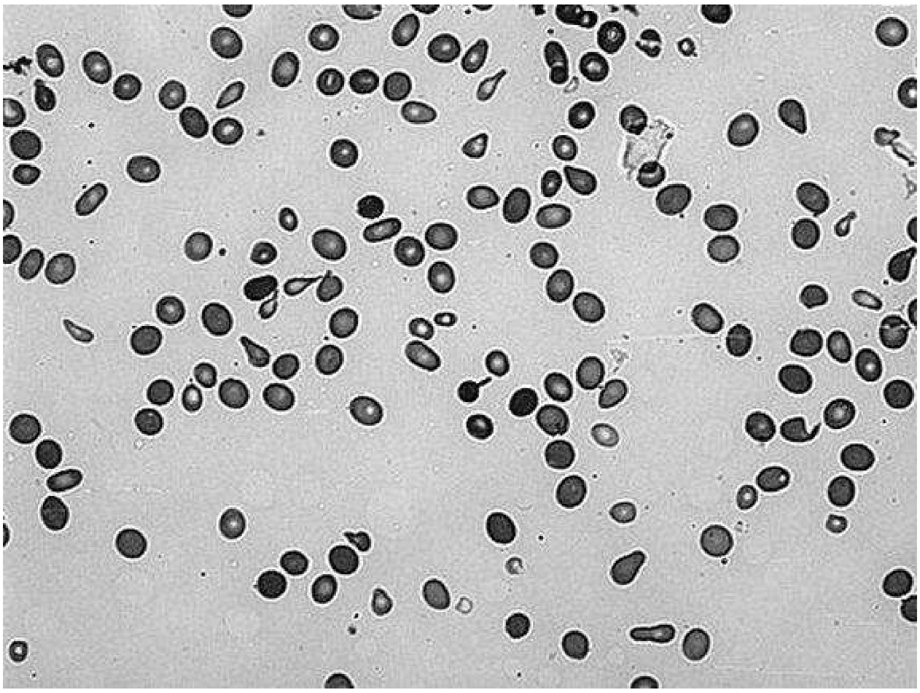


Figure 2.17: shows Poikilocytes which are RBCs appeared as variety of shapes including teardrop-shaped cells, oval-shaped cells, smaller and larger RBCs Mary, (2004).

Other more morphological shapes (Fig. 2.18 a-k) include: Acanthocytes (Spike/Spur Cells) that resemble the spurs on cowboy boots, Codocytes (Target Cells): resemble targets or "bull's eyes", Dacrocytes (Teardrop Cells) that resemble teardrops or raindrops, Degmacytes (Bite Cells) that resemble cells that look as if they have a bite taken out of them, Drepanocytes (Sickle Cells) that resemble sickles, Echinocytes (Burr Cells) that resemble burrs, Elliptocytes/Ovalocytes: elliptical or oval-shaped cells, Keratocytes (Horn Cells) that resemble horns, Microspherocytes which are looked smaller than normal size, Macrocytes which are looked larger than normal size, Pyropoikilocytes, Schistocytes (Helmet Cells) that resemble Army helmets, Stomatocytes (Mouth Cells) the cells are swollen, so they look as if they are mouths, Anisocytosis: Variation in RBC size/diameter which is measured depending on Red Cell Distribution Width (RDW) i.e. If the RDW is >14.5%, this indicates a heterogenous population of RBC's, which means you will likely see a variety of sizes of RBC's on the slide. This is associated with iron deficiency, megaloblastic or hemolytic anemia.

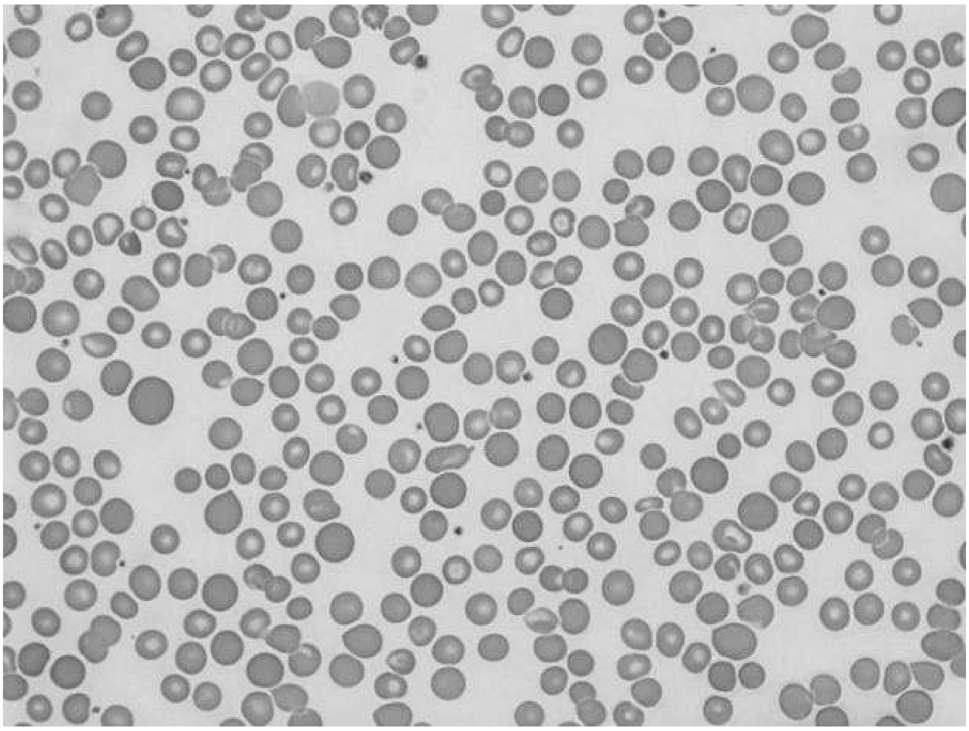


Figure 2.18-a: shows Marked anisocytosis, or variation in RBC size Mary, (2004).

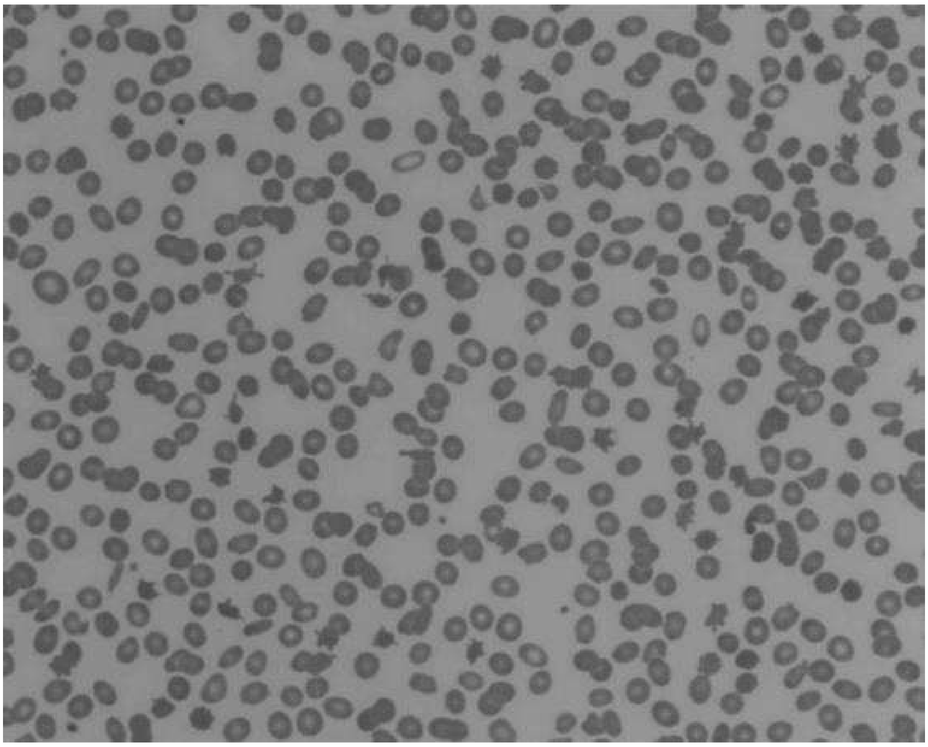


Figure 2.18-b: Acanthocytes resemble spurs on cowboy boots, but they have uneven projections (spicules) Mary, (2004).

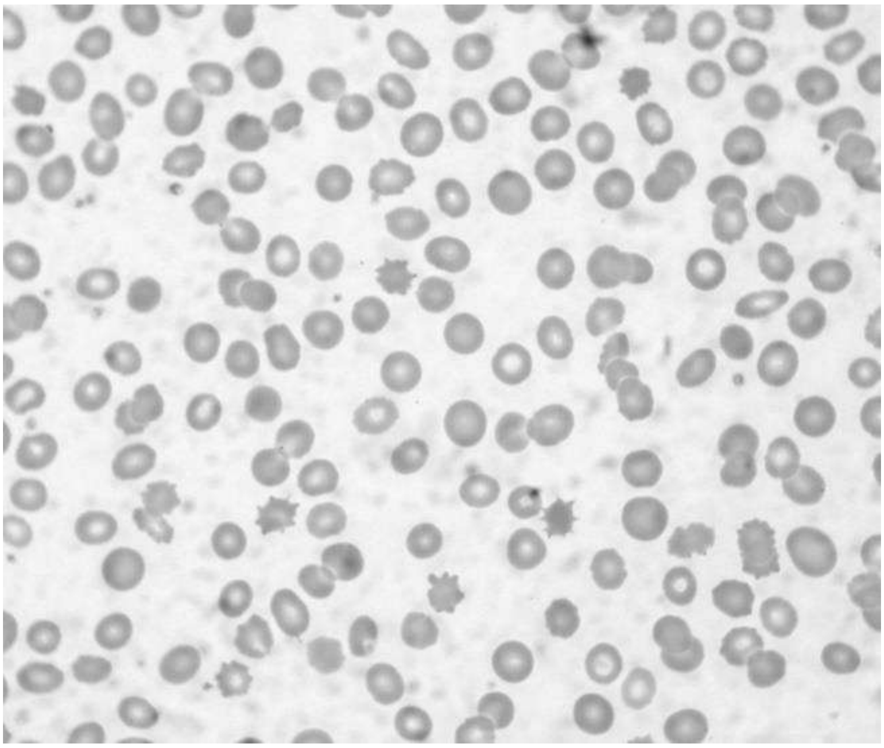


Figure 2.18-c: Acanthocytes are the RBCs seen with projections of spicules around the surface, (Spike/Spur Cells): resemble the spurs on cowboy boots Mary, (2004).

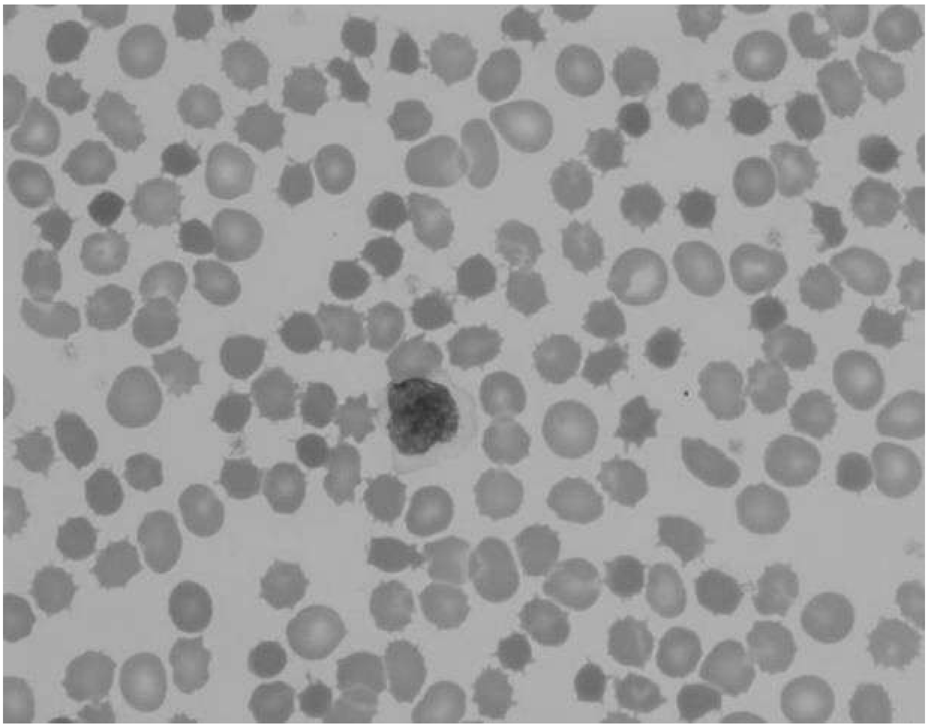


Figure 2.18-d: shows RBCs with numerous acanthocytes Mary, (2004).

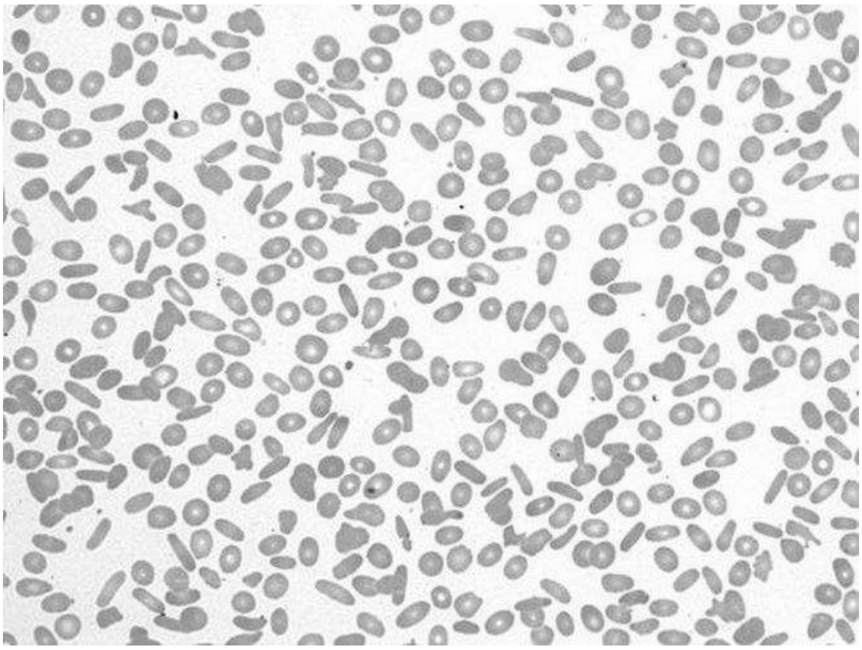


Figure 2.18-e: A slide contains numerous elliptical shaped elliptocytes Mary, (2004).

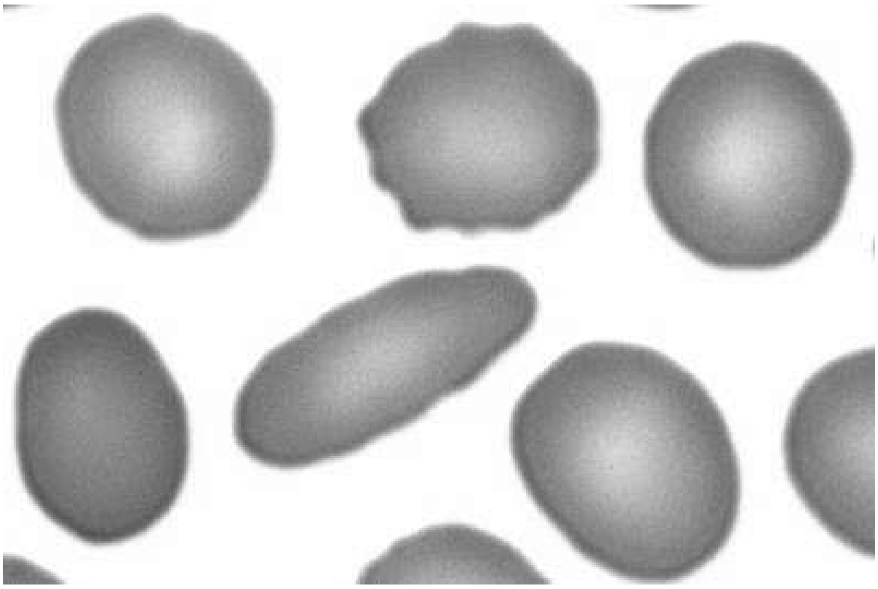


Figure 2.18-f: Shows an elliptocyte and a couple of ovalocytes Mary, (2004).

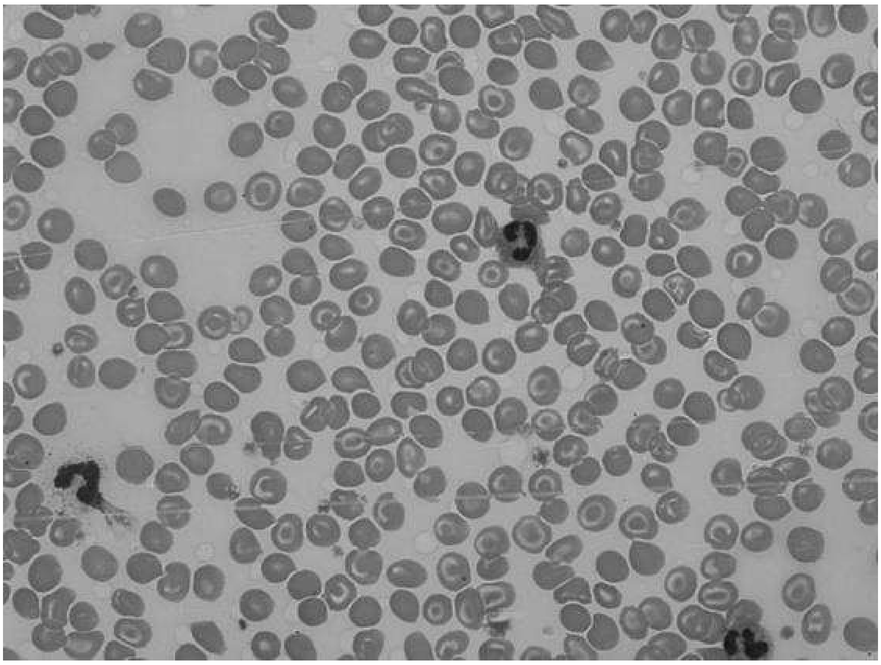


Figure 2.18-g: Shows a Codocytes, or Target Cells, resemble targets, a bullseye or Mexican hats Mary, (2004).

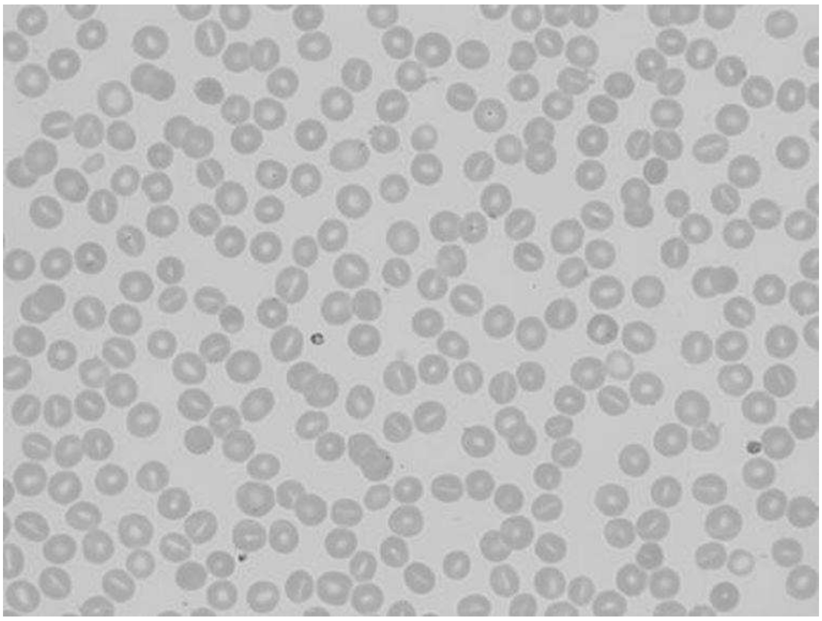


Figure 2.18-h: shows Stomatocytes/Mouth Cells/Slit Cells: which are seen in: Hereditary stomatocytosis Hemolytic anemia, Overhydration (too much water, edema, too much IV fluid) as also referred to as "volume overload", Alcoholism, and Liver disease Mary, (2004).

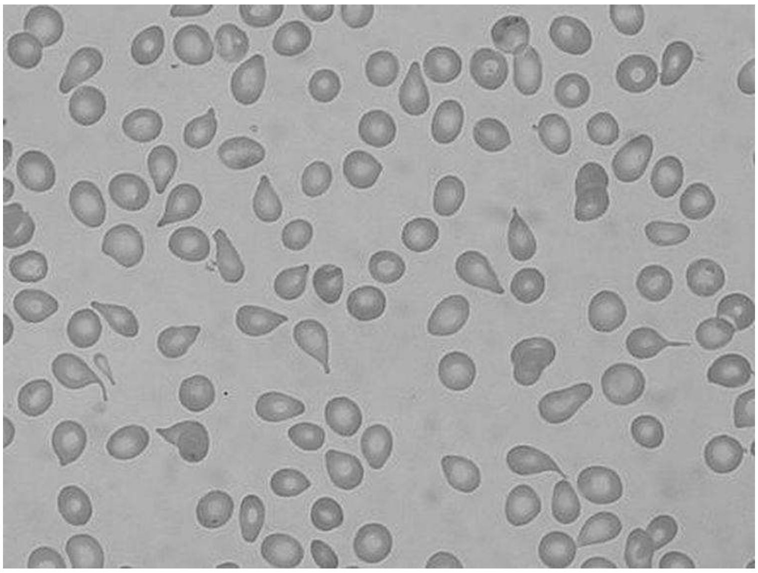


Figure 2.18-i: Dacrocytes are a result of "squeezing" through the spleen Mary, (2004).

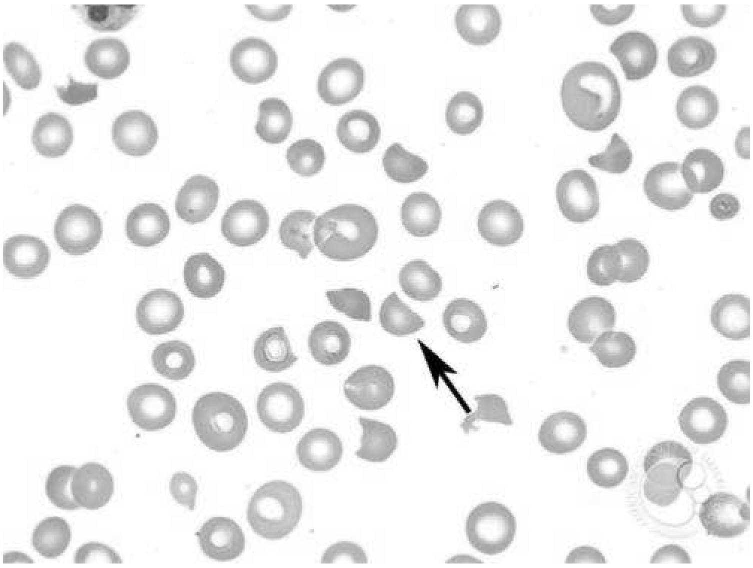


Figure 2.18-j: Degmacytes/Bite Cells: Bite cells are caused by the removal of hemoglobin by the spleen. Glucose-6-phosphate dehydrogenase deficiency also causes the formation of bite cells as hemoglobin breaks down and Heinz bodies form. Bite cells may contain one or more "bites" Mary, (2004).

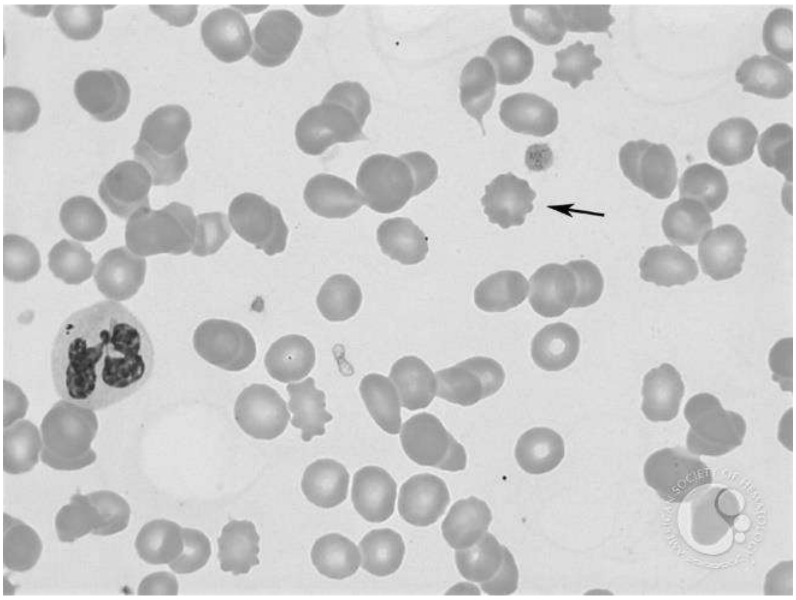


Figure 2.18-k: shows an Echinocytes are similar to acanthocytes, however, the spicules are smaller and even Mary, (2004).

Relative to morphological effects, Mona et al, (2015) also, have studied the cellular response of blood and hepatic tissue to different doses of γ-irradiation. The results showed although relative viscosity and conductivity of hemoglobin were significantly elevated in rats exposed to a single dose of 2 Gy, these elevations were statistically non-significant in irradiated rats exposed to 4 and 6 Gy as compared to control animals. All irradiated animals showed significant reduction in WBCs count after a single dose of 6 Gy ($p < 0.01$), 4 Gy and 2 Gy ($p < 0.05$), compared to non-irradiated animals. On the other hand, non-significant changes were observed in other hematological parameters as compared to control group (Table 2.1).

Blood smears from irradiated groups showed non homogenous stain distribution within the erythrocytes as compared to control group (Fig. 2.19). Erythrocytes from 2 Gy-irradiated rats showed contracted hemoglobin at the periphery of the cell, while those irradiated with 6 Gy, hemoglobin was concentrated at one side of the erythrocyte. As regards to rats exposed to 4 Gy, pale stain central regions and clumping appearance were observed.

Table 2.1. Hematological parameters in control and the different irradiated animals (Mean ± SD) Mona et al, (2015).

Parameters	**Groups**			
	Con	**2 Gy**	**4 Gy**	**6 Gy**
WBCs × 10^3 (cell/μL)	8.5 ± 3.39	2.18 ± 0.57	3.4 ± 1.22	4.2 ± 1.41
RBCs × 10^6 (cell/μL)	7.81 ± 0.59	8.16 ± 0.34	7.8 ± 1.19	8.03 ± 0.99
Hb (g/dl)	13.8 ± 0.87	14.6 ± 0.61	13.2 ± 2.76	13.45 ± 1.05
Plts × 10^3 (cell/μL)	737.25 ± 155.17	642 ± 104.12	656.5 ± 58.16	617.25 ± 129.16
HCT (%)	44.08 ± 2.77	46.15 ± 2.13	41.9 ± 7.53	44.08 ± 4.33
MCV (fl)	56.45 ± 1.58	56.58 ± 0.38	53.55 ± 2.61	55.08 ± 2.34
MCH (pg)	17.73 ± 1.27	17.88 ± 0.5	16.8 ± 1.5	16.85 ± 1.02
MCHC (g/dl)	31.33 ± 1.39	31.65 ± 0.79	31.33 ± 1.32	30.58 ± 0.72

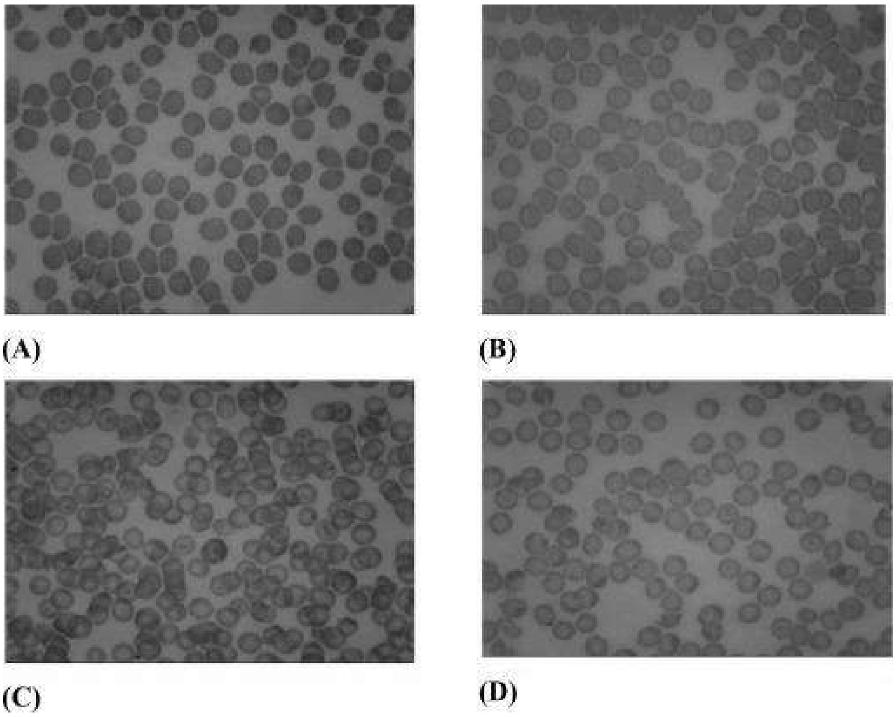


Figure 2.19: Photomicrograph from light microscope of rat blood cells (×40). Control group (A) and irradiated animals with 2, 4 and 6 Gy (B, C and D, respectively) Mona et al, (2015).

Gamma radiation doses of 500–1000 Gy induced alterations of the red blood cell (RBC) membrane at the level of lipid bilayers and skeleton proteins as well as hemoglobin states inside the cells. Much less is known about the cellular response to low doses of IR such as those typical for medical diagnostic procedures, normal occupational exposures or cosmic-ray exposures at flight altitudes, and there are only a few reports on their action on RBCs (Kaczmarska et al, 2011). In addition, IR causes severe cellular damage and stress both directly, by energetic disruption of DNA integrity, and indirectly, as a result of the formation of intracellular free radicals (Simone et al, 2009). On the other hand, infra-red (IR) is able to regulate several genes and factors involved in cell-cycle progression, survival and/or cell death, DNA repair and inflammation modulating an intracellular radiation-dependent response (Di Maggio et al, 2015). Although the relative hemoglobin viscosity levels in all irradiated rats were increased, but rats exposed to 2 Gy showed significant elevation ($p < 0.01$), compared to both control and 6 Gy groups. The same results were observed in Hb conductivity level of 2 Gy exposed group ($p < 0.05$), compared to control and 6 Gy exposed groups (Fig. 2.20).

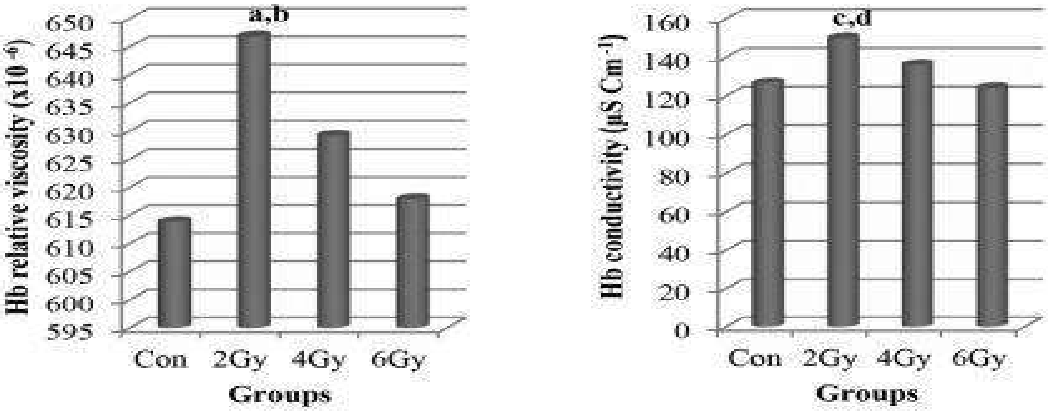


Figure 2.20: Mean values of hemoglobin relative viscosity and conductivity in control and the different irradiated animals. (a: significant Vs Con ($p<0.01$), b: significant Vs 6Gy ($p<0.01$), c: significance Vs Con ($p<0.05$), d: significance Vs Con ($p<0.05$), d: significance Vs Con 6 Gy ($p<0.05$) Di Maggio et al, (2015).

Ionizing radiation causes severe cellular damage and stresses both directly, by energetic disruption of DNA integrity, and indirectly as a result of the formation of intracellular free radicals (Simone et al, 2009). Among the key cellular components that are sensitive to γ-radiation are leukocytes which dropped sharply after exposure to the different doses of γ-irradiation. This reduction may be due to irradiation damage of lymphocyte DNA since there is no lethal damage to RBCs because they lack nuclei. However, other damages to erythrocytes may influence the quality of RBC concentrates. The present results are in line with those of Maks et al, (2011) and De Oliveira et al, (2013) who reported that whole blood irradiation damaged lymphocyte DNA, but there is no lethal damage to RBCs. However, they did not observe damage to the hemoglobin structure, as assessed by the degree of hemoglobin denaturation and electrophoresis.

The viscosity of Hb solution can vary greatly depending on the solute molecules (Hb) which possess the native helical conformation or shaped in coils. Often kinetics of denaturation from helix to random coil can conveniently followed by measuring changes in the solution's viscosity over a period of time (Pajonk & McBride, 2001). Our results showed a pronounced increase in the Hb viscosity and conductivity in rats exposed to 2 Gy. The viscosity enhancement means Hb unfolds (Multhoff & Radons, 2012), which destabilizes the remaining structure and simultaneously collapse to random coil (Pallister, 1999). This is accompanied by an increase in the fractional volume of molecule, so that the specific viscosity increases. In addition, the change in Hb conductivity gives line of evidence about the degree of unfolding with formation of new groups exposed to the surface besides the polar hydrophilic groups leading to increasing of electrical conductivity. These abnormalities in the physical character of Hb were observed as contracted hemoglobin at the periphery or at one side of the erythrocyte of irradiated groups' blood smear photomicrographs. The relationship between radiation and inflammation seems somewhat paradoxical. At high doses, radiation is generally pro-inflammatory. On the other hand, low dose radiation has a long history of use in the treatment of inflammatory disease. This suggests the involvement of multiple mechanisms that may operate differentially at different dose levels (Raymond, 1990). Radiation treatment is obviously a two-edged sword. On the one hand, sub lethal doses of IR induce a nuclear DNA damage response.

Further study introduced by Deyi Xu et al, (2012), to reveal the alterations in the ultrastructure of RBCs due to gamma irradiation doses (25–35 Gy). The changes seen under microscope were the concentrations of plasma electrolytes and the killing effect of lymphocytes in samples of blood exposed to different doses of γ-ray irradiation and the changes were as dose, storage times and time dependent as well as the environment (invitro/invivo). Also, as the dose of irradiation was increased, the proportions of echinocytes, sphero-echinocytes and erythrocytes with a degenerated shape increased, illustrating storage times that the changes of ultra-structure are dose-dependent. The relative RBCs response to irradiation have been presented in Fig. (2.21-A-D).

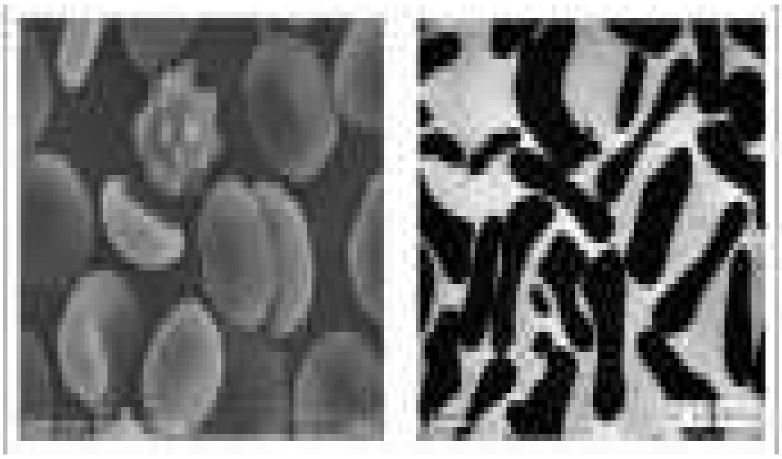


Figure 2.21-A: Scanning electron microscope picture of red blood cells subjected to 15 Gy irradiation, after 7 days of storage. Original magnification 6,000x. The dominant cells are discocytes and only a few irreversibly changed red blood cells can be seen (Deyi Xu et al, 2012).

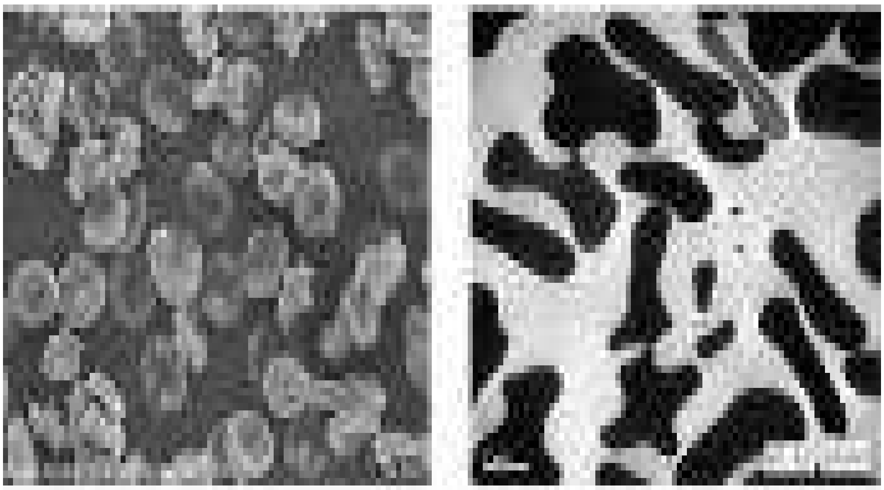


Figure 2.21-B: Scanning electron microscope picture of red blood cells subjected to 35 Gy irradiation, after 21 days of storage. Original magnification 2,500x. Numerous echinocytes and sphero-echinocytes can be seen. echinocytes and sphero-echinocytes can be seen (Deyi Xu et al, 2012).

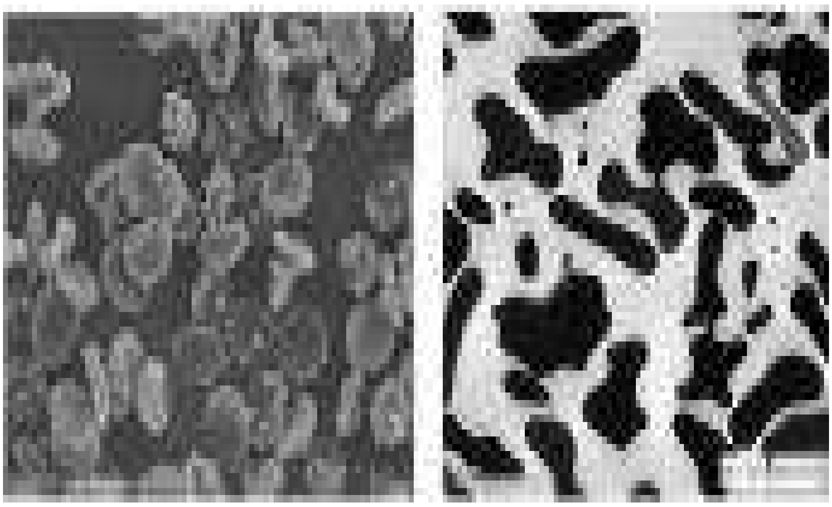


Figure 2.21-C: Scanning electron microscope picture of red blood cells subjected to 45 Gy irradiation, after 21 days of storage. Original magnification 2,500x. Sphero-echinocytes and degenerated forms dominate among irreversibly changed cells (Deyi Xu et al, 2012).

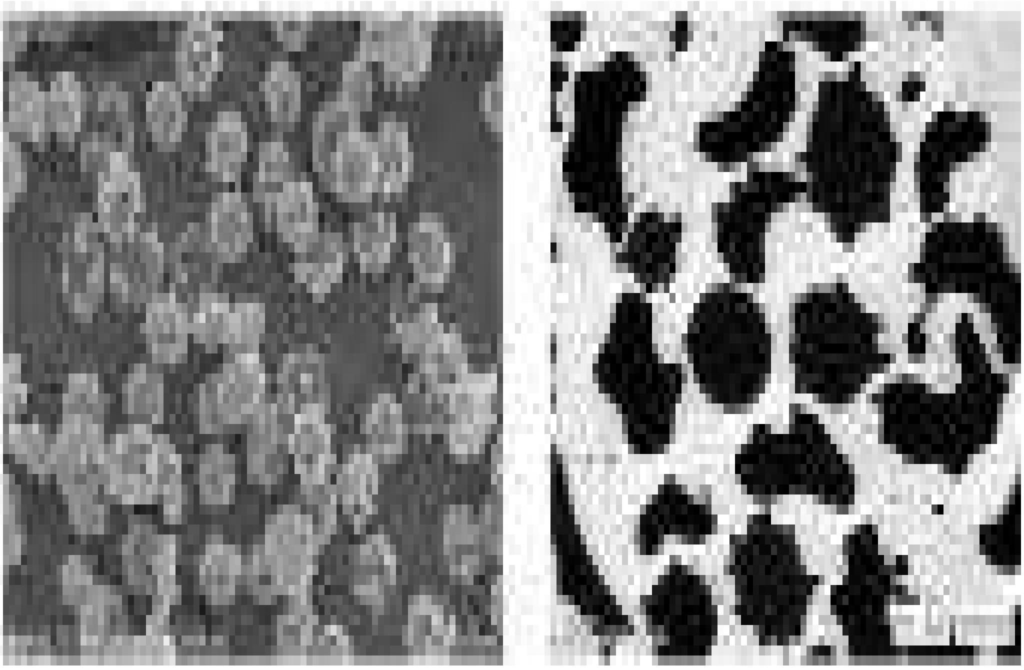


Figure 2.21-D: Scanning electron microscope picture of red blood cells subjected to 55 Gy irradiation, after 28 days of storage. Original magnification 2,500x. Almost all cells are irreversibly changed cells (Deyi Xu et al, 2012).

The standard radioactivity dose of radiopharmaceuticals in adults is based on the ideal standard weight of a patient, 70 kg. (Hansen et al, 2006) and the parameters such as pregnancy and sometimes renal function are considered limiting factors in the radiation dose delivered to the patient. Obtaining acceptable image quality in an obese patient frequently requires use of an activity higher than used in a patient of ideal weight. However, the radiation dose to the patient recommended by the International Commission on Radiological Protection limits the increase in activity, and hence the dose may not be high enough to produce an adequate study for proper interpretation due to a reduced signal-to-noise ratio and increased scatter in the acquired image. In positron emission tomography (PET), for example, an increase in the injected dose according to patient weight can be used to overcome poor image quality due to scatter, but the dose cannot exceed 925 MBq (25 mCi) (Everaert et al, 2003). A common procedure used in myocardial perfusion imaging is to calculate the activity on the basis of patient weight and adjust upward for heavier patients by using a fixed formula dose such as 11.47 MBq (0.31 mCi)/kg for ^{99m}Tc agents or 1.48 MBq (0.04 mCi)/kg for ^{201}Tl or the following general equation:

$$Patient\ dose = \frac{Standard\ Dose\ \times Patient\ weight\ (Kg)}{Standard\ weight\ (70\ Kg)}$$

Another option to overcome this limitation and improve image quality is to prolong the acquisition time or use a multidetector system for higher statistical counts (Karesh et al, 2006; Hansen et al, 2006).

The withdrawal blood samples were sent to department of histopathology and have been processed and visualized by transmitted light microscope to obtain a magnification of 1.0×10^3 for the histological changes induced by irradiation in the RBCs.

Chapter Three

Methodology

Chapter Three
Methodology

3.1 Area of the study:

The following study has been carried out as retrospective and minimum invasive experimental work to collect the relevant data from the Radiation & Isotopes Center of Khartoum (RICK), Nuclear Medicine Department during June 2014 –2018.

3.2 Variables of the study:

The variables of this study imply the Ages, gender, body mass index (BMI) and count of blood components (WBCs, RBCs, HGB and Platelets (PLT)).

3.3 Sampling of the study:

This study was performed among a sample size of 350 patients who referred for bone scintigraphy at RICK. With different ages and body mass index (BMI) as derived from the patient weight divided by the square of height in meter (weight in Kg/height in meter^2). The ages have been sampled as 18-28 with interval of 10 years and the BMI sampled as underweight ($\leq$ 18.49), normal BMI (18.5 – 24.9), overweight (25 – 29.9), obese (30 – 39.9) and morbidly obese ($\geq$ 40 Kg).

3.4 The method of the study:

3.4.1 *Sample & technique:*

The targeted sample consist of 350 cancer patients referred for bone scintigraphy for metastasis assessment at RICK – Sudan during 2014- 2018. The patients have been informed for relative preparation (hydration, hair shaving and fasting) and on the due date they did laboratory test for WBCs and RBCs as routine blood checkup for cancer's patients before radioactive dose administration for bone scintigraphy. Then the radioactive dose has been eluted from ^{99m}Tc generator based on its daily time activity formula ($I = I_0\, e^{-\lambda t}$), where I_0 refers to initial activity and I refers to activity after elapsed time t and based on the disintegration constant λ) as total volume for all patients prepared for scan. Then the individual patient dose has been estimated based on body mass index (weight in Kg/height in meter^2) and further the relative amount has been mixed with MDP for each specific patient. The administrated dose composed of Technetium-99m (^{99m}Tc)/MDP; is given intravenously to each patient and the bone scan started after three hours for image acquisition as stated by Collier et al, (1987) with bladder voiding. At this moment a 5 cc of blood sample has been withdrawn from each patient (*patient informed consent was signed by the patients*) and sent to laboratory for further blood analysis and data collection related to blood components such as: WBCs, RBCs using automated cell counter (Sysmex KX-21) in addition to Haemoglobin (Hb), and Platelets after taking patient informed consent. the obtained data has been analyzed using Statistical Package for Social Sciences SPSS program.

Chapter Four
Results

Chapter Four
Results

The following section presenting the results related to bone scintigraphy that has an increasing demand in Sudan with special consideration to breast cancer that influencing the high incidence of patient who referred to bone scan with relative parameters and furtherly presenting the effect of radioactive dose of bone scintigraphy in blood components as follows:

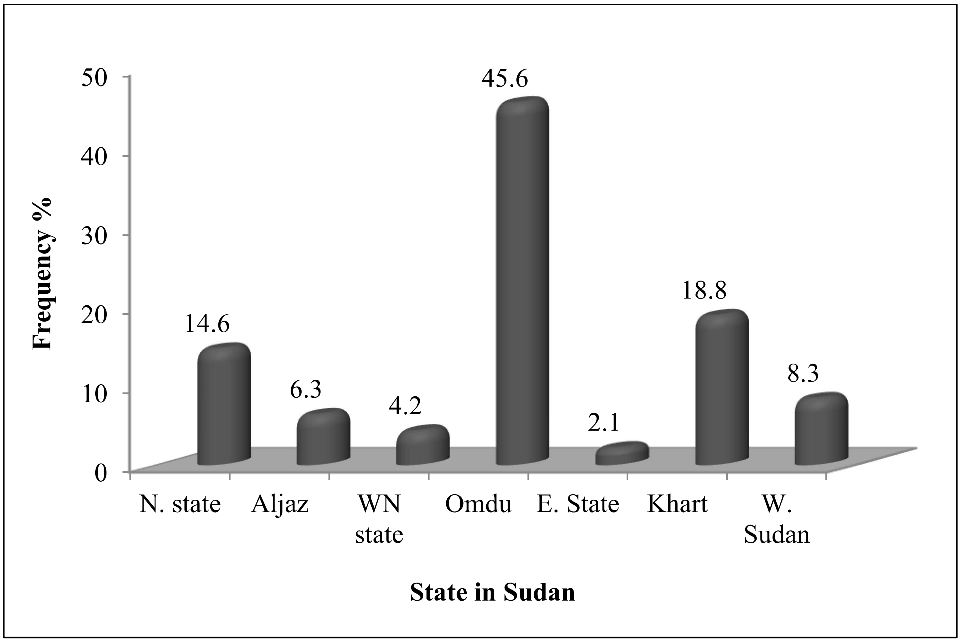


Fig. 4.1: shows the frequency % of cancer cases referred for bone scan at RICK during the selected study period distributed based on geographical status.

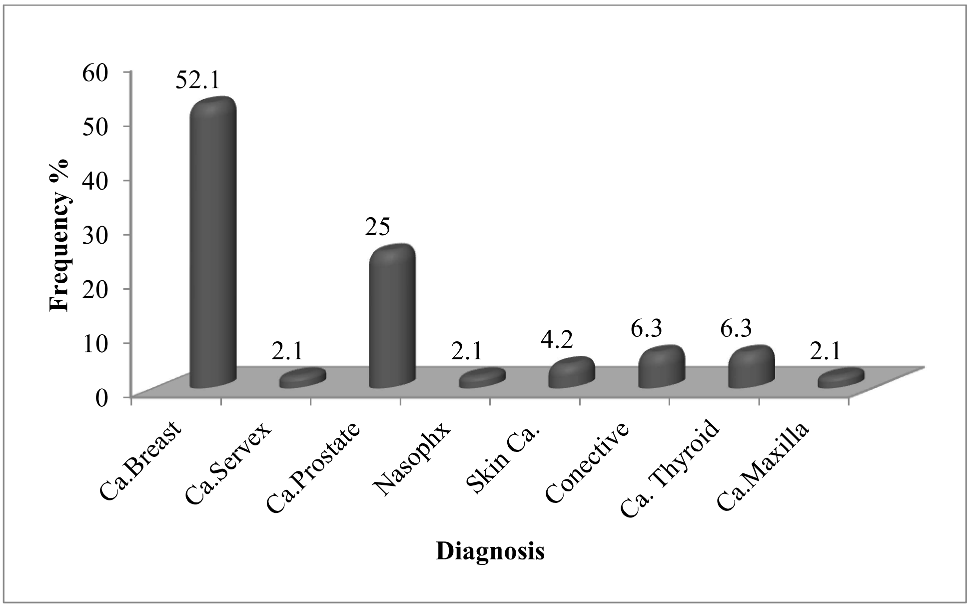


Fig. 4.2: shows the common cancer types in Sudan based on the selected sample at RICK during the study period

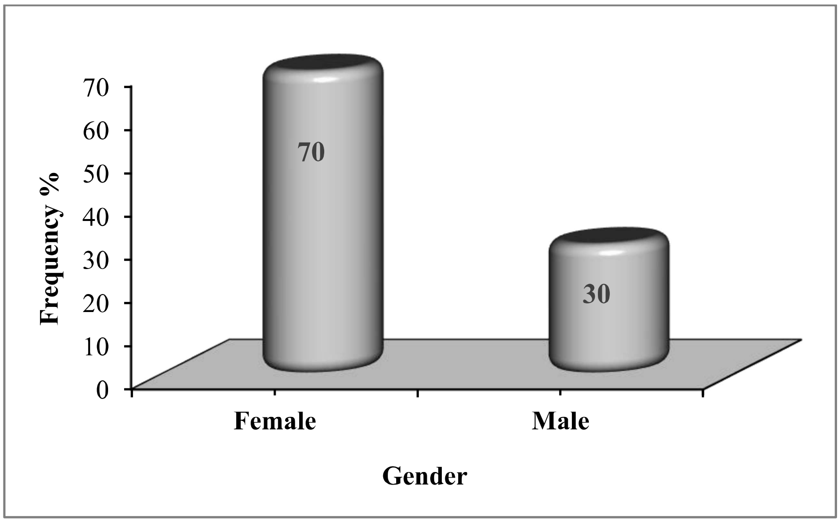


Fig. 4.3: shows the frequency% of Sample underwent bone scintigraphy distributed based on gender.

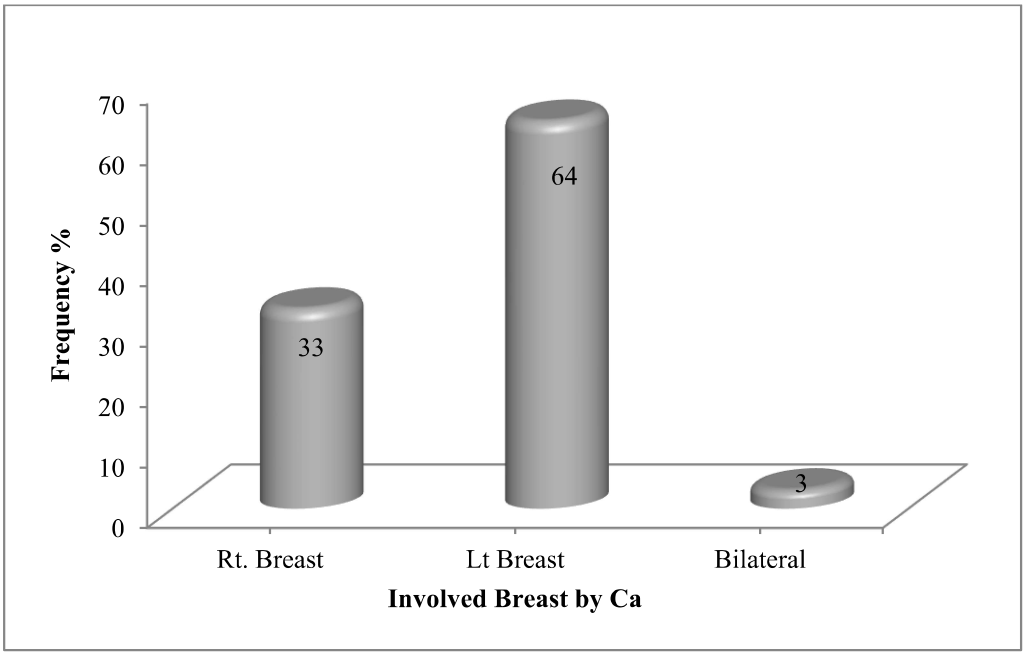


Fig. 4.4: shows the percentage distribution of breast cancer based on body symmetricity

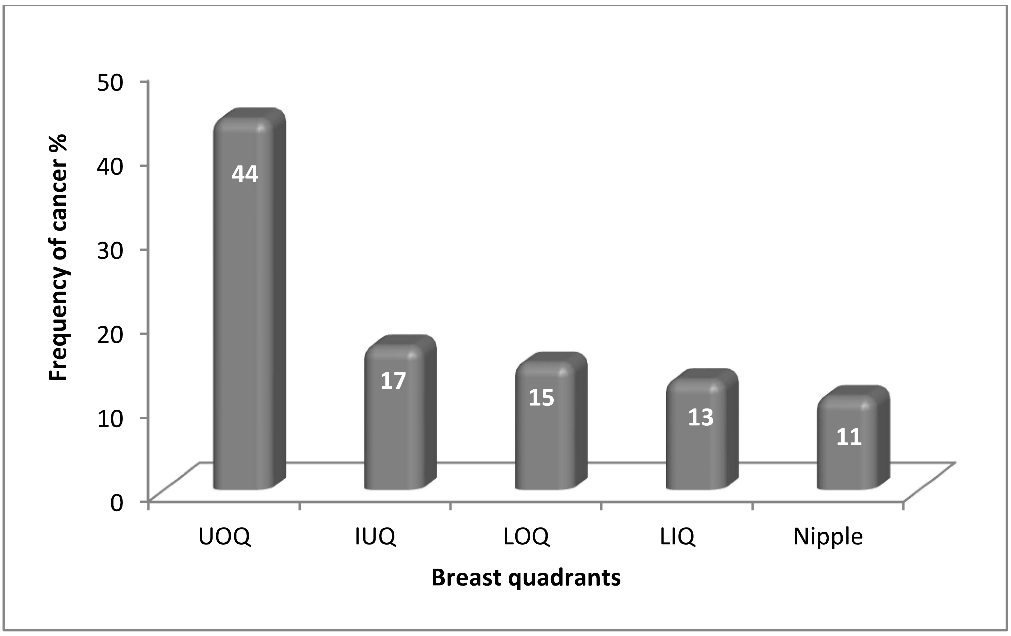


Fig. 4.5: shows the common involved quadrants of breast by cancer in percent

Fig. 4.6: shows the percentage distribution of breast cancer involvement based on women age.

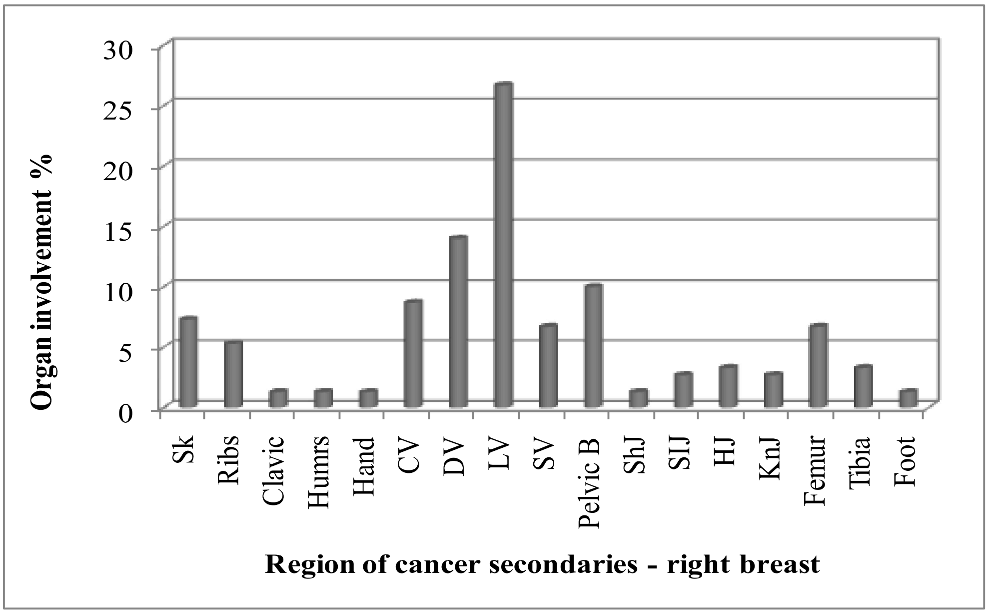


Fig. 4.7: shows the percentage of common anatomical regions of cancer secondary among women for right breast:

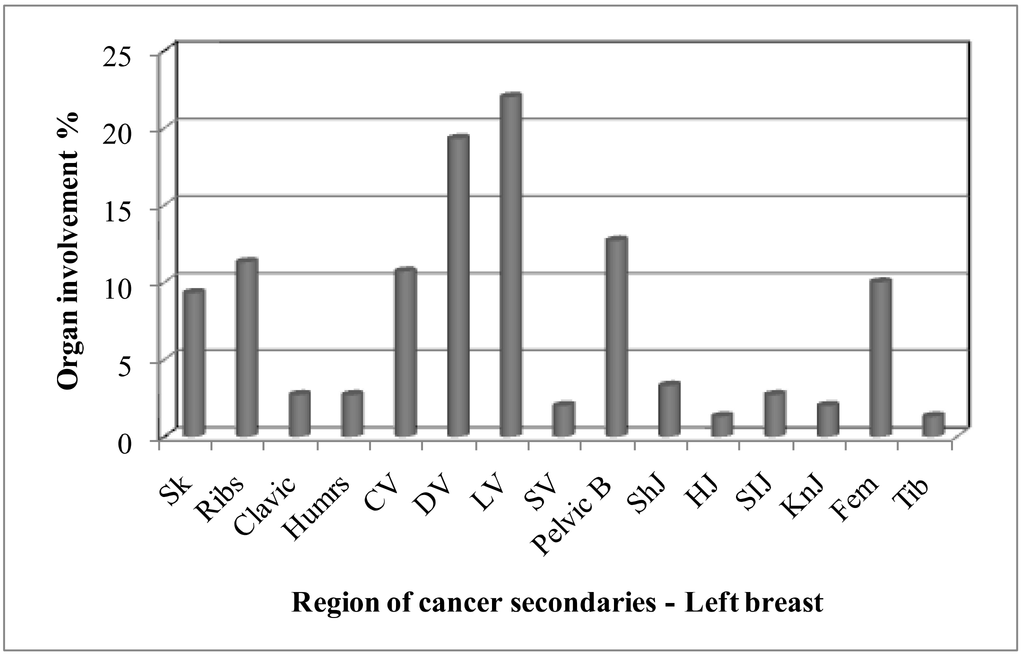


Fig. 4.8: shows the percentage of common anatomical regions of cancer secondary among women for left breast:

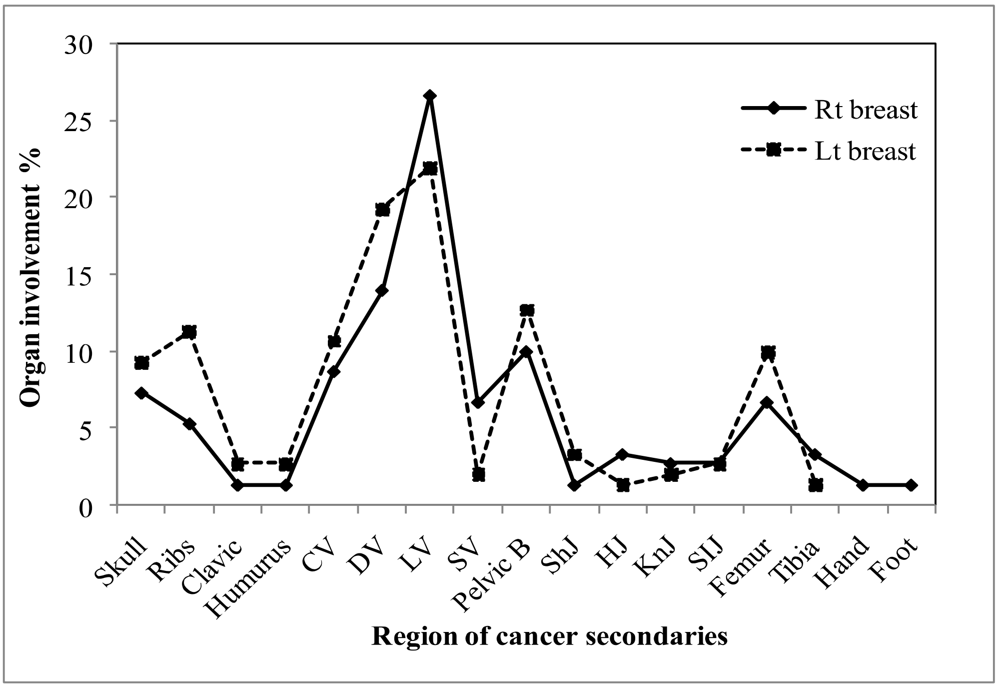


Fig. 4.9: shows the comparative metastatic percent of cancer to skeletal system from right and left breast cancer

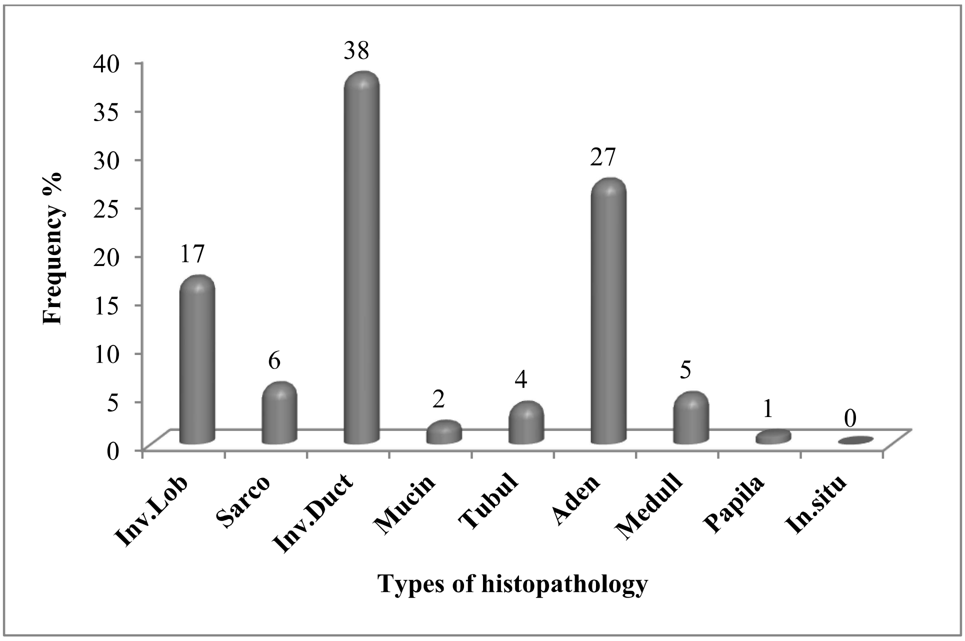


Fig. 4.10: shows the common histological types of breast cancer percent in Sudan

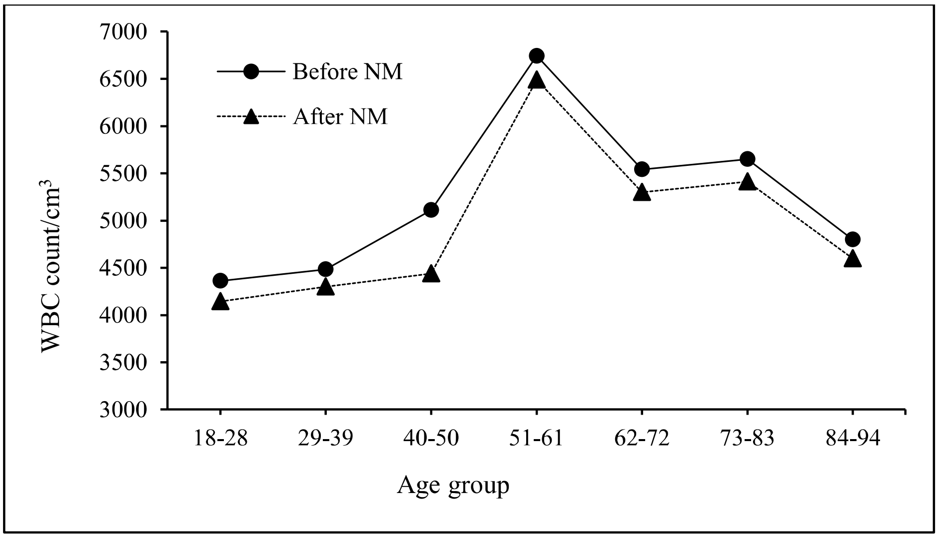


Fig. 4.11: shows the correlation between WBC count and the age group before/after interval time of radioactive dose injection for bone scintigraphy

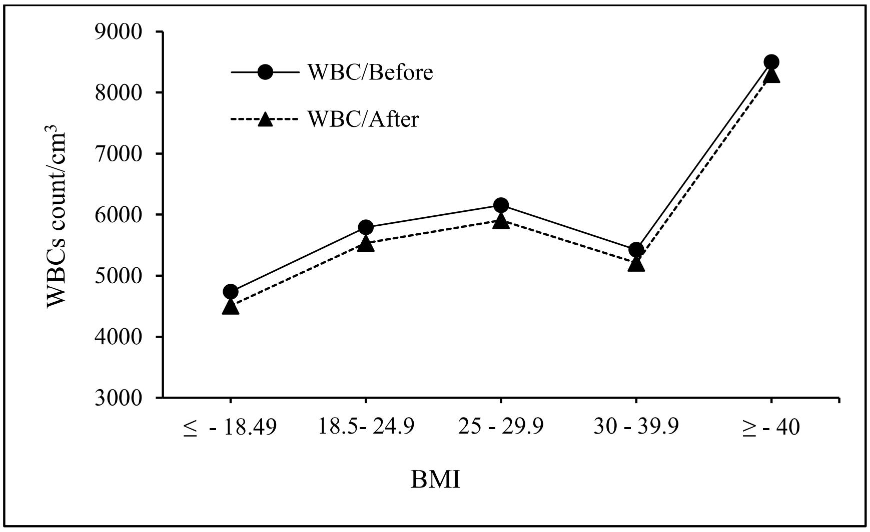


Fig. 4.12: shows the correlation between WBC count/cm3 and the BMI before and after interval time of bone scintigraphy (≤ 18.49 for underweight, 18.5 – 24.9 for normal, 25 – 29.9 for overweight, 30 – 39.9 for obese, and ≥ 40 Kg for Morbidly obese)

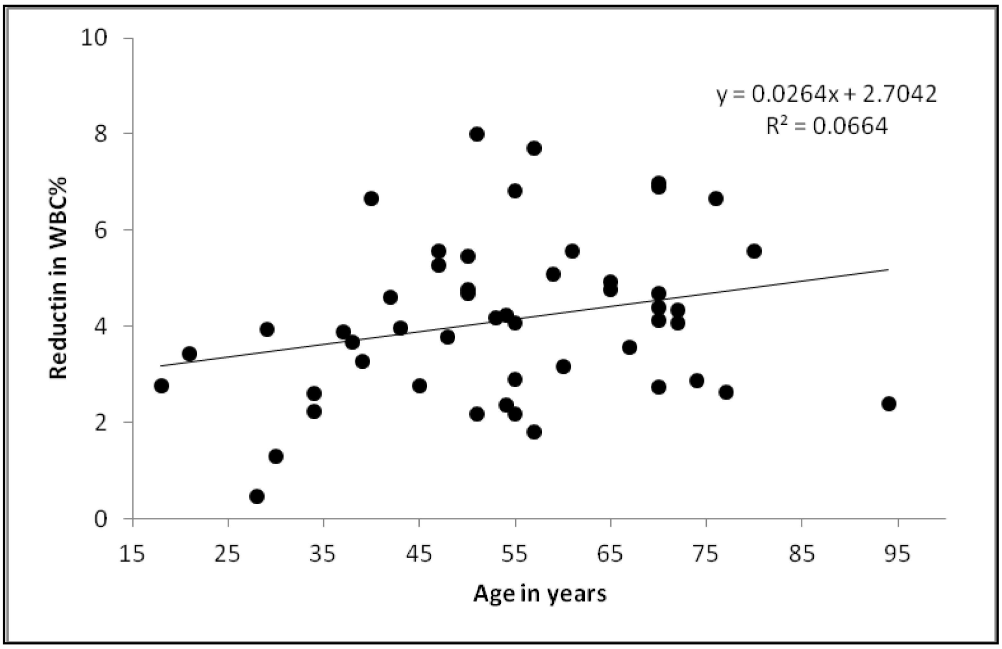


Fig. 4.13: shows the correlation between the reduction in WBC and the age after interval time of bone scintigraphy

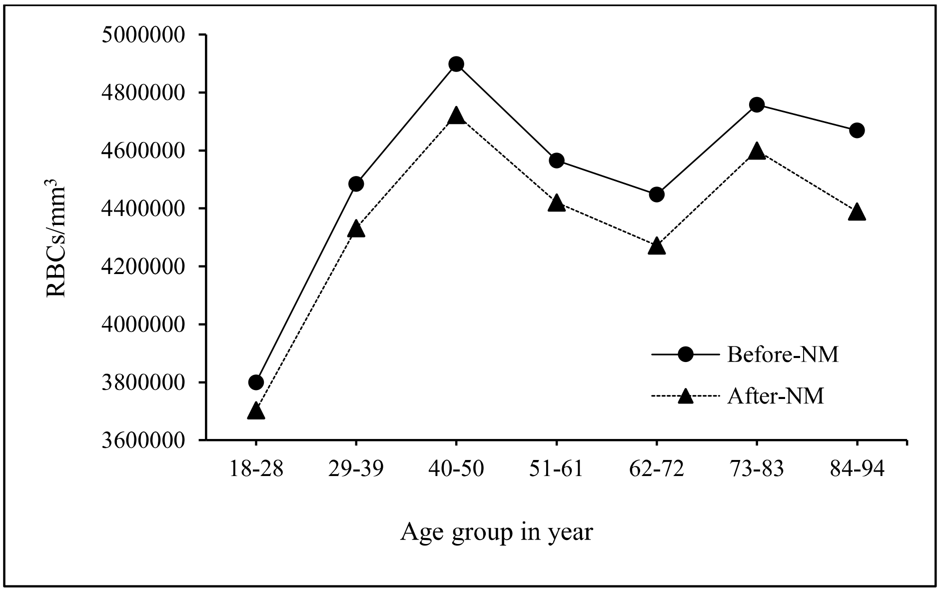


Fig. 4.14: shows the correlation between RBCs and the age groups in years before/after interval time of bone scintigraphy.

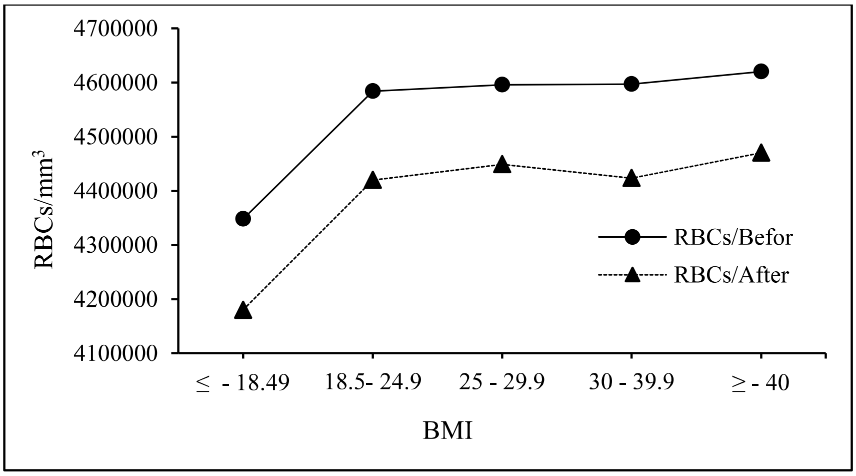


Fig. 4.15: shows the correlation between RBCs and the BMI before/after interval time (3 hours) of bone scintigraphy. (≤ 18.49 for underweight, 18.5 – 24.9 for normal, 25 – 29.9 for overweight, 30 – 39.9 for obese, and ≥ 40 Kg for Morbidly obese).

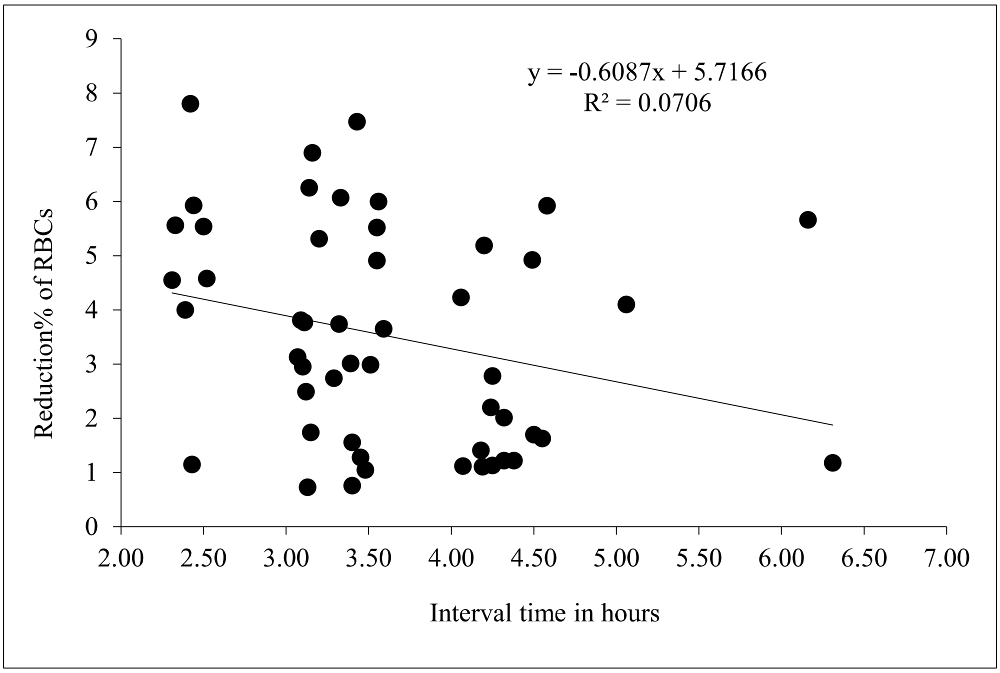


Fig. 4.16: shows the correlation between the reduction in RBCs and the interval time of bone scintigraphy

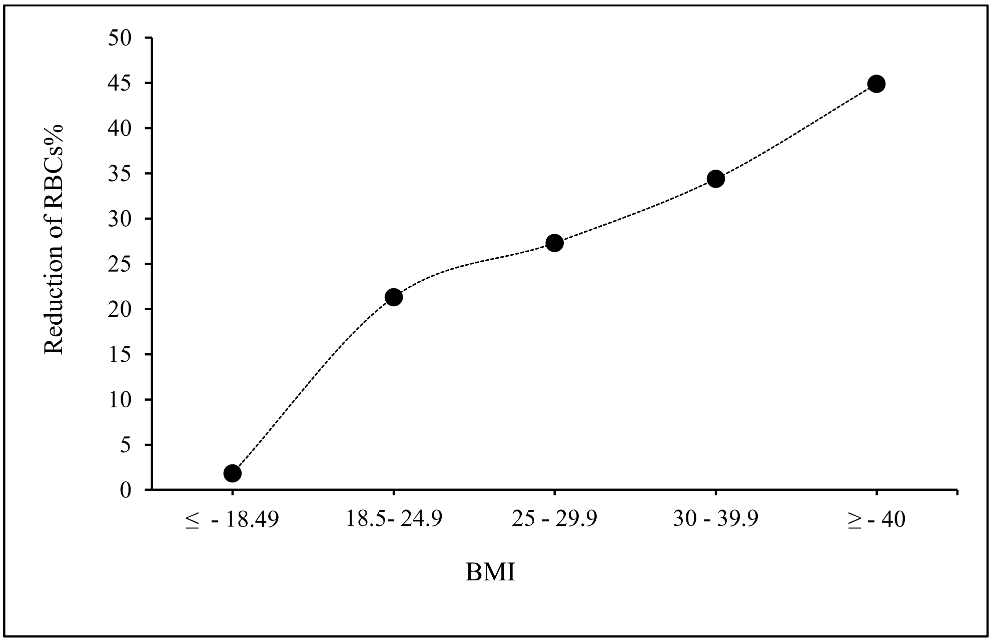


Fig. 4.17: shows the correlation between reduction of RBCs% and the BMI after interval time (3:00 - 3:30 hours) of bone Scintigraphy.

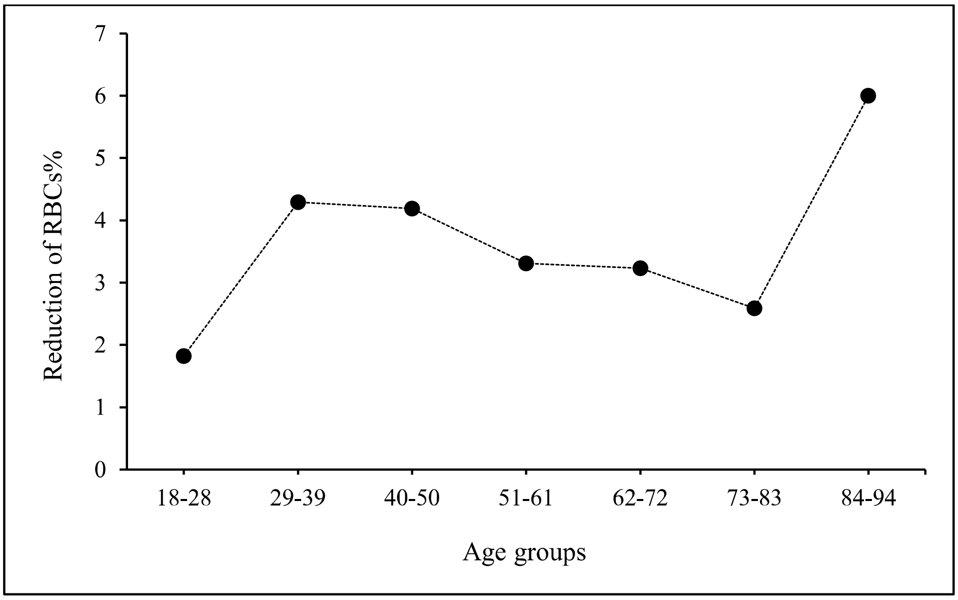


Fig. 4.18: A correlation between the reduction of RBCs% versus the age groups after the interval time of bone scintigraphy.

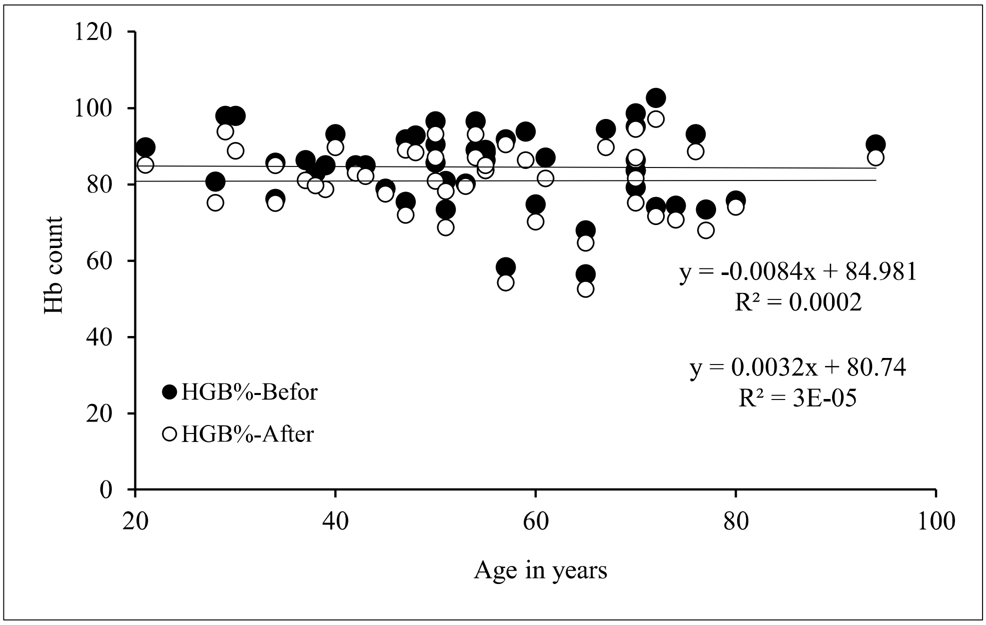


Fig. 4.19: shows the correlation between hemoglobin HGB and the age before/after interval time of bone scintigraphy.

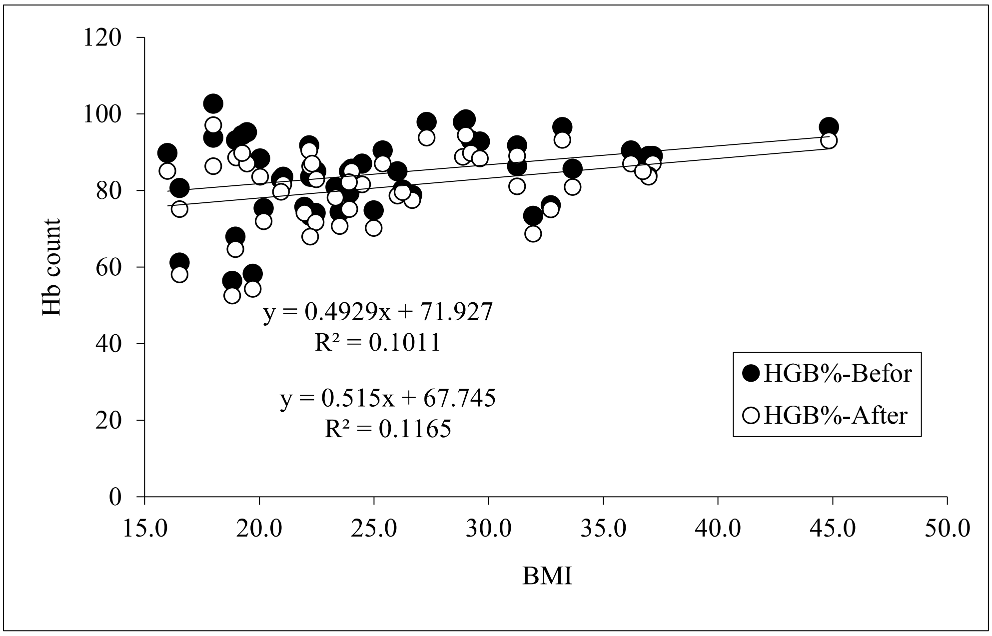


Fig. 4.20: shows the correlation between HGB and the BMI before/after interval time of bone scintigraphy.

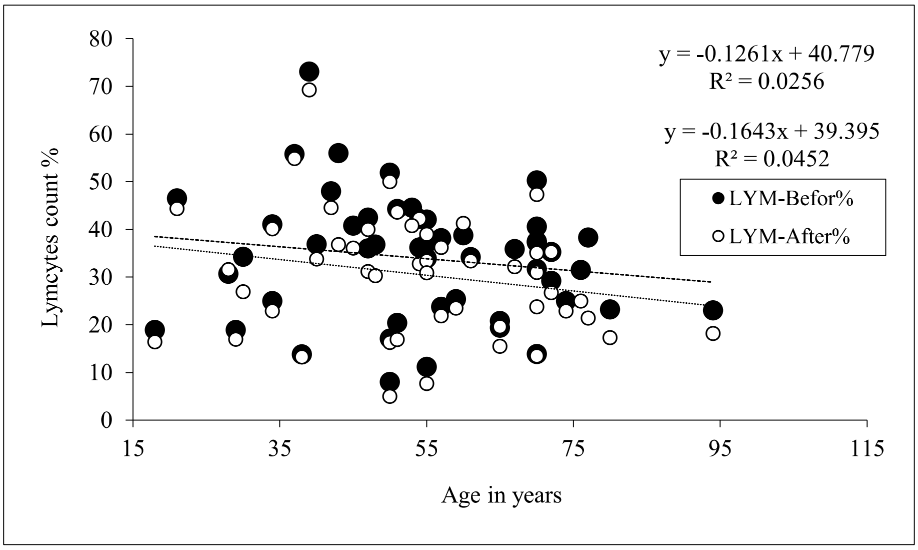


Fig. 4.21: shows the correlation between age in years and Lymphocytes % before and after interval time of bone scan

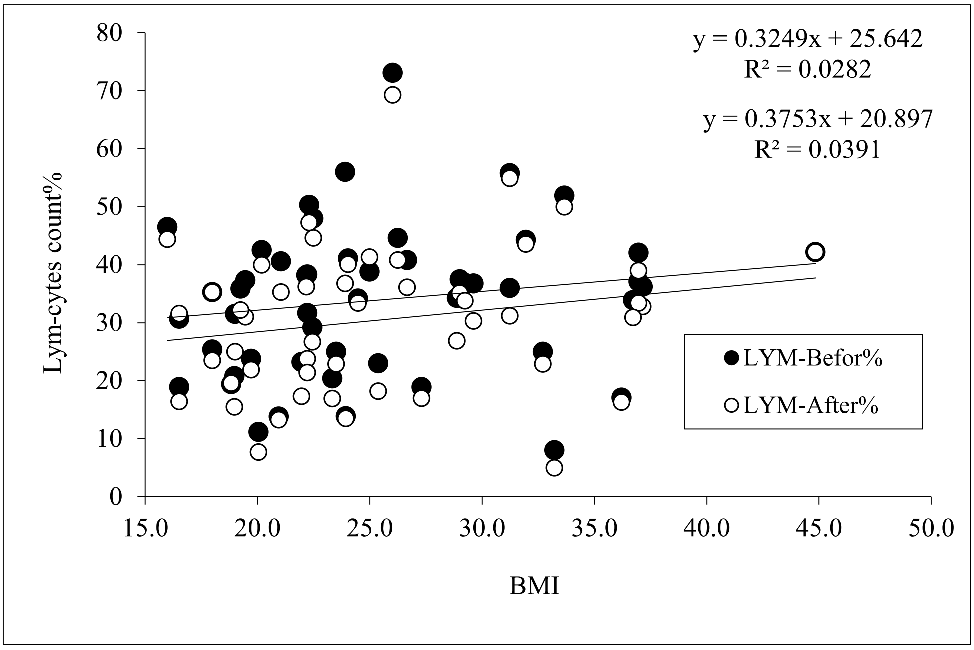


Fig. 4.22: shows the correlation between Lymphocytes% versus BMI before and after interval time of bone scan.

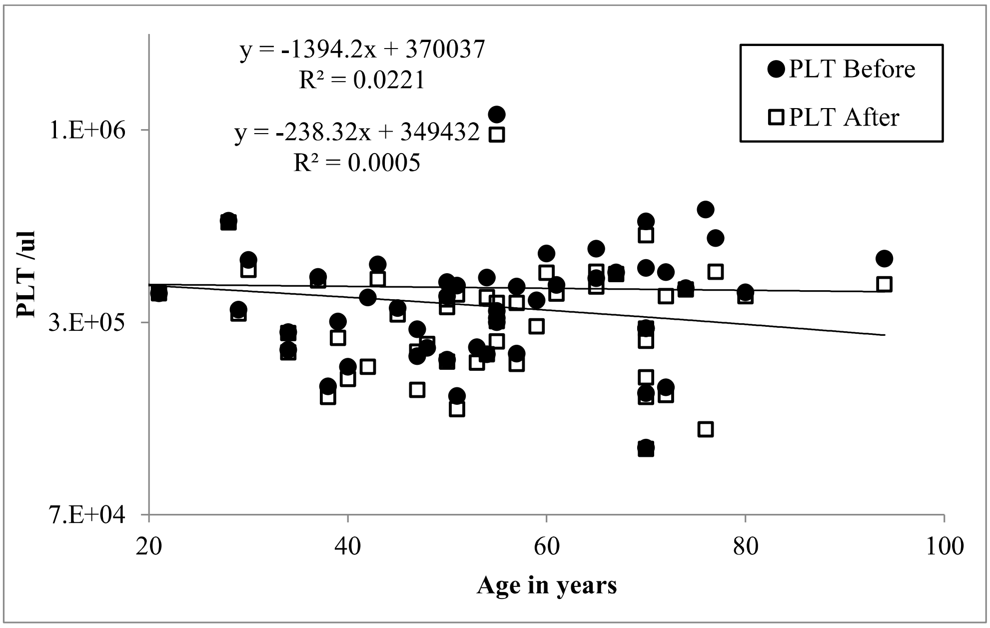


Fig. 4.23: shows the correlation between Age in years and PLT count before and after the interval time of bone scan.

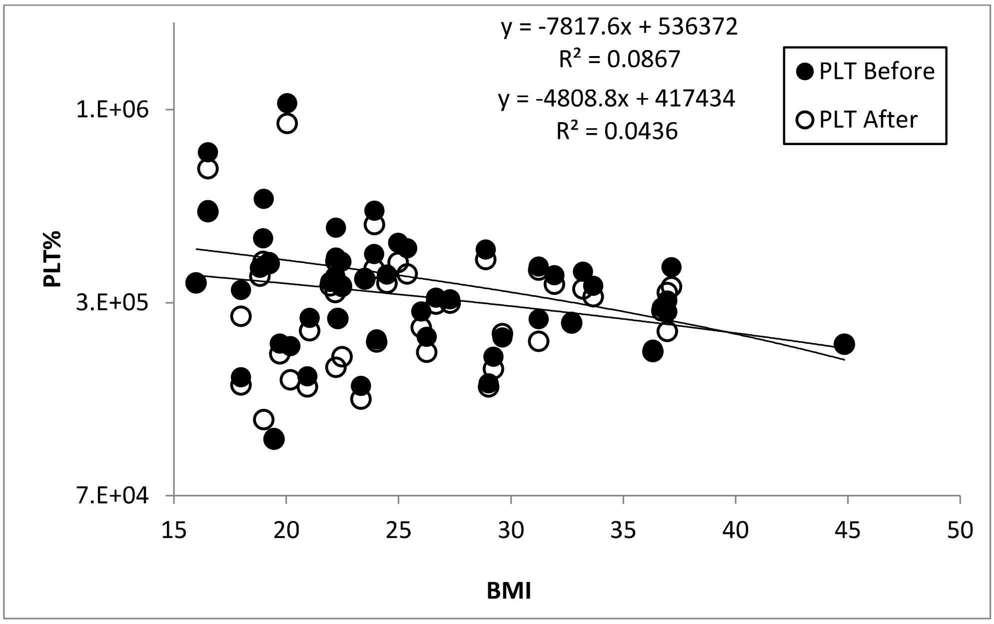


Fig. 4.24: shows the correlation between BMI and the PLT % before and after interval time of bone scan

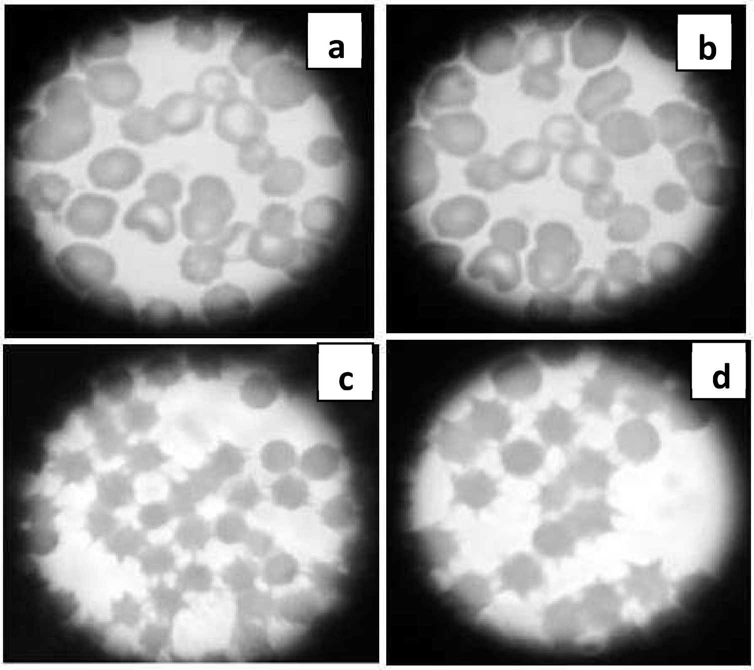


Fig. 4.25: Morphological deformities involving RBCs after interval time of bone scan in nuclear medicine (‘a’ = control group (0.0 mCi), group ‘b’ =15 mCi, group ‘c’ = 20 mCi and group ‘d’ = 25 mCi).

Chapter Five
Discussion & Analysis

Chapter Five
Discussion & Analysis

Relative to bone scintigraphy with consideration to breast cancer as example in the current study and the radioactive dose of bone scintigraphy effects in blood components; the study revealed that: in Fig. (4.1), that shows the frequency % of cancer cases referred for bone scan at RICK during the selected study period distributed based on geographical status. It reveals that the high incidence of cancer was in Omdurman state which representing 45.6 %, then Khartoum state (Khartoum & Bahri) which represents 18.8 % and in North state which represents 14.6%. The high incidence in Omdurman and Khartoum could be ascribed to extension of the towns as well as the recent exodus to capital and big cities due to lack of medical specialized services and better basic community services. Considering this argument; the health workforce together with health institutions distributed inequitable (Three specialized medical centers in the middle of the country i.e. Radiation Isotope Center Khartoum (RICK), Gezira Institute for Cancer treatment and Molecular Biology (GICMB), and Shendi Cancer Center), and more than 60% of health worker staff are working in secondary and tertiary facilities (Ebrahim et al, 2017; Gafer et al, 2016). The other state encountered with considerable incidence was the west of Sudan taking 8.3 %, Aljazeera state taking 6.3 % as agreed by Ali et al, (2014); Saeed et al, (2016).

These patients who have been referred from different provinces in Sudan for bone scan; the majority of them were breast cancer type and representing 52.1% relative to all cancer types Fig. (4.2) with an increasing scale as agreed with Elamin et al, (2015). Then followed by prostate cancer which represents 25 %. Such result also, agreed by Bray et al, (2018), where they predicted that

Ca. has been increases annually among females. While other studies stated that prostate cancer and Nasopharynx are the most common cancer in Sudan among male group.

The predominant cancer cases of Ca. breast have been distributed based on gender as in Fig. (4.3). The distribution showed that: the female represented the predominant cases with a 70% compared with 30% male relative to total sample size (350 patients). The high frequency percent in female could be ascribed to the high incidence of breast cancer which referred to bone scan in addition to cervical carcinoma in contrast with male who presented for bone scan to assess the metastasis of nasopharyngeal and prostate cancers. Among these patients i.e., 70% of the sample; the left breast involved by cancer representing 64% while the right one represents 33.6%, and bilateral was 3% (Fig. 4.4). This result is an agreement with the study done by Nosheen et al, (2013) which indicate that the carcinoma of the breast affects the left breast with percentage of 66% slightly more than the right breast which has 31% and bilateral breast cancer 3%, while bilateral breast cancer has zero percentage. Which indicate that bilateral breast cancer incidence is very rare. This result is an agreement with the study carried out by Chaudary et al, (1984), in which they reported that, the incidence of bilateral breast cancer with percentage of 1.3 from 521 patients. All this result indicates that the bilateral breast carcinoma represents very small proportion of all breast carcinoma cases. Furtherly as in Fig. (4.5) that shows the common involved quadrants of breast by cancer. It reveals that when the breast has been divided into four quadrants plus the nipple site, the upper outer quadrant (UOQ) shows the most involved site by cancer taking 44% from the total sample, as well as other types of diseases such as benign tumors (fibroadenoma and cyst), and the susceptibility of this quadrant by cancer and other diseases could be ascribed to retch lymphatic and other types of epithelial tissue which considered as a common targeting by cancer (Philippa, 2005). Other quadrants as Inner upper quadrant IUQ, Lower outer quadrant LOQ, Lower Inner Quadrant LIQ and the nipple shows the following percentages 17%, 15%, 13%, and 11% respectively, such result is in agreement with the study carried out by Gulam et al, (2012).

These patients presented with LUOQ of Ca. breast being distributed based on age groups as in Fig. (4.6) which reveals that the breast cancer could involve younger ladies in the ages of 20-30 years and increases with aging taking a high incidence around 38% among age group of 40-50 years old and 24% in women with age group of 50-60 years old, then decreases with aging, however this result is differ for the same case in developed country in which breast cancer is predominant among the

age group of 20-43 years old as 12% (Hicky et al, 2008). This finding is in agreement with Anderson et al, (2008); they found that the breast cancer is so predominant among black women and commonly above the age of 40 years old. The decreasing incidence following the ageing could be ascribed to deceased of patients; one notation is that: all younger patients (20-30 years old) developed aggressive and most susceptible cancer types to hormones such as adenoid carcinoma.

The cancer cases originated at LUOQ tend to give metastasis general skeletal system and organs; hence the common anatomical regions being striking by right and left breast cancer metastasis have been presented in Fig. (4.7 & 4.8). which they revealed that: the right breast is commonly gives some considerable metastasis to the Lumber vertebrae (LV) with a percentage of 26, the dorsal vertebrae (DV) with a percentage of 14, the pelvic bone (Pelvic B) with a percentage of 10, the cervical vertebrae (CV) with a percentage of

8, the skull with a percentage of 7.3 and femur bone with percentage of 6.7. The common metastatic property from breast cancer is due to estrogen receptor positive subtypes (ElAyass et al, 2009). [6]. This finding is an agreement with the literature review which stated that the breast cancer commonly gives metastasis to bone (Salim and Alhaj, 2008) [24]; however, there are some organs more susceptible to metastasis than other parts as our study shows that within the skeletal system there is most common region for secondary such as LV, DV and Pelvic bone. The researchers assume that the success of secondary growth is due to opportunity of the cell impaction, good climate and blood supply, in this view Marina and Ivan, (2008). stated that growth of secondary tumor is mortgaged to factors of cell growth. The routes of skeletal metastasis are direct extension or invasion, lymphatic spread, hematogenous dissemination and intra-spinal spread. Skeletal metastases of breast cancer will mainly occur from lymphatic spread and hematogenous dissemination. While the left breast is commonly giving some considerable metastasis to the Lumber vertebrae (LV) with a percentage of 21, the dorsal vertebrae (DV) with a percentage of 18, the pelvic bone (Pelvic B) with a percentage of 11, the ribs with percentage of 10, the cervical vertebrae (CV) with a percentage of 9 and the femur bone with a percentage of 9. This finding is agreed with Koizumi et al, (2003) which concluded that bone is the most common sites of breast cancer secondary. However, the results show that within the skeletal system there is most common region for secondary such as pelvic, upper leg bone (femur) and ribs but the spine is the most common site of bone metastasis (LV and DV). This finding is agreed with Gray and Ignac, (2006) in which they stated that the breast cancer is most commonly affects the spine, ribs, pelvis, and proximal long bones.

The comparison between right/left breast cancer metastasis, Fig. (4.9) revealed that: metastasis from both breasts to human system have showed same preferences; as to metastasize to certain organ higher than others i.e. the left and right breast cancer give metastasis to LV, DV and the Pelvic bone as most higher than others parts of skeletal system, they also show the same phase of metastasis to other skeletal system segments i.e. identical metastasis, this could be due to symmetrical net of lymphatic drainage as well as the blood supply arteries and the drainage veins. However, the right breast usually appears to give higher frequency% relative to left one.

The distribution of common histological types among these breast cancers presented in Fig. (4.10), which revealed that: the common histological types of breast cancer are Invasive ductal carcinoma (IDC) that representing 38% from the total sample; which is in agreement with the study carried out by Gautam et al, (2010); as well Li et al, (2005) and Terfa et al, (2010) who mentioned that: the most common subtype accounting for 70–80% was the IDC. The other less common types were Adenoid carcinoma 27%, Invasive lobular carcinoma (ILC) 17% in addition to minor percent of other types of histology, however carcinoma in situ taking 0% indicating the lack of breast screening program in Sudan or not publicly known.

Fig. (4.11) shows the correlation between WBC count and the age group before/after interval time of radioactive dose injection for bone scintigraphy. The data reveal that the WBC count increases eventually following the age group increment from 18 – 61 years old and then started to decreases but usually remain within the normal range (4000 – 7000/cm^3) as agreed with the study done by Biino et al, (2011). And as well same result had been presented by Valiathan and Asthana, (2016), and Maulik et al, (2014). Such normality is ascribed to normal human physiology (production and optosis). However, the WCB count decreased by 3.8% (221.8) in average after the interval time of 3 hours of ^{99m}Tc administrated to patient, relative to initial count which is so significant at (P value = 0.00, t = 17.6), indicating that either the radiation destroying the WBC or could change their morphology causing the detector uncapable to distinguish and depict them or could be due to suppression of blood forming organs as stated by Sharma et al, (2012).

Fig. (4.12): shows the correlation between WBC count and the BMI before/after interval time of bone scintigraphy. It revealed that: the WBC increases as the BMI increases from ≤ 18.49 (underweight) up to 25 – 29.9 (overweight) then decreases among obese (30 – 39.9) and peaking among Morbidly obese (≥ 40 Kg) but remains in normal range. The activity dose (15±2.9 mCi) of bone scan reduces significantly the WBCs by 3.8% at P-value = 0.00 and P=value = 0.05) relative to age and BMI respectively. However, in both cases of aging and BMI variation, WBCs remains fluctuating within the normal ranges which is due to normal host physiology. But after the interval time of ^{99m}Tc dose administration, the WBCs count decreases by 3.8 % relative to initial count, which is so significant at (P-value = 0.05). The response of WBC to irradiation could be due to large target volume they possess for radiation photos and considerable radio-sensitivity (Mohamed et al, 2015). Also, the BMI together with the massive umber of RBCs/mm^3, their small size, frequent rapid production and the radio-resistivity of RBCs could play a major role in the significance effect in WBCs and RBCs. Such role notable significant effects in WBCs compared with RBCs as obvious variation in t-test significances (P-value 0.00 for WBCs versus age and P-value 0.05 for WBCs versus BMI).

Fig. (4.13): shows the correlation between the reduction in WBC% and the age after interval time of bone scintigraphy. The data shows that as the age increases as the reduction of WBC% increases, indicating that: either the radio-sensitivity of WBC increases by aging or most probably due to natural reduction of immunity by ageing. The correlation between the age and the reduction of WBC% could be fitted in the following equation: $y = 0.03x + 2.7$, where x refers to Age in year and y refers to reduction of WBC%.

Fig. (4.14): shows the correlation between RBCs and the age before/after interval time of bone scintigraphy. It shows that RBCs count has increases from 18 to 50 years old then decreases following ageing but remains within the normal amount along the age of man increment with an average of (4560800) cells/mm^3 in contrast with the normal range $4.8 \times 10^6 - 5.8 \times 10^6$ cells/mm^3 or 6.46×103 / mm^3 to 7.93×103 / mm^3 for male and 4.2×10^6 to 5.2×10^6 cells/mm^3 or 6.56×10^3 /mm^3 to 7.33×10^3 / mm^3) for females (Maulik et al, (2014). However, after the interval time of bone scintigraphy the RBCs reduced by an average of 3.6% (165600 cells/mm^3) relative to initial count and at an average dose of (15±2.9 mCi) as the t-test showed insignificant (P-value = 0.31) reducing impact of radiation dose in the number of RBCs which is ascribed to damage of cellular membrane of RBCs (Selim, 2010). Comparing the impact of radiation dose in WBCs and RBCs, the impact was so insignificant in case of RBCs as it could be ascribed to small size and massive number of RBCs/mm^3 compared with WBCs count. And the general reduction in WBCs and RBCs could be due to: either destruction of mature circulating cells, or failure of instrument to detect the blood corpuscles (WBCs & RBCs deformity) or cessation of WBCs and RBCs production which is occurs at high exposure doses (Manisha et al, 2011; Sharma et al, (2012).

Fig. (4.15): shows the correlation between RBCs and the BMI before/after interval time of bone scintigraphy. The data shows that: RBCs count has been increases as the BMI increases form underweight (≤ 18.49) up to normal BMI (18.5 – 24.9) then persist semi constant in normal range among overweight (25 – 29.9), Obese (30 – 39.9) and morbidly obese (≥ 40 Kg). However, the average radioactive dose of bone scan (15±2.9 mCi) reduces the RBCs insignificantly (P value = 0.32) by 3.6% relative to initial count. The massive umber of RBCs/mm^3, their small size, frequent rapid production and the radio-resistivity of RBCs could enhance the negative effects of radiation.

Fig. (4.16): shows the correlation between the reduction in RBCs and the interval time of bone Scintigraphy. It reveals that the RBCs% decreases by the increment of interval time of bone Scintigraphy, indicating that the increment of internal exposure dose from Tc-99m resulted in more damage to RBCs. The correlation between RBCs and the interval time of bone Scintigraphy could be fitted in the following equation: $y = -0.6087x + 5.72$, where x refers to interval time of bone scan and y refers to reduction of RBs % and the correlation was insignificant ($R^2 = 0.07$).

Fig. (4.17): shows the correlation between reduction of RBCs% and the BMI after interval time of bone Scintigraphy**.** The data shows that: the reduction of RBCs% encountered among underweight group as minimum and eventually increased following the increment of BMI to be steeper among normal and overweight but usually remain within the normal range, however it increased rabidly among morbidly obese groups. After the interval time of bone Scintigraphy for all patients; the average reduction in RBCs was 3.6% relative to normal average count which is insignificant as P-value = 0.3. such insignificance could be attributed to broad normal range of RBCs count and the intensive number/mm^3.

Fig. (4.18): A correlation between the reduction of RBCs% versus the age groups after the interval time of bone scintigraphy. It shows that the reduction of RBCs% increases following the age group (18-28 years) increment upto the age group of (29-39 years); then got decreases gradualy but at age group (73-83 years) the reduction of RBCs% peaking rabidly and seriously leading to an average reduction in RBCs of 3.6%. Such reduction indicating that the aging of man would result in increment of RBCs radiosensitivity but the RBCs count themselfe would not influenced by the age.

Fig. (4.19): shows the correlation between hemoglobin HGB and the age before/after interval time of bone scintigraphy. The data shows that the amount of hemoglobin in g/dl doesn't have significant effect by aging generally (P-value = 0.21). However, the HGB count has been decreases insignificantly (P-value = 0.34) after interval time of bone Scintigraphy by 3.1% relative to the average normal value. As HGB carried by RBCs; hence its influence by radiation follows the same effect as RBCs and therefore the insignificant reduction ascribed to same factors and manifested as quick fatigue and excessive breathing rate among overweight and obese individual when got exercise.

Fig. (4.20): shows the correlation between HGB and the BMI before/after interval time of bone scintigraphy. The data reveals that: HGB increases slightly following the increment of BMI but showed insignificant correlation (P-value = 0.31) between them throughout all weights which. Such fact could ascertain the quick fatigue and excessive breathing rate among overweight and obese individual when got exercise.

While after administrating Tc-99m i.e. after interval time of bone scan, the HGB count decreases from the initial count by 3.1% relative to its average normal value.

Fig. (4.21): shows the correlation between age in years and Lymphocytes % before and after interval time of bone scan. It shows that the Lymphocytes count generally decreases insignificantly (P-value = 0.3) following the aging increment and the correlation between them was fitted in the following equation: y = -0.07x + 37.4, where x refers to age in years and y refers to Lymphocytes % (R^2 = 0.02 & 0.04 before and after applied radioactive dose). However, the count of lymph% after interval time of bone scan decreases by 10.3% (3.5) relative to initial count and their correlation follows the equation: y = -0.13x + 36.9 where x refers to age in years and y refers to Lymphocytes %. The reduction% was insignificant (P-value = 0.4) and the general amount persisting and fluctuating within the normal level as age increases.

Fig. (4.22): shows the correlation between Lymphocytes% versus BMI before and after interval time of bone scan. The data shows that the lymphocytes % increases insignificantly (P-value = 0.3) following the increment of BMI and continues in same manner and fluctuating within the normal level. However, after the interval time of bone scan; the Lymphocytes decreases by 10.3% from the initial count and their correlation fitted in the equation: y = 0.4x + 19.1 where x refers to BMI and y refers to Lymphocytes %. Also, such reduction was insignificant (P-value = 0.3) and persists with same manner but fluctuating within the normal level.

Fig. (4.23): shows the correlation between Age in years and PLT count before and after the interval time of bone scan. The analysis revealed that the PLT count does not influenced by the aging normally, however it does so and decreases significantly (P-value = 0.01) by 12.5% (42020) after the interval time of bone scan following aging, relative to the initial count, indicating that the PLT count radiosensitivity increases by aging. And the correlation between Age and PLT count after interval time of bone scan could be fitted in the flowing equation: $y = -238.3x + 34943$ where x refers to age in years and y refers to PLT count.

Fig. (4.24): shows the correlation between BMI and the PLT% before and after interval time of bone scan. It reveals that the PLT count % decreases significantly (P-value = 0.04) as the BMI increases, which could be fitted to the following equation: $y = -7817x + 53637$, where x refers to BMI and y refers to PLT %. While after the interval time of bone scan, the total count of PLT% deceases significantly (P-value = 0.02) by 12.0% following the increment of BMI, and the correlation could be fitted to the following equation: $y = -4808x + 41743$ with significant correlation at $R^2 = 0.04$ where x refers to BMI and y refers to PLT %.

Fig. (4.25): Morphological deformities involving RBCs after interval time of bone scan in nuclear medicine. It revealed that: among patients in group ‘a’ (0.0 mCi) representing the control group, RBCs appeared as normal shape and size, patients in group ‘b’ (15 mCi) in which some RBCs lose their biconcavity and increased in diameter (10 ±0.4 μm), patients in group ‘c’ (20 mCi) in which RBCs developed spikes mimicking Tribulus terrestrial (zygophyllaceae) fruit like (Kevalia and Patel, 2011) which known as anisocytosis and poikilocytosis shape deformity, and patients in group ‘d’ (25 mCi) in which RBCs appeared with intensive anisocytosis and poikilocytosis with shrinking size.

Therefore, and based on these results and facts; the acquisition and procedures of NM examinations, better carried out by using intelligent robotic system as suggested by Hosny et al, (2018) and Emre, (2019).

Chapter Six
Conclusion & Recommendation

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6.1 Conclusion:

The study ends up with the facts that: the high demand of Bone scintigraphy in Sudan was influenced by the high incidence of breast cancer which represents 64% in left breast and predominant among age group 40-50 years old. The right and left breasts cancer commonly gives metastases to lumbar vertebrae (26.7%, 22%), then dorsal vertebrae (14%, 19%), the pelvic bone (10%, 12.7%), the ribs (5%, 11.3%), the cervical vertebrae (8.7%, 10.7%), the skull (7.3%, 9.2) and the femur bone with percentage of (6.7%, 10%) respectively. And the left breast cancer showed relatively high metastatic percent to skeletal system segments (58.0%) than the left breast cancer 42.0%, with specific preference to lumbar vertebrae.

The high incidence of cancer was in Omdurman state representing 45.6%, Khartoum state (Khartoum & Bahri) represents 18.8 % and in North state which represents 14.6%. Among these states carcinoma of the breast was most predominant (52.1%) followed by prostate cancer which represents 25 %. The study revealed that: blood components have some relation with ageing, BMI and gender. For instance: WBC count increases eventually following the age group increment from 18 – 61 years old and then decreased; but usually remain within the normal range (4000 – 7000/cm^3). Also, it increased as the BMI increases from ≤ 18.49 (underweight) up to 25 – 29.9 (overweight) then decreases among obese (30 – 39.9) and sudden peaking among Morbidly obese (≥ 40 Kg) but remains in normal range. On the other hand, RBCs count increased from 18 - 50 years old then decreased following ageing but remains within the normal amount along the age of man. And also, it has been increases as the BMI increases form underweight (≤ 18.49) up to normal BMI (18.5 – 24.9) then fluctuating normally among overweight (25 – 29.9), Obese (30 – 39.9) and morbidly obese (≥ 40 Kg).

The level of hemoglobin did not influence by ageing and only increase slightly insignificant (P-value = 0.31) following BMI increment within the normal range. Lymphocytes count generally decreased continuously insignificantly (P-value = 0.3, R^2 = 0.02 & 0.04 before and after applied radioactive dose) following the aging increment. While in correlation with BMI; the lymphocytes% increases insignificantly (P-value = 0.3) following the increment of BMI and continues in same manner and fluctuating within the normal level. Then after the interval time of bone scintigraphy (3.0 - 3.5 hours) with an average radioactive dose of 15±2.9 mCi; the WBCs count decreased significantly by 3.8% at P-value = 0.00 and 0.05 relative to age and BMI respectively. The RBCs reduced but insignificantly (P value = 0.31) by an average of 3.6% relative to initial count. The RBCs% appeared less than normal among underweight patients (BMI < 18), but increases and fluctuating normally as BMI increased and got abnormal increment among morbidly obese patients (BMI ≥ 40). The reduction of RBCs% increased following the ageing through 18-39 years old and by 73-83 years old became prominent with an average reduction of 3.6%. The reduction also seen in HGB level by 3.1% and the Lymphocytes decreased insignificantly (P-value = 0.42) by 10.3% relative to normal average level. The analysis also, revealed that: the PLT count does not influenced by aging but decreased significantly (P-value = 0.04) as the BMI increases. However, after interval time of bone scan; it decreases significantly (P-value = 0.01) by 12.5% following aging, and significantly (P-value = 0.02) by 12.0% following the increment of BMI relative to the initial count. The radioactive scintigraphy dose also induced morphological deformities in RBCs such as: loss of biconcavity and increased in diameter (10 ±0.4 μm) at 15 mCi. And at 20 mCi; the RBCs developed spikes mimicking Tribulus terrestrial (zygophyllaceae) fruit like which known as anisocytosis and poikilocytosis shape. And at 25 mCi; RBCs appeared with intensive anisocytosis and poikilocytosis with shrinking size

6.2 Recommendation:

After successful achievement of thesis objectives, the ultimate points worth to be recommended could be summarized in the following points:

- Wider advanced studies implying large sample size, and advanced characterization technology as invitro and in vivo have to be contemplated.
- Characterization of induced histological effects by NM radioactive dose in other blood components and the vital organs would be as encourage-able researches.
- Studies to establish dose indexing for common nuclear imaging cases together with minimum biological effects should be carried out.
- Encouraging the invention of new technologies to be applied in diagnosis instead of NM imaging to avoid radiation exposure and the relative risks
- Simulation of induced biological effects before applying radioactive dose in NM imaging
- Also, the researcher recommends that: NM examination and any hazardous examination better done by intelligent robotic system to avoid radiation exposure and the relative non-stochastic effects
- Motivate the synthesis of drugs that prevent the seeding of cancer foci in skeletal system.

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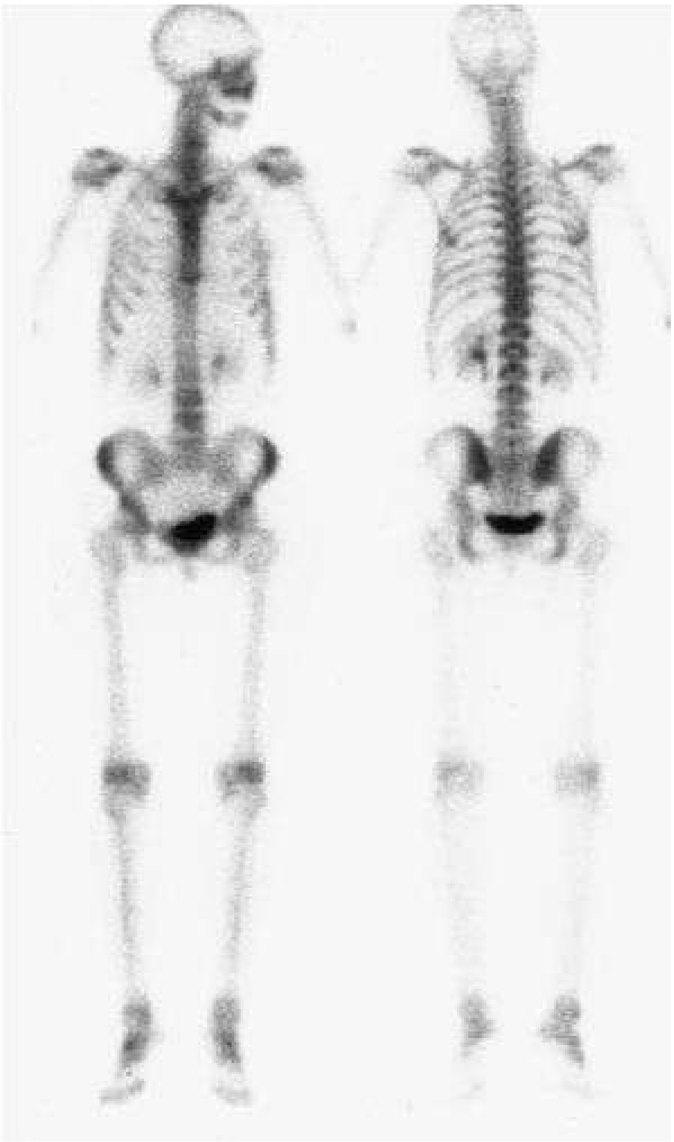
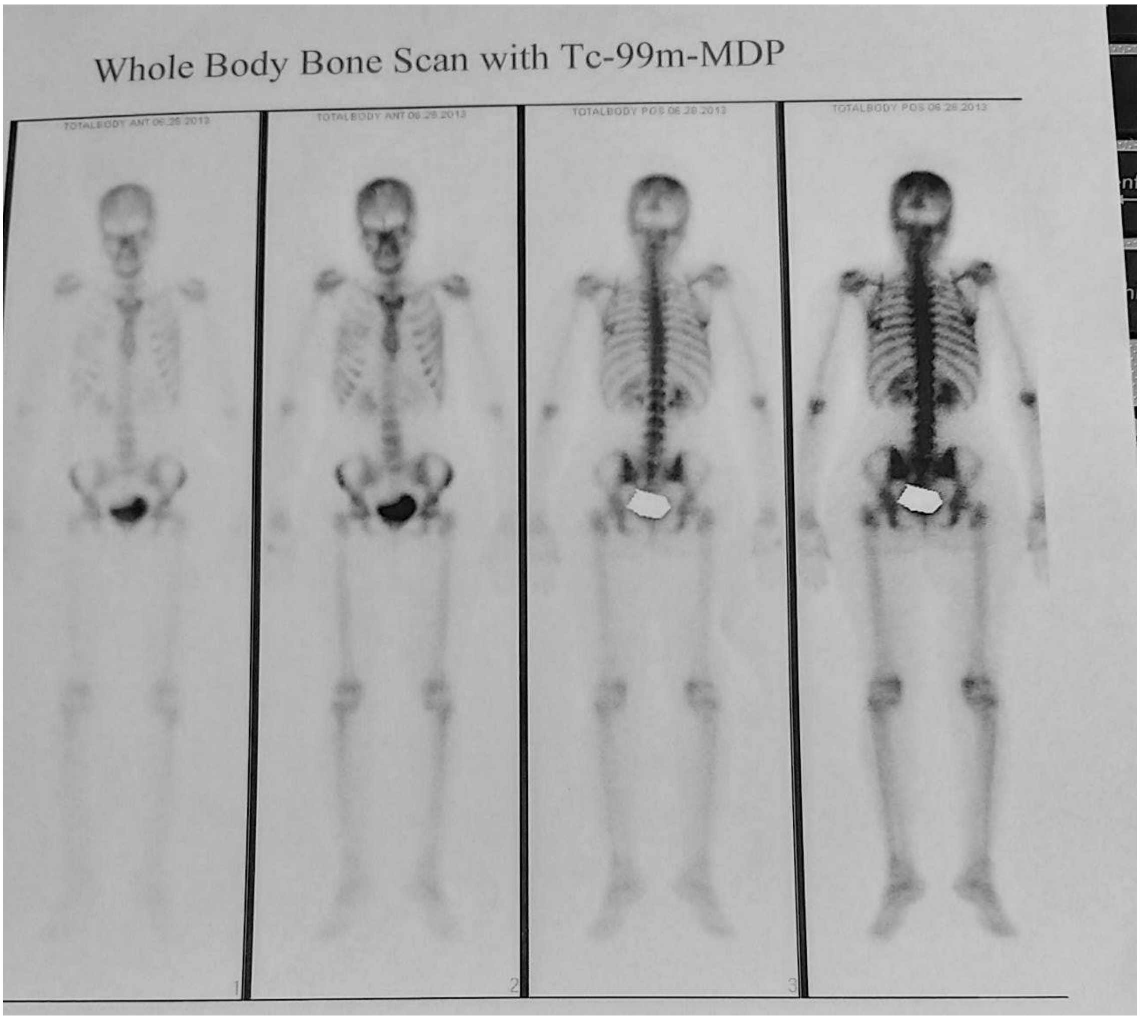
Appendices

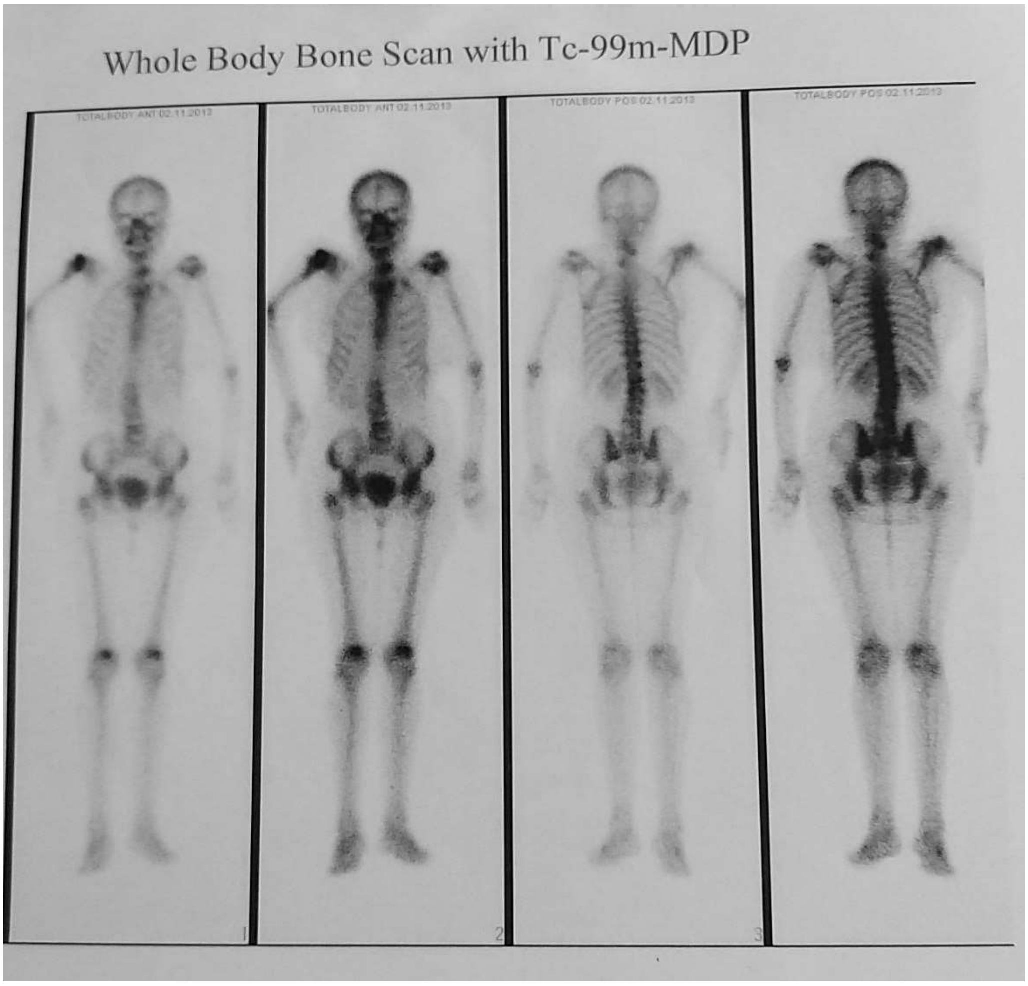


Adult ^{99m}Tc-MDP bone scan, anterior and posterior views (Ca. breast case with normal bone uptake)

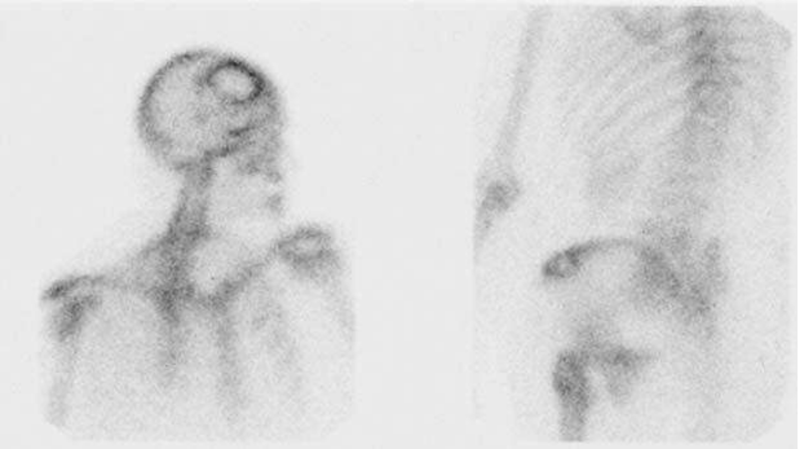


Adult ^{99m}Tc-MDP bone scan, anterior and posterior views (Ca. breast case with normal bone uptake)

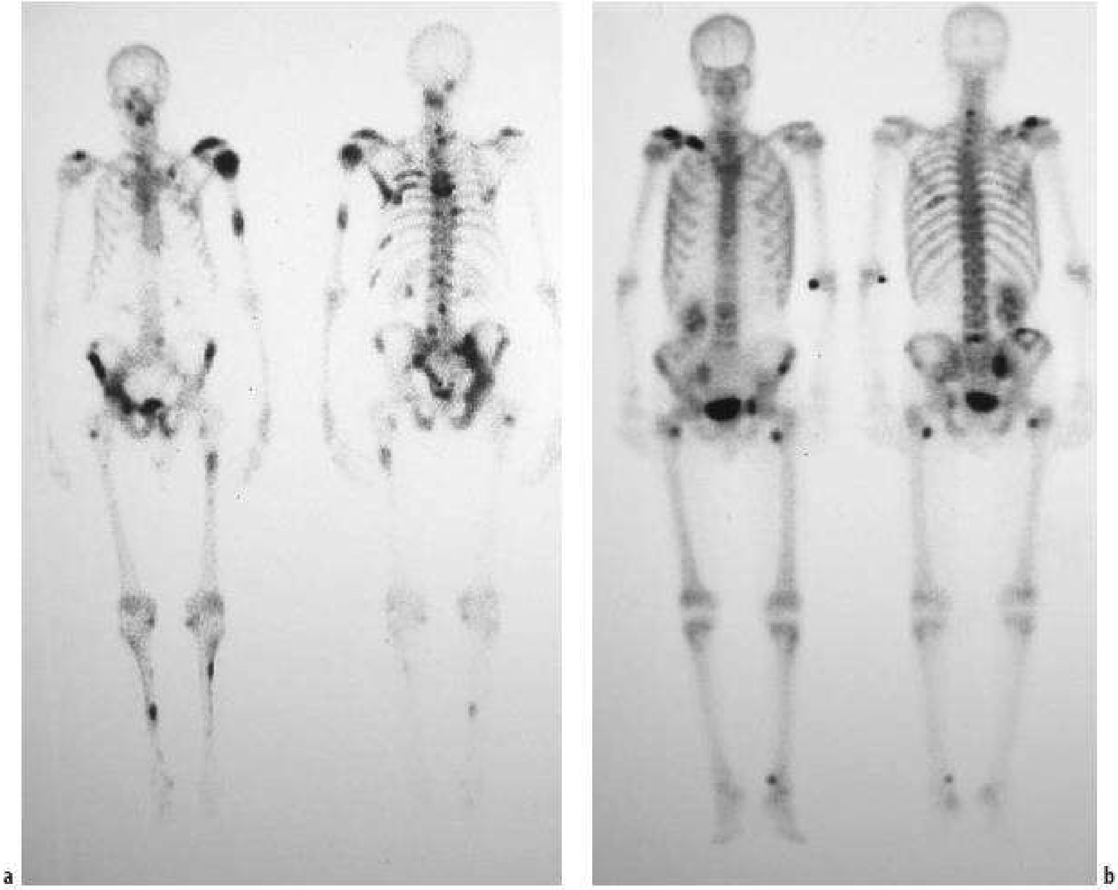
Adult ^{99m}Tc-MDP bone scan, anterior and posterior views (Ca. breast case with prominent bone uptake at dorsal, lumber vertebrae and head of the femur bone)



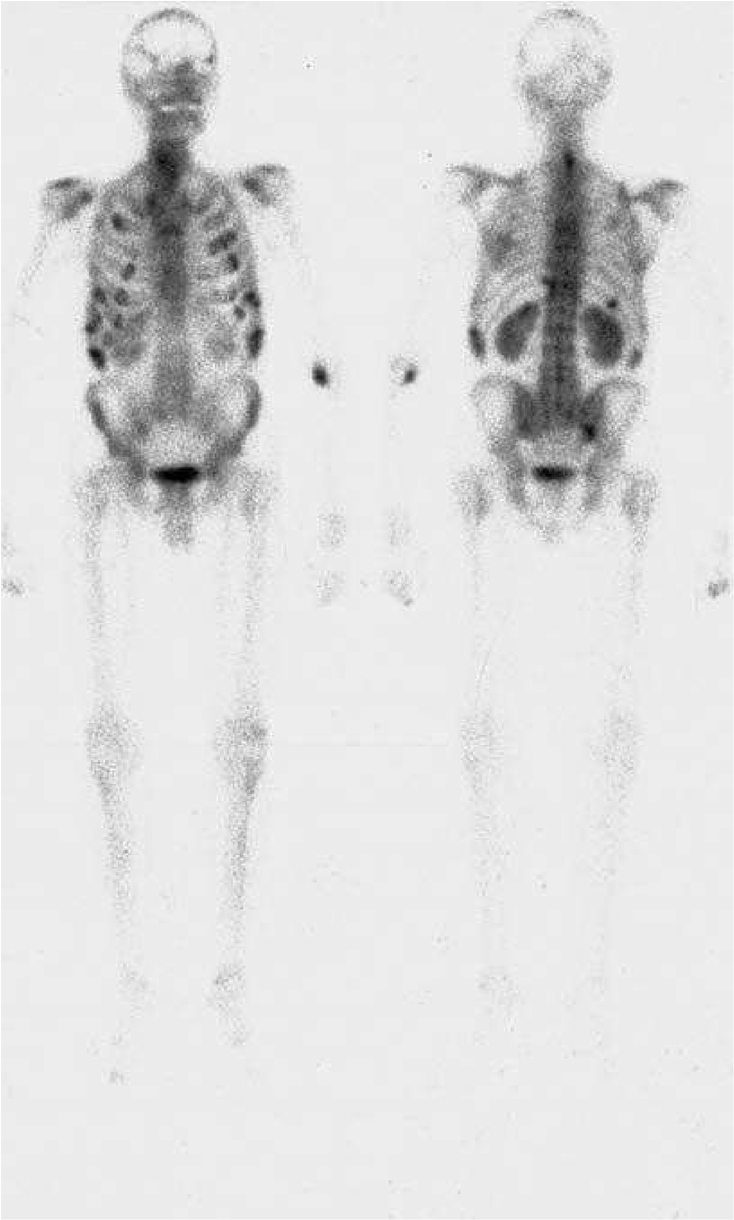
Adult ^{99m}Tc-MDP bone scan, anterior and posterior views (Ca. breast case with prominent bone uptake at dorsal, lumber vertebrae, pelvic bone and head of the femur humors bone)



Oblique spot views of the skull and pelvis with osteolytic metastases from primary renal carcinoma



Widespread skeletal metastases from primary prostate carcinoma. b Metastases from renal carcinoma, absent left kidney (nephrectomy).



Myeloma with multiple rib and vertebral pathological fractures

Posterior view of multiple vertebral fractures due to osteoporosis (Cancer)