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A Quantitative Prospective Study for Whole Body- Diffusion MRI and PET-CT in Detection of Primary and Metastatic Malignant Lesions

Ahmed Mohammed Ahmed Abu Ali

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A Quantitative Prospective Study for Whole Body- Diffusion MRI and PET-CT in Detection of Primary and Metastatic Malignant Lesions

Prepared by:

Ahmed Mohammed Ahmed Abu Ali

B.Sc. Medical Imaging Science, Arab American University, Palestine.

Supervisor: Dr. Mohammed Hjouj.
Co-Supervisor: Dr Mosab Maree

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Prepared by: Ahmed Mohammed Ahmed Abu Ali

Registration No: 21910032

Supervisor: Dr. Mohammad Hjouj

Co- Supervisor: Dr. Mosab Maree

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The names and signatures of the examining committee members are:

1- Head of Committee: Dr. Mohammad Hjouj Signature:

2- Internal Examiner: Dr. Hussein AL-Masri Signature: Hussein ALMasri

3- External Examiner: Dr. Muath Daraghmeh Signature:

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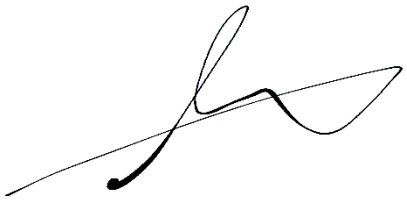
Dedication

I dedicate this dissertation to my parents, my little family my wife and children, to my sister and brothers. To the people of occupied Palestine.

Ahmed M.A. Abu Ali



Declaration

I certify that this thesis submitted for the degree of master, is the result of my own research, except where otherwise acknowledged, and that thesis has not been submitted for a higher degree to any other university or institution.

Signed: 

Ahmed Mohammed Ahmed Abu Ali

Date: 22.05.2022

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Praise be to “Allah” in the first and in the last.

I would like then to thank my thesis advisor Dr. Mohammad Hjouj, his office was always open whenever I ran into a trouble spot or had a question about my research or writing. He consistently allowed this paper to be my own work, but steered me in the right the direction whenever he thought I needed it.

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Abstract

The idea of having an integrated nuclear medicine unit consisting of a scanner with a compatible source of isotopes like cyclotron to work efficiently in Palestine is almost impossible due to many issues beginning from political issues and ending with financial issues. Moreover, the nature of materials that have been used in nuclear medicine is radioactive which could increase the ability of causing other malignancies. PET scan can sometimes show areas of high activity, which may be mistaken for cancers like inflammatory conditions. In order to avoid all these pitfalls that might interfere with the diagnostic process, it is necessary to start looking for an alternative to support oncologists and their patients to use another safe, valid, available in abundance and lower cost technology called Whole Body Diffusion MRI. It can project areas of restricted water diffusion for pathologies and for tumors through the whole body in places where cellular activity is increased with decreasing of relevant water diffusion in the same area.

A prospective data collection for 33-oncology patient, who advised previously to do PET scan had been agreed to participate in our study for WB-DWI MRI scanning in a period not exceeding ten days between PET and MRI. 60% are male participants (n=20) and 40% female (n=13), ages of participants are ranging between 18-74 years old with an age average of 48 years old, body weight average is 83kg with a maximum and minimum weight are125kg and 56kg respectively. Their primary diseases varied between non-Hodgkin lymphoma (NHL), Hodgkin lymphoma, endometrial, prostate, pancreatic, and gastric, thyroid cancer, pathological fracture and skin lesions.

Result in PET shows 181 hypermetabolic lesion distributed in the four zones (head-neck, chest, abdomen-pelvis and musculoskeletal). WB-DWI MRI shows most of the same lesions restricted in diffusion with extra small subcentimetre lesions totally 251 lesions in count. Comparison between standard uptake volume (SUV) and apparent diffusion coefficient ADC) which shows most high SUV (SUV>2.5) have ADC < 1.1 $x10^{-3}$ mm^2/s.

Statistical quantitative analysis shows a significant positive correlation between number of detected lesions in both modalities, in the same zone for each patient, at p

value < 0.05 (p=0.00004) and R-value = 0.178, 0.434, 0.606 and 0.840 for head-neck, chest, abdomen-pelvis and musculoskeletal respectively. A comparative correlation between ADC and SUV shows a significant negative correlation between SUV and ADC at p value < 0.05 and R-value= -0.3073.

WB-DWI MRI can be used in some lymphoma cases for follow up as an alternative for PET scan in case no access is available for PET imaging, DWI can be used also for localized tumors follow up to monitor the response for treatment after chemotherapy or radiotherapy either post-surgical resection. Oncology and radiology departments recommended activating diffusion sequence in each MRI study for oncology patients in order to assure the idea of diffusion restriction for follow up studies.

Table of Contents

List of Tables

List of Figures

List of Appendices

Definitions

- MRI: magnetic resonance imaging, a form of medical imaging procedures.
- PET/CT: positron emission tomography/ computed tomography, a form of medical imaging procedures.
- DWI: diffusion-weighted image, sequence in MRI that depends on diffusion of water molecules to create a signal for restricted molecules.
- b-value: gradient amplitude and duration used in DWI sequence.
- ADC**:** apparent diffusion coefficient (DWI direction).
- ^{18}FDG: Fluoro-deoxy-glucose is an isotope utilized to screen glucose collection in the cells with increased metabolism.

Abbreviations

- MRI: magnetic resonance imaging.
- PET/CT: positron emission tomography/ computed tomography.
- DWI: diffusion-weighted image.
- ADC: apparent diffusion coefficient.
- ^{18}FDG: Fluoro-deoxy-glucose.
- WB: whole body.
- DWIBS: diffusion-weighted image background suppression.
- 3D: three-dimensional.
- MIP: maximum intensity projection.
- SUV: standard uptake volume.

Chapter 1: Introduction

This chapter outlines the background section and context section 1.1, 1.2 of the research, and its purposes section 1.3, Section1.4 describes the significance and scope of this research and provides definitions of terms used. Finally, section 1.5 includes an outline of .the remaining chapters of the thesis

1.1 Background

Medical imaging technology has a major role in the field of oncology in the diagnostic process. Early detection, staging and planning for the fractions of radiotherapy and chemotherapy sessions cannot be done without medical imaging (Koh & Thoeny, 2010). Regarding neoplasms and malignancies, it is important to realize which imaging modality is much more suitable than other modalities to ensure a proper diagnosis for the oncology patients (Xu et al., 2014).

However, medical imaging in general including X-ray, mammography and computed tomography (CT) specially has a major role in malignancy staging. MRI either is playing an important role in the process of staging for oncologists with multi appearance criteria in all sequences for each lesion nature with respect to high contrast and spatial resolutions. CT is more available in the most medical imaging centres, by using contrast enhanced CT, the value of output results is improved due activity of malignant lesions in cases of parenchymal multi-phase enhancement especially in abdominal lesions in the area of liver or kidneys, according to the blood vascularity of the lesion (El-Galaly et al., 2018).

The main conflict for strong-disease-plan management is early detection of cancers before any metastatic activity begun, to achieve that, the choice of appropriate screening tools must be made by the treating physician to detect and treat before losing the rudder to make control over the disease.

Later on, scientists developed many medical imaging technologies that exploits the physiological and functional properties for the organs inside the human body, by using hybrid-imaging techniques to project images for the organs or tissues with another registered image of the functional activity of the same organ in identical to be the same at the voxel level. This method used in the integration of hybrid PET-CT for oncological activity detection over the whole body for all tissue types (Cook & Goh, 2018).

Positron Emission Tomography (PET) is one of these leading technologies that had been considered as a superior modality in evaluating the nature of body lesions as benign or malignant (Akay et al., 2013). In addition, PET CT has advanced marking properties in the process of locating the primary and metastatic tumours by evaluating organ and tissue functions, by identifying changes at the cellular level, PET may detect the early onset of disease before most of the other imaging tests can (Baranska et al., 2019).

However, the idea of having an integrated nuclear medicine unit consisting of a scanner with a compatible source of isotopes like cyclotron to work efficiently in Palestine is almost impossible, due to many issues, beginning from political issues and ending with financial issues. In general, the nature of materials that have been used in nuclear medicine is radioactive, that means it is a source for ionizing radiation that could harm the biological tissue, which could increase the ability of causing other malignancies (Fonti et al., 2019).

PET scan can sometimes show areas of high activity, which may be mistaken for cancers like inflammatory conditions (Tomizawa et al., 2017). PET scans are a very costing form of imaging, and are not readily available such as CT and MRI (Usuda et al., 2021). In order to be diagnostically effective and for all these pitfalls of PET scan, it is necessary to start looking for an alternatives to avoid expose the patients to all of previous mentioned situations.

One of the most available, safe, and promising technologies is the magnetic resonance imaging modality (MRI) which is reliable, updated and considered as a wide field of research in medicine because of its role in the improvement of diagnosis in general and in oncology in special; each MRI exam consists from many sequences for interpretation of whole tissue types.

One of these power sequences called diffusion (DWI) that modified in the last years to enable the option of scanning whole body within a few minutes (Hamstra et al., 2007). This sequence has the power to detect the lesions regardless it is a primary or a metastatic lesion (Messina et al., 2020), this sequence could be used as an alternative for PET scan if the strength of DWI approved in opposite to the previously mentioned challenges of PET scan.

To the best of our knowledge, diffusion based MRI sequence is available in the most MRI scanners in Palestine. Conversely, nuclear medicine imaging technology replacement by DWI imaging technique in a different modality is an apparently unconvincing idea for the concerned medical staff especially since there is no previous studies covering this subject in our area.

Regarding the published studies concerned in discussing the above-mentioned topic, there is an obvious limitation in the number of participants, used b-values and technical sequence building issues. A larger number of participants will be used to increase the accuracy of our results; also, DWI sequence with multiple b-value will be built to ensure our image quality results and using different scanning geometric parameters to improve image findings.

The study will focus on a special different set of parameters to build a new DWI sequence with multiple b-values based on recently published papers while the b-values that have been used in the recent previous publications were set by default by the manufacturer of the scanner.

Finally, our study will be comprehensive to the population of our area. In more details, the nature of samples will be randomly selected through oncology clinics at An Najah National University Hospital, patients who will be asked to do a PET scan in order to evaluate their oncology disease by their oncologists, will be asked to have a Whole Body Diffusion Weighted Image (WB DWI).
The results will be analysed statistically and compared with PET scan findings to make a conclusion about WB DWI efficiency.

1.2 Context

The fields of concern in this study are the exact track of the most of oncology patients during the process of diagnosing their disease, beginning from oncology clinics, crossing towards different medical imaging sections, and finally the sessions of suitable care of therapy. It is not the end of the journey; this cycle will be repeated until the aimed care is being delivered with more sessions of following up the regression or progression of the disease.

Oncology patients at this status need any contribution to reduce the difficulties that face them during fighting their disease. Patients targeted in this study are very critical on many levels; they have special situations after taking into account their psychological and physical suffering.

1.3 Purposes

In this study, the effectiveness of WB DWI sequence will be evaluated, in detection and characterisation of different whole body malignant lesions, by comparing the appearance and absence of lesions which had been already scanned in PET- CT using ^{18}FDG isotope to the finding WB-DWI MRI. By modifying a DWI MRI sequence for whole body, including a dual b-value to be able for getting an Apparent Diffusion Coefficient (ADC) mapping.

All that to differentiate and characterise the lesions each one by their signal appearance on different b-values and ADC signal intensities.

The main inspiring causes that lead us to think in using DWI-sequence as an alternative to PET-CT after reviewing relevant published papers are:

1. The nature of materials that used in nuclear medicine is radioactive, that means, it is a source for ionizing radiation that could harm the biological tissue, which could increase the ability of causing other malignancies.

2. PET scans can sometimes show areas of high activity, which may be mistaken for -cancers like- inflammatory conditions.
3. The idea of having an integrated nuclear medicine unit consisting of a scanner with a compatible source of isotopes like cyclotron to work efficiently in Palestine is almost difficult due to many issues beginning from politics, and ending with financial issues.
4. PET scan is a very costly form of imaging, and are not readily available such as CT and MRI.

5. MRI scanners are widely available in Palestine, we are talking about one MRI scanner for around each 400.000 people, on other hand, Palestine has a population of around 5.500.000 people, has only three limited PET-CT scanner using only ^{18}F-FDG isotope which is a disastrous problem in the field of oncology. On other hand, the recommended population for each PET scanner is around one million people as reported (Al-Bulushi et al., 2013).

6. The process of applying for PET CT scan has many obstacles in Palestine starting from getting the financial coverage from the Ministry of Health or insurance company, pre-booking for the imaging session and finally getting a reported result of the exam in a time period not less than 20 days for the total process for the most oncology patients. Actually, this is a very serious problem, which may lead to an impact on the psychological status of the patient, which in turn would negatively affect the diagnosis and treatment process.
7. The scan time during examination for the whole body in PET-CT is around two hours including isotope pharmaceutical uptake preparation, which is a long time compared to whole body DWI-MRI that needs only 20 minutes without need for any previous preparations.

After finishing this study, it will be possible to answer the following questions:

1. Is the WB DWI scan able to detect all kinds of malignant tumours that had been reported in PET scan images?
2. Is there any relation between high SUV for cancer tissue in PET and water molecule diffusion since there is high cellular division rate?

1.4 Significance and Scope

It is a necessary concept in the diagnostic field that the first priority is related to the patient's interest, hence, the design of any diagnostic plan must conform to the patient's interest, safety, comfort, and medical efficacy. Our study will be comprehensive to the population of our area.

In more details, Samples will be representative of the most categories of patients who will be asked to have a PET scan in order to evaluate their diseases in Palestine.

Patients will be requested to have a whole body diffusion weighted image magnetic resonance scan; the results will be compared to make a conclusion about WB-DWI efficiency in detection of body malignant lesions.

1.5 Thesis Outline

By viewing the reminder of this thesis, you will find the following chapters sequentially in order, chapter (2): literature review with subtopics, chapter (3): methodology of the study and the design of our research, chapter4: the result of the research, chapter (5): the discussion of the results and chapter (6) will be our conclusion about the findings of our study.

Chapter 2: Literature Review

This chapter will summarize an overview about MRI and PET scan modalities in the field of oncology including many technical specifications for each modality.

Many literatures have discussed the efficacy of PET in detection of tumours, primary or metastatic regardless of their origins, but here, their opinions about the fact of the MRI-DWI sensitivity in detection of these lesions will be reviewed.

To be more precise, three major topics will be listed, topic1 will mention the PET scan superiority in the field of oncology, topic 2 will describe the main MRI sequences that sensitive to lesions in oncology for follow up imaging, and topic 3 and 4 will deeply handle the sequence of DWI. By dealing with many important subtopics including a historical background about DWI, sequence of events for DWI, image acquisition and image contrast, b-values and ADC, lesions appearance on DWI, the idea of whole body scan and many technical issues regarding DWI including normal physiological signal, micro-perfusion effect, DWI conditional artefacts. Finally, at the end of this topic, the exception criteria for DWI restriction will be reviewed with touching some pitfalls of DWI in the field of oncology.

2.1 PET scan In Oncology

Most of the articles, that discussed the possibility of using WB-DWI as an alternative tool for diagnosing the progression of oncological diseases, mentioned the PET modality as it is a perfect modality in detection malignant lesions.

In fact, PET is the superior modality for it, but it is important to disagree with the point of the idealism of PET, due to its faults in the clinical, economical and technical levels.

PET/CT was used as the gold standard for lymphoma staging for correlation study with MRI(Stéphane et al., 2013). In 2019, researchers described the efficiency of PET in lymphoma and said: This test was previously recommended as a gold standard approach (EuroNet-PHL-C1/Interimphase/LP1), with sensitivity and specificity for nodal disease detection of 87.5 percent and 85.6 percent, respectively (Baranska et al., 2019). The patient may be exposed to ionizing radiation from ^{18}F-FDG, which is a potential drawback of PET/CT (Tomizawa et al., 2017). PET and PET/CT have long been regarded as the most reliable and well-established imaging modalities for cancer diagnosis and follow-up. The main disadvantages include the large doses of ionizing radiation, the cyclotron required, the physiologic changes of ^{18}FDG buildup, and the diagnostic difficulties induced by respiratory artefacts(Akay et al., 2013).

In 2011. a study performed by Chieh Lin and his colleagues, they assumed the reference standard is ^{18}F-fluoro-deoxyglucose PET/CT and they had neglected the disadvantages of PET at the physiological levels (Lin et al., 2011).

It is important for all in the field to know and cover the main pitfalls, especially if it is affecting the patient's interest. Moreover, the financial issues are so important to assure of appropriate diagnostic process. It has been reported in an approximate comprehensive comparison study for the cost of each FDG-PET/CT, MR examination including WB-DWI and CT scan, they found the costs are 756$, 116$ and 88$ respectively. Furthermore, the clinical criteria for PET is not as to be (Usuda et al., 2021).

PET has been investigated for the most prominent false positive results, it has been found that malignant tumours with low metabolic activity or less than 1.0 cm in diameter often give false negative results; false positives for benign diseases have been reported with active inflammation or infections. Therefore, ^{18}FDG is not a cancer-specific (Chang et al., 2006). On other hand, it was reported that the smallest detectible volume of tumour was 3.95 mm^3 in diameter on PET (Adler et al., 2017).

2.2 MRI in Oncology

Every imaging modality has its own technical characteristics with different viewing and differentiation methods for tissue types and pathology according to which modality it supposed to be used.

In general, MRI also has the same concept, but in another mechanism, if just refreshed our memory to get back to the basics of MRI, more than one sequence of imaging will be found, that separated in acquisition, parameters, timing, and number of frequencies or shots.

Some of these sequences will show a good signal from fatty tissues, others will highlight the collection of fluids, and some others will exploit some physical phenomena at intercellular level (Abildgaard, 2015).

The interesting sequences used in this study are STIR and DWI sequences, due to their sensitivity for lesions in the human body tissue (Eissawy et al., 2021). MRI has typical resolutions of around $1.5\times1.5\times4$ mm^3 and less in some sequences, and has a resolution of 50-500µm (Barsanti, 2015).

2.3 Diffusion Weighted Image and STIR MRI Based Scanning

In routine MRI scanning for selective organs or systems, STIR and DWI sequences are presented always in any exam especially for those which requested by oncology physicians. Brain, neck, gastrointestinal, musculoskeletal and general neuro imaging exams are depending so much on these tow sequences (GRoth MD, 2016).

If it is selective for a specific organic imaging, so these sequences can be used as station packages for whole body scanning with some technical modifications to project lesions free from background normal tissues specifically in DWI.

DWI can differentiate benign from malignant lesions in prostate, breast, liver lung and thorax (Usuda et al., 2021). DWI can help likewise in separating non-cancer tissue from neighbourhood cancer backslide after therapy, introducing as central hyperintense regions on high-b-value DWI with comparing low ADC (Messina et al., 2020). WB-DWI is a harmless method that may effectively distinguish the spreading of the cancer lesions in oncology patients when used as an alternative to PET/CT (Akay et al., 2013).

The most encouraging successions are those that utilization some type of fat saturation, STIR imaging is generally used to recognize bone marrow lesions since it is a strong sequence for identifying cancer, oedema, and disease in bone marrow (Tokuda et al., 2004). STIR imaging could decrease the quantity of false positive results (Sun, 2020). STIR gives better worldwide fat suppression over a long field of view, the burdens of STIR is diminished SNR in light of fractional loss of proton signal during the inversion time (Kwee et al., 2008). Moreover, by reviewing the competent articles it has been found that the most suitable sequence for anatomical correlation is STIR.

Many papers that interested in this topic has reviewed the ability of DWI and STIR to screen and detect body lesions specially the metastatic ones, some of them covered the depth of the topic, many others were superficial without any hint for the technical issues importance.

2.4 DWI Technical and Clinical Aspects

By a thorough review to the published DWI results in oncology, it has been found that there is no definite final acredited adjustment of the sequence parameters to get the optimal results of lesions projection, parameters including: b-value, ADC intensity, b-value intensity and imaging geometry issues, in this topic, theses subtitles will be discussed in details.

2.4.1 DWI Acquisition:

In the beginning, the basics of diffusion sequence, sequence of events, the main concept and how DWI sequence is being sensitive for abnormal tissue will be slightly overviewed.

DWI is a sort of functional imaging innovation created in recent decades; it is a measurement method that has been used to define the quality and quantity of water molecules diffusion in-vivo tissues, the random motion of water atoms, especially when portability is limited to explicit directions (McRobbie et al., 2017). Therefore, it is able to attribute the variations of a specific tissue before any obvious variation for the conventional imaging techniques, and later on to measure the apparent diffusion coefficient in order to be sure if there is lesion DWI restriction or not.

DWI sequence consists of a 90º–180º degree spin- echoes of Radio frequency pulses with large and equal gradients placed on either side of the 180º-degree pulse (Zhao et al., 2021). Figure (2.1) is demonstrating the sequence of events for DWI sequence.

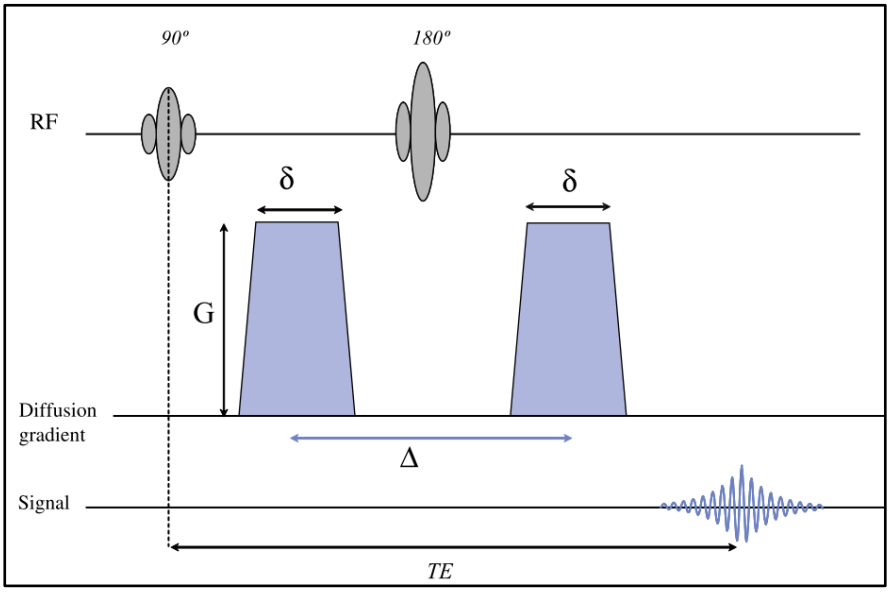

Figure 2.1: Basic sequence of events for DWI. For imaging. **δ** denotes the pulse width and **Δ** the center-to-center spacing. **G** is the magnitude of the diffusion-weighting gradient (McRobbie et al., 2017).

Diffusion sequence depends mainly on the physical phenomena that exists in the living biological tissues which known as Brownian motion that depends on the random motion of water molecules (Tang & Zhou, 2019). Figure (2.2) is illustrating the principle of

Brownian motion in the tissue according to presence of cells by increasing their quantities, water molecules, extracellular and intracellular space.

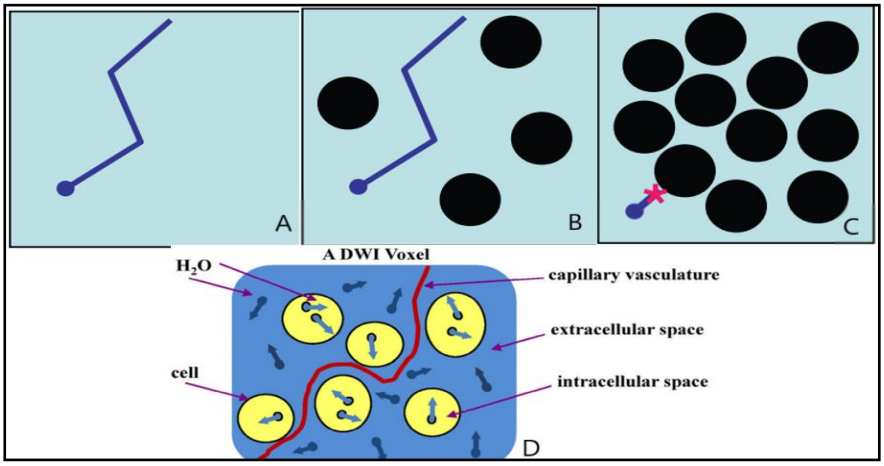

Figure 2.2: (A) Random Brownian motion, (B) less normality of diffusion with high ADC, (C) restricted diffusion with low ADC, (D) an image voxel of diffusion (Tang & Zhou, 2019).

2.4.2 b-Value:

Regarding this issue, firstly it is important to have a clear idea about b-value of DWI, it is the amount of DWI weighting factor, the strength of gradient used and the duration of applying the gradient, b-value unit is s/mm^2.

Using a larger b-value a worse image quality will be. "When the b-value is more than 1000 s/mm^2, the SNR and spatial resolutions are lower, the magnetic sensitive artefacts are more serious, and the image quality is significantly reduced" (Zhao et al., 2021).

Usuda and his colleagues in there experimental study for WB-DWI had used a b-value: 0 and 1000 s mm $^{-2}$ (Usuda et al., 2021). Zhao also used b-values: 300, 500 and 800 s mm $^{-2}$ (Zhao et al., 2021). Eissawy on other hand used 50 and 900 s mm $^{-2}$ (Eissawy et al., 2021). Many others used a range of b-values without mentioning the reason of selecting those values to make their studies. In fact, the only needed b-value is two values, in order to enable

the software from calculating the ADC to measure the quantity of restriction (Abildgaard, 2015). Therefore, there is no need for three b-values.

> " For mono-exponential assessments of ADC values, the use of two b-values (>100 and between 500 and 1000 μs μm−2) has been recommended to avoid perfusion effects and to obtain accu-
> For monoexponential assessments of ADC values, the use of two b-values (>100 and between 500 and 1000 μs μm−2) has been recommended to avoid perfusion effects and to obtain accurate ADC values " (Karki et al., 2015).

Therefore, each method in the previous studies that used a b-values the first less than 100 s/mm^2 and the second less than 500 or more than 1000 s/mm^2 are at risk in their results of micro-perfusion effect.

2.4.3 Apparent Diffusion Coefficient (ADC):

ADC maps are registered in accordance with framework programming involving mono remarkable fitting in which each voxel mirrors the tissue diffusivity in unit: mm^2/s, ADC value is cannot be measured in DWIBS (Eissawy et al., 2021).

In fact, DWIBS is MRI DWI-based sequence that can be modified to be able to generate ADC quantitative mapping, actually, this what had been done in this study.

"DWIBS could not characterize a suspected hip joint bony lesion either inflammatory or metastatic deposit. The case was finally interpreted as inflammatory lesion based on the ADC value applied on WB DWI" (Eissawy et al., 2021), for more clarification, they scanned each patient two separated DWI-based scan, one on DWIBS to get a MIP 3D image like PET scan image, and other scan for WB-DWI with multiple b-value to get ADC mapping.

This method really needs more time and costs without any additional benefits. On other hand, they could only modify the DWIBS to generate more b-values, for example b=100 and b=1000, then ADC could be ready to reconstructed and quantified from the raw data images. ADC signal of malignant tumour in various b-values was fundamentally lower contrasted with benign tumour (Zhao et al., 2021). ADC can be used to exclude T2 shine

through effect or to differentiate benign lesions from malignant by showing if there is restriction or not (Tomizawa et al., 2017).

Proof has aggregated from various clinical experiments on that ADC is unusual in growths; that raised ADC, which mirrors a raised non-cell portion. That hyperintense ADC following treatment can demonstrate that cancer cells have been killed (Sinkus et al., 2012). It has been reported that ADC value is less in lymphoma nodes and higher in health lymph nodes (Kirchner et al., 2017). Benign lymphoma will not show any DWI restriction on the contrary of malignant lymphoma, which will show different degrees of restriction on ADC Mapping, necrotic malignant lymph node will show a marginal restricted diffusion due to high cell activity around the necrosis with no restriction. Moreover, Central portion of abscess will show a restricted DWI due to high activity of inflammatory cells (Bhatt et al., 2017).

According to the published data regarding ADC value, it had been mentioned that healthy lymph node would show an ADC value that considered being large (ADC > $1.1x10^{-3}$ mm^2/s), lymphomatous nodes will appear as low ADC value (ADC < $1.1x10^{-3}$ mm^2/s) (Baranska et al., 2019).

We conclude from the previous literature review about ADC appearance criteria that malignant tissue has a drop in the signal on ADC image in different degrees, according to the tumor type and nature of cellularity.

2.4.4 Image Contrast and Lesions Appearance:

Malignant growths have overall higher cellularity and accordingly less diffusion with ordinary tissue of comparable density. In addition, cancer cells begin from tissue-explicit cells and hence show trademark properties that differ between tissues (Karki et al., 2015). Therefore, any lesion that gives hyperintense or isointense signal on high b-value DWI, hyper-spot lesion on reconstructed DWIBS with signal drop on ADC mapping image will be highly considered a malignancy (Sun, 2020).

2.4.5 Normal Physiological Signal:

As it is known. PET has many false positive findings due to improper patient preparation as a technical issue. Alternatively, due to hypermetabolic areas in a non-malignant tissue as happening in areas with active fibrosis or areas with a tissue parts that could be infected. Either due to normal physiological signals from brain, spleen or kidneys by execration of urine with diluted injected isotope (Chang et al., 2006).

Almost the same tangles are existing in WB-DWI especially with DWIBS reconstruction for whole body imaging. It is necessary for all who concerned in WB-DWI to know the limits of this imaging technology before starting to use it, limits that inherently existed which making improper signal from normal locations to be detected, or misdetection of signal from abnormal tissues. Hyperintense signal in DWI as a normal physiological signal could be seen in the following organs: brain, spinal cord, plexus nerves, salivary glands, tonsils, adrenal glands, spleen, gallbladder, kidneys and ureters, bowels, bone marrow, testes and prostate (Boerhout et al., 2013).

2.4.6 Microperfusion Effect:

> "Free water estimates from diffusion MRI are assumed to account for freely diffusing water molecules in the extracellular space, but may be biased by other pools of molecules in rapid random motion, such as the intravoxel incoherent motion (IVIM) of blood, where water molecules perfuse in the randomly oriented capillary network" (Pevzner, 2017).

> "In living tissues there are physiologic motions unrelated to diffusion that can mimic diffusion processes and confound in vivo measurements. In particular, the use of low b-values is sensitive to the microcapillary perfusion effects within the image voxel. Hence, accurate estimation of the apparent diffusion coefficient (ADC) of tissues in the body is dependent on the proper choice of b-values" (Koh & Thoeny, 2010).

It has been has recommended a specific set of b-values which are at least two values to manage us from getting an accurate ADC mapping, the first value should be >100 s/mm² and the second value: between (500-1000) s/mm² (Karki et al., 2015).

"Perfusion contamination is increased by inclusion of b-values too low and noise contamination is increased by use of b-values too high" (Koh & Thoeny, 2010). "In practice, what we measure in PGSE is related to the actual diffusion coefficient but may contain contributions from other movement sources (Karki et al., 2015).

Microcirculation in pseudo-random capillary systems is one such source of incoherent-intravoxel motion. Bulk flow and motion will also seriously degrade the measurements and lead to image artefacts. Additionally the imaging gradients can contribute to the diffusion weighting, although with large diffusion gradients this effect is normally minimal. Because of this, it has been usually referred to the apparent diffusion coefficient, which can be calculated from ADC image ln for cases where an equal TE applies to both weighted and unweighted images.

Alternatively a range of *b*-values can be applied and a 'least-squares' fit can be performed. This should give a more accurate value of ADC" (McRobbie et al., 2017).

The recommendations for a specific set of b-values, which are at least two values to manage us from getting an accurate ADC mapping, the first value should be >100 s/mm² and the second value: between 500-1000 s/mm² (Karki et al., 2015).

2.4.7 Rules and Exceptions for DWI Restrictions:

Depending on the context of the previous paragraphs, it is necessary to summarize the following about diffusion restriction:

1. Benign lesions regardless its location with no matter if it show a high signal intensity or not, will not make any diffusion restriction with some consideration to other types of benign lesions that make restriction which will be mentioned later.

2. Malignant lesions anyway and regardless its primary or metastatic, will have a hyperintensity signal on high b-value DWI.

3. Malignancy in general, and due to high cellular activity within the same space of tissue will cause the water molecules in the extracellular space to be restricted in its random motion. Therefore, it will show a drop in ADC signal, which means, it makes a DWI restriction.

As respect to our knowledge, and because every base has exceptions, it has been found that DWI-MRI has a known false positive findings and false negative also, it has been reported-in 2017 in a pictorial review-that each benign lesion that has a high cellular activity for example Warthin's tumor, will give a false positive findings. Abscess either has a high inflammatory cells activity, which will be the same appearance. Malignancies with low cellular activity will have false negative findings (Bhatt et al., 2017).

2.5 Summary and Implications

After a brief review for the concerned articles in this topic, it has been found that studies had been done with respect to our knowledge in the area of Europe, East of Asia and some other countries that so far from our region in the Middle East. Therefore, the lack and necessary indigence of this kind of experimental studies were a great motivator for us to start in this study.

Palestine has a major problem as mentioned previously in the idea of having a complete unit for molecular and nuclear imaging due to political issues. Therefore, it is important for not losing sight of the fact that, the issue affects first oncology patients in occupied Palestine, due to the crowding of patients on a single limited device in the city of Nablus. We are talking about three limited PET-CT scanners that serve around sex million people.

West Bank and Gaza Strip needs at least another four PET/CT modalities with their accessory units from cyclotrons and isotopes. On other hand, MRI devices are available in abundance and distributed constantly in the whole Cities. All what needed to do is to approve the benefit of this technology to use it as an alternative until the PET related crisis is resolved, then it will be easy to build a standard imaging protocol as an alternative after proper coordination with the Oncology and Radiology Committees under supervision of Palestinian Ministry of Health.

Moreover, most of those papers had recommended expanding the range of the study and increasing the number of samples to decrease the factors of errors in the results. They did not consider the potential false positive results for PET in oncology, also STIR sequence can be used not only for anatomical correlation for WB-DWI, it is an informative sequence in cases of multiple myeloma in bone marrow where DWI sequence has failed due to interferences with artifacts specially in long bone.

DWI sequence, papers depended dramatically on DWIBS sequences that have been modified already by the manufacturer, there is papers that deny the ability of DWIBS to generate ADC mapping to predict the presence of restriction, and they had to scan DWI twice, one for DWIBS image and other with multi b-values and ADC.

On other hand, it is possible to build a single sequence with multi b-values, ADC mapping, and DWIBS with 3D MIP reconstruction for the whole body in a single session without having to scan DWIBS separately.
All that were in a total scan less than three minutes for each station in total number four stations from vertex of the head to above knee joints.
We tried to enhance the quality of images by trying to avoid perfusion effect that caused by improper setting of b-values, which could create a pseudo-hyperintense signal as a false positive signal. The PET scan has been considered as our reference standard modality despite its disadvantages, lesions appearance on both modalities will be compared, during that, efforts will be intensified to provide an answer if there is a relation between high standard uptake volume (SUV) in hypermetabolic lesions and extracellular water diffusion since the two states share high cellular activities.

Chapter 3: Research Design

After ending this chapter, the following sections will be involved: 3.1.1 methodology, 3.1.2 research design, 3.2 criteria regarding participants, 3.3 used instruments, 3.4 procedures and timeline, 3.5 analysis method used in this study, 3.6 ethics and limitations.

3.1 Methodology and Research Design

3.1.1 Methodology:

In this section, the method used in this study will be discussed according to introduced research questions. The method is experimental for the MRI modality, in more specific for the DWI sequence, which is very sensitive for extracellular water molecules diffusion for detection of malignant body lesion without injection any contrast media. Only depending on the physical phenomena of water diffusion that exists in whole body tissue types in modified parametric sequence that controls the sensitivity of the sequence to detect only the malignant lesions that detected previously on PET scan as hypermetabolic spots, also the overall findings for WB-DWI and ^{18}FDG-PET will presented then compared.

A conclusion will be for the correlation between MRI and PET according to findings of WB-DWI scan for the quantified lesions on both modalities and measured ADC for high SUV hypermetabolic lesions that confirmed on both modalities also.

After having the result. The questions of the study will be answered, which are interested in correlation between ability of lesions detection in PET-CT and WB-DWI MRI in one hand, and on another hand, if there is any relation between high SUV for cancer tissue in PET and water molecule diffusivity in WB-DWI, since there is high cellular division rate and cellular activity.

This study suggested focusing on a modified protocol set of MRI exam based on two sequences only:

1- Whole Body STIR sequence as a background reference image, for anatomical correlation and for bony lesions, total scan time= 3:18 minutes in four stations.
2- Whole Body Diffusion sequence for detection of malignant lesions with two b-values (b=150 s/mm² and 800 s/mm²) with ADC mapping for malignancy confirmation, and exclusion of abscess, the addition of quantitative analysis of ADCs might help to differentiate benign findings from malignant tumors, total scan time for the four stations=13:18 minutes .

The total population of patients are 30 patient per month; the period for data collection is limited for two months only. Therefore, 60 patient are our total population who requested to do PET scan.

Steps Involved:

1. A 33 patients from oncology clinic at An Najah National University Hospital had been included, who advised to perform a PET scan by their clinicians. Each patient will be reported for the PET scan wherever it will be done. In opposite they will be asked to perform a WB-DWI MRI scan in a period not exceeding 10 days from PET scan and prior to any medical intervention. During this period, it has confirmed by treating oncologists that no noticeable changes could be happened on the size and function of lesions, for approximately 18 minutes of scan for whole body by MRI.
2. The predicted needed period is not less than two months and not more than four months for collecting the needed numbers of samples, analysis of results and extracting the statistical data.
3. Three senior boarded (7-25 years) experienced radiologists will report each WB-DWI MRI scan from the Department of Diagnostic and Interventional Radiology at An Najah National University Hospital- separately in blind manner without reviewing PET scan or PET report to make sure of high accuracy level of our study results.
4. The final step is comparing the findings of WB-DWI MRI with the result of PET scan; the result of comparison will be analyzed statistically and sorted in tables to summarize the conclusion about this imaging technology.

3.1.2 Research Design:

The study will be comparative between PET and WB-DWI MRI. It is a prospective because patients-who had been advised to PET scan, also asked and waited to do WB-DWI. Quantitative due to the analysis method used to describe findings regarding the degree of correlation between the quantities of lesions discovered by PET and MRI using Microsoft Excel 2017.

The clinical radiological findings on PET scan are our reference in this study; it will be considered as our gold standard. On other hand, WB-DWI MRI findings will be the variable that need to be evaluated it's technical parameters in order to see it's sensitivity in detection and not to attenuate the signal of lesions at the same time by modifying its b-value.

A background about WB-DWI MRI faults already covered, in addition to the most locations of false positive findings. Moreover, the main pivotal subject is when to treat the positive lesions as a true positive finding, all that will be after a proper analysis to the findings after comparing with the gold slandered.

3.2 Participants

This study will focus on all oncology patients at An Najah National University Hospital; patients who have one of the following criteria will be excluded:

1. Age less than 18 years old, due to legal issues.
2. Claustrophobia will need a general anaesthesia.
3. Patients who have any history of metallic implants, peacemaker and any device implants due to safety issues.
4. Patients that may need general anaesthesia.
5. Patients who will not agree on the procedure.
6. Unconscious, disoriented and all patients who are contraindicated for MRI.

The selection process is random, regardless if their PET scan is negative or positive; the ability of WB-DWI MRI to show the true positive and negative results needs to be evaluated.

Oncology clinics at An Najah hospital are dealing with a variety of oncology patient types. The number of patients who requested for PET are almost 30 patients monthly, this study obliged to be committed to the time period of two months, which means having a total populations of 60 patients. To calculate sample size, a statistical calculator has been used after taking into account the confidence level, margin of error, population proportion and the total population size, the values were respectively: 90%, 5%, 4% and 60 as a total population. The resultant needed sample size was 25 patient at least.

3.3 Instruments

WB-DWI MRI was performed using a definite set of organised imaging protocol that specially built for this study. The hardware tools were 1.5 Tesla MRI system (Ingenia, Philips Healthcare), 70cm magnet bore diameter with an operating release system 5.3, head-neck-brain coil 8 channels, two anterior body coil 16 channels, posterior build in body coil 12 channels, multi-station moving imaging table system with a maximum load 250kg and 275cm travel limit. Omega HP gradient system Max amplitude: 45mT/m, Max slew rate: 120mT/m and fastest rise time: 0.275ms.

The software including a whole body survey only with anterior and lateral view for whole body, whole body STIR sequence in four coronal stations (head and neck, thorax, abdomen pelvis and femur), WB-DWI single shot echo planar imaging sequence in a four axial stations series (head and neck, thorax, abdomen pelvis and femur). Table (3.1) summarizes in details the used modified technical scanning parameters for the used sequences.

Table 3.1**:** Technical scanning parameters for the used MRI sequences.

Sequence	Survey	STIR	WB-DWI
FOV mm	265*530*400	300*453*270	460*294*300
Voxel mm	1.04*1.29*200	1.66*2.37*6	3.5*3.5*6
Stations	5 COR/SAG	4	4
TR/TE ms	3.5/14	8285/64	5836/68
b-value s/mm^2	NO	NO	150, 800
SENSE	NO	2 (RL)	2.5(AP)
Fast mode	NO	TSE,39	EPI SS
Shim	default	default	Volume
Gap mm	---	1	1
IR	NO	160 ms delay	180 ms delay
Align overlap	30mm	30mm	30mm
Reconstruction matrix	---	320	288
Scan time	1:09 min	3:18 min	13:18 min

Gradient performance is accepted due to its effect in enhancing the magnetic field homogeneity, table movement during scanning enabled us to get a whole body scan with multi station acquisition, and PHILIPS scanner software offers an option to stich the stations together by MOBI-VIWE technology. So a whole body scan with a very fewer susceptibility edges artefact gained.

Because diffusion sequences use the Echo Planner Imaging technique, they are a fast scan. On other hand, DWI sequence are very sensitive to magnetic field inhomogeneity, it has been considered DWI for a specific organs with Shimming is very necessary for DWI, a volume shimming is used to reduce the effect of inhomogeneity due to large scan fields to cover whole body and due to variety of anatomy. In addition, all body organs need to be projected free from artefacts.

Only areas of abnormality in the extracellular space diffusion will appear as a high signal. To make it free from normal micro perfusion effect in capillaries, a modification was applied for the sensitivity of DWI sequence for detection of restricted water molecules that caused by malignant lesions in a way by not using too much b-value and not too small one. As noticed while reviewing the previous literatures, as a result, a reason for false positive signal will be avoided.

3.4 Procedure and Timeline

The process of data collection was designed to be clear from errors and mistakes as much as possible, participants have a ready data of interest that has been archived and stored in an external location, PET scan DICOM images with PET reports, and pathology, medical history and ID of the patients are accessible.

2.4.1 Study Stages:

The access requested regarding this study from oncologists who participated in data collection, the process of inspection about data had been divided into stages:

- ✓ **Stage1:**

Topic, proposal editing and getting the primary confirmation from the advisor. Later on, we have been asked to apply for the IRB committee to have the approvals, the requested documents and forms had been filled and assigned according to Al Quds University and An Najah National University Hospital policies. A coordination with the oncologists to provide us with needed participants and clinical data at An Najah Hospital has been done.

A big time was spent for the financial coverage and funding procedures, many obstacles were encountered, including logistical support.

- ✓ **Stage 2:**

Callings started to invite patients for participating in this study after informing them of the details of the study and its purpose, by phone. A good percentage of them had met us in affirmative, an initial appointment for MRI has been booked for them, and the others refused

due to transportation, health status issues and due to COVID-19 pandemic to avoid infection according to their immunity status.

✓ **Stage 3:**

Receiving for patients started in radiology department at An Najah Hospital-Nablus, PET scan has been confirmed to be proceeded before MRI in a period that not exceeding ten days, there is a confirmation from referral oncologists that patients did not receive any medical intervention regarding their oncological status between PET and MRI.

Consent forms had been assigned by patients or their families; data of MRI has been acquired successfully for 33 patients without any obstacles inside the radiology department.

Patient's preparation protocol for any routine MRI scan was done, the position was head first, supine and arms on by sides, iso-center for the first scan was on glabella for brain scan, the survey was modified to scan whole body in multi station mode automatically, head-neck, chest, abdomen pelvis and thigh, all stations contain anteroposterior and midsagittal images. STIR and WB-DWI mainly used the option of moving table during scanning for each station to bring the desired scan field of view to the iso-center, which in turn reduces the effect of magnetic field inhomogeneity for large fields.

Reconstruction was done using Mobi-View option to stich images together; the entire body appeared in one view on both views. However, planning for STIR and WB-DWI sequences will be easy due to scan align option, STIR was reformatted in the same technique, whole body STIR image in the coronal view as a the result with homogeneous peripheral signal.

As for WB-DWI acquisition and reconstruction. Sequences had been set to have two b-values (b=150,800) s/mm^2, with automatic registration of the images of different b-values. The validity of acquired ADC value is high according to the pervious recommendations by the publishers by not using too low or too high values, the algorithm of ADC threshold mapping has been standardized, then maximum intensity projection (MIP) for lesion projection has been applied in addition to background tissue signal suppression.

Later on, the resultant raw data processed with Mobi-View for the entire stations to have surface-rendered images for the whole body, which called whole body diffusion weighted image with background signal suppression (DWIBS).

It is important to mention that it is possible to use any b-value for WB-DWI to reconstruct DWIBS, actually, it has been noticed the strength of background normal tissue signal suppression in high b-values, each time low b-value used for DWIBS; it will project more normal tissues that could obscure lesions, in three-dimensional reconstruction of DWIBS.

The PET scan images of interest are archived in the PET Center Friend's Society-Nablus; the data has been accessed and extracted on an external storage unit. Clinical history and patient's data had been collected and sorted in tables, in order to make it easy and clear for radiologists to interpret the images of MRI according to their clinical history.

Findings of the WB-DWI MRI were interpreted using all acquired MRI images, any suspicious lesion on STIR that gives a high signal intensity on DWI, mainly on the high b-value, and showing drop of signal on ADC that means it is showing a diffusion restriction, it will be considered a malignant lesion and will be treated as a positive finding.

The criteria of lesions classifications is depending on their signal intensity on DWI and ADC. On other hand, presented lesions will be compared to their appearance on PET images with considering normal physiological signals to be excluded on both PET-CT and WB-DWI MRI.

The identical presented lesions on both modality will be treated as true positive findings. Lesions that confirmed on PET which didn't show any DWI restriction but gives a high b-value signal intensity will be treated as a true positive also, lesions that appears on DWI which haven't any activity on PET will be described as radiologists medical opinion, if not significance, it will be considered as false positive signal.

The true negative must be identical after confirmation of negativity on both modalities, the false negative either will be presented on PET but absent on WB-DWI.

2.4.2 Stages Timeline:

The progress of planned stages were illustrated for timeline in timetable, (table 3.2) of the scientific research that had been done.

Since 2020, Aug until 2021, Sep, there was no activity regarding data collection, at the beginning of 2022, data collection started after having the financial coverage in addition to approved acceptance from the CEO of An Najah Hospital and Radiology Chief Manager.

Table 3.2**:** The timetable of research activity during performing stages of thesis.

Periods	**Stages**	**Status**
Aug.2020-jan.2021	Topic, proposal and IRB approval	Defenced and accepted
Oct.2020-Sep.2021	- Preparations of MRI protocols -Financial coverage	Done successfully 70% coverage
Dec.2021-Feb.2022	Data collection	MRI scan PET and medical history of patients
Feb.2022-March.2022	Data analysis Result formulation	--------

3.5 Analysis

In details for each patient, age, weight, gender and number of lesions separately according to body zones (head-neck, chest, abdomen-pelvis and musculoskeletal) had been sorted in a table using Microsoft Excel, average, maximum and minimum values for age and patient's weight values in addition to gender percentage had been calculated for the participated patients.

The table that contains the data which will be used will be duplicated. The first contains values regarding number of lesions that had been detected by PET scan, and it will be used as a reference gold standard. The other will have a different number values representing for the lesions which detected using WB MRI, in this way, the level of correlation between both modalities will be describe after measuring the performance level of WB-DWI MRI in lesions detection for the same quantified lesions on PET.

After getting the number of lesions using MRI, areas that show a restricted diffusion and high metabolic rate (high SUV) will be correlated in a table with a comparison between SUV and ADC quantitatively to assess if there is any correlation.

There is many statistical formulas to evaluate the results of studies, regarding this topic, many literatures used chi-square for determining whether there is a statistically significant difference between the expected frequencies in results for each modality, others used kappa index to measure the degree of agreements between both modalities. Pearson's correlation method is more suitable to describe our results statistically, since there is no need to evaluate the performance of PET. Only need to test if there is a statistical significant correlation between two deferent variables, one of them is the gold standard and the other is under assessment (MRI) since there is an expecting for a positive correlation between them.

The same statistical analysis method will be used also in this study to evaluate the nature of relationship between both SUV and ADC since there is a prediction for a negative correlation between them.

3.6 Ethics

According to the recommendations of the research committee at Al Quds University, we applied to the IRB approval, the application form and checklist had been filled with details of predicted requirements of our study with respects to any conditional complication that might happen during proceeding the stages of the study. Fortunately, in Jan 2021 we

received a committee’s decision letter that informed us with agreements to go ahead in our proposal idea, there is no any ethical conflict related to our scientific mission.

Chapter 4: Results

The process of data collection performed in stages, to be clearer; lesions of interest had been quantified by reviewing PET reports for each patient, the exact location for each hypermetabolic lesion was confirmed and classified according to its region. The same method has been used for lesions defining after reviewing MRI reports, which has been reported by three well-experienced boarded radiologists.

This chapter will summarize the resultant values of needed lesions for both modalities; each modality findings will be viewed and described separately in a titled section.

4.1 General Information about Participants

By looking to table (4.1) in appendix A, a 60% are male participants (n=20) and 40% female (n=13), ages of participants are ranging between 18-74 years old with an age average of 48 years old, body weight average is 83kg with a maximum and minimum weight are125kg and 56kg respectively.

Regarding participants medical oncological history. Five patients had been requested to do PET scan due to their primary Hodgkin lymphoma (HL); seven patients have non-Hodgkin lymphoma (NHL). Two patients have breast cancer and the remaining patients have: left foot alveolar rhabdomyosarcoma, endometrial cancer, gastric CA (infiltrating poorly differentiated signet ring adenocarcinoma), prostate cancer, anterior mediastinal mass (biopsy: poorly differentiated carcinoma), pancreatic tumour (intra-ductal papillary mucinous neoplasm, low grade), thyroid cancer, L4 vertebral body pathological fracture, skin lesions (biopsy result suggestive of mycosis fungoides) and left perihilar lesion and occipital brain lesion.

4.2 Distribution of Hypermetabolic Lesions According to Body Zones

Four geometric zones has been considered for the whole body for each patient as the following: head-neck, chest, abdomen-pelvis and musculoskeletal for 33 patient, that means a total of 132 geometric zone for the total 33 patient, each zone for each patient has been checked qualitatively and quantitatively for presence or absence of hypermetabolic lesions. It has been found that 85 zone have a negative findings with no presence of any abnormal metabolic activity. On other hand, 47 zone showed a spots of hypermetabolic activity in a total number of 181 lesion with assurance of malignancy by the reporting PET radiologist, without any suspicious physiologic or inflammatory hypermetabolic activity. Table (4.2) explains clearly and concisely the distribution of hypermetabolic lesions for PET exams. In the next sections, each zone will be briefly described with its related lesions in addition to other findings that could be a potential malignant with no absolute metabolic hyperactivity.

4.2.1 PET Findings (Head-Neck zone):

Including brain and all anatomical details in this area. It has been noticed that from a 33 patient, there is a 23 patient have a negative hypermetabolic malignant activity in the area of head and neck. The remaining 10 patients have a positive hypermetabolic activity in a total of 17 active lesion, in a different locations in the area of head and neck, most of them are presented as a lymph node with hyperactive metabolism. There is two in the thyroid gland with nodular activity, one has a maxillary sinuses hyperactivity, one has nasopharyngeal and one patient has a suspicious right frontal lobe hypodense area. Lesions that have not been confirmed in malignancy or viewed as a suspicious to inflammatory activity even if showing hyperactivity had been neglected by the research team.

Table 4.2**:** Number of positive hypermetabolic lesions according to related body zone in PET-CT.

Zone	lesions
Head, Neck	17
Chest	70
Abdomen-Pelvis	69
MSK	25
Total PET Lesions	181

4.2.2 PET Findings (Chest zone):

The entire chest organs including lungs, mediastinum, oesophagus, trachea and related lymph nodes in the chest zone whether mediastinal either axillary, all had been evaluated for each patient.

It has been found 18 patient from 33 patient that have a negative hypermetabolic activity in the chest zone, the remaining 15 patients have a hypermetabolic malignant active lesion in a total of 70 lesion.

There is many enlarged lymph nodes with no evidence of hyperactive metabolic rate; they are distributed in the area of mediastinal area, supradiaphragmatic area, axillary area, hilar area, subcarinal area, lungs, oesophageal activity and chest zone skin hypermetabolic lesions.

The research team had agreed to neglect lesions that have not been confirmed in malignancy or viewed as a suspicious to inflammatory activity even if showing hyperactivity in the chest zone.

4.2.3 PET Findings (Abdomen-pelvis zone):

This area has a variation in anatomical characteristics, abdominal solid organs including liver, spleen, urinary system, with adrenals, gastrointestinal system in addition to pelvic organs which extending from lower abdomen to be ended at the symphysis pubis level. Moreover, lymphatic system is highly complicated also; it has been managed to quantify each active lesion in this zone.

It has been found that 17 patients have a negative active lesions whither solid neither lymphatic, the remaining 16 patient have a total of 69 active hypermetabolic lesion that is varying to be lymphatic mostly, parenchymal, subcutaneous metastatic in the abdominal wall, gastrointestinal wall and glandular hypermetabolic lesions.
The research team had agreed to neglect lesions that have not been confirmed in malignancy or viewed as a suspicious to inflammatory activity in the abdomen-pelvis zone even if showing hyperactivity.

4.2.4 PET Findings (Musculoskeletal (MSK) zone):

It is highly important to cover whole MSK system including bones, cartilage, ligaments, tendons and connective tissues.
It has been noticed that between 33 patients, there is 27 patient were negative to any hypermetabolic findings in their MSK whither in bones neither in muscles.

The remaining six patients had in total of 25-hypermetabolic lesion, which had been distributed in the bones mainly in the spine, ribs and uptake along axial and proximal appendicular bone marrow, gluteal subcutaneous nodules, gluteal cleft, teres major and latissimus dorsi muscles and many other connective tissues.

Most patients had a hypermetabolic signal in the area of shoulder and knee joints due to inflammatory process as mentioned by PET radiologist.

The research team had agreed to neglect lesions that have not been confirmed in malignancy or viewed as a suspicious to inflammatory activity in the musculoskeletal zone even if showing hyperactivity.

4.2.5 MRI Findings (Head-Neck zone):

The same technique was followed in quantifying lesions in whole body for all patients for divided body zones.

Lesions, which showed only a true diffusion restriction had been included in our calculations, DWI signal with T2 shine through was not included according to the radiologist's opinion.

Each lesion in the area of head and neck was quantified with confirmation of true restriction by measuring the ADC using a free hand region of interest to include only lesions with ADC value less than 1.1 x 10^{-3} mm^2/s; table (4.3) is summarizing the net findings of MRI for each body zone.

Table 4.3**:** Number of positive true restricted lesions according to related body zone in MRI.

Zone	lesions
Head, Neck	59
Chest	72
Abdomen-Pelvis	101
MSK	19
Total MRI Lesions	251

It has been found that from 33 patient, there is 13 patient have negative findings, were 20 patient have a positive true restriction lesion in a total of 59 lesion, submandibular LNs, cervical LNs, nasopharyngeal restriction and supraclavicular LNs.

There was many sub-centimetre size lesions that showed to us as a true restriction with an ADC value was ranging from (0.2-1.1) x 10^{-3} mm^2/s, this number variation is what forming

the differences between PET and MRI due to absence of these small lesions on PET with keeping in our minds that most of hypermetabolic PET lesions were confirmed on DWI as a true restriction.

4.2.6 MRI Findings (Chest zone):

18 patient from a total of 33 had a negative findings in the chest zone, 15 patient showed a different areas as a restricted diffusion which distributed in infraclavicular, axillary, lungs, mediastinum, supdiaphragmatic, perioesophageal and hilar regions.

ADC values was confirmed as a true restriction to be in the range from 0.2 x 10^{-3} mm^2/s to 1.1 x 10^{-3} mm^2/s for the most hypermetabolic PET lesions in a total of 72 lesion.

4.2.7 MRI Findings (Abdomen-pelvis zone):

In this zone, 101 lesions confirmed as restricted diffusion for 21 patient, 12 patient had negative findings with neglecting all T2 shine through lesions that did not show any restriction in ADC. The distribution of lesions were retroperitoneal LNs, pelvic LNs, inguinal LNs, spleen hailer LNs, liver, mesenteric LNs, intra-abdominal soft tissue masses and uterine-cervix tumours. Most of these lesions had been presented in PET as hypermetabolic lesions, ADC values were confirmed for a true restriction which range from (0.3-1.1) x 10^{-3} mm^2/s.

4.2.8 MRI Findings (Musculoskeletal (MSK) zone):

STIR sequence was our basic tool for evaluation of MSK lesions, which is very sensitive for any abnormality in the area of bony tissues and related connective tissues.

DWI sequence was useful also in some cases for evaluation of non-bone marrow areas.

It has been found 19 lesion for five patients distributed in humerus, sacral bone, tensor fascia lata muscle and lamina of L4 lumbar spine.

It has been managed to detect area of pathological fracture in spine and measuring ADC for restricted DWI of right lamina, which showed ADC value 0.48 x 10^{-3} mm^2/s which appeared previously as hypermetabolic area on PET.

4.2.9 SUV versus ADC:

During the process of lesions quantification related to each body zone, it has been noticed that not all lesions had been marked by its own SUV; the mentioned lesion's SUV had been measured for their ADC the same lesion on WB-DWI by a freehand ROI by participated radiologists, according to the literatures.

It has been noticed that SUV values more than 2.5 is considered as a malignancy with hypermetabolism. On other hand, ADC value less than 1.1 x $10^{-3}mm^2/s$ is highly indication for a true restriction on DWI MRI images by ADC mapping (Kirchner et al., 2017).
It has been managed to count a 45 different lesion's site on both modalities by PET reports and MRI images; in (table4.4, A/B), the correlation comparison between ADC and SUV is sorted below.

Table 4.4-A**:** Comparison between SUV and ADC values for different lesions crossing whole body for 33-oncology patient.

Anatomical Region	**SUV**	***ADC**
Thyroid gland	6.05	0.8
RT retro pectoral LNs	7.03	0.5
RT hilar	3.07	1.1
Retroperitoneal LNs	3.03	1.05
Supraclavicular LN	5.45	0.56
Supradiaphragmatic mass	4.82	0.7
Uterine and cervical mass	28	0.32
External iliac LN	20	0.68
Cervical LN	4.7	0.2
Splenic hilar LN	4.5	0.7
Nasopharyngeal	11.7	0.6
Cervical LN	4.4	0.45
Middle lower abdomen	2.92	0.96
Pelvic LN	5.36	0.9
Mesenteric mass	6.7	1.05
LT supraclavicular LNs	5.45	0.67
Supradiaphragmatic LN	4.82	0.97
Uterine and cervical	28.3	0.62
LT external iliac	20.41	0.624
Thyroid gland	6.05	0.89
LT lower cervical	4.7	0.37
RT retro pectoral LNs	7.03	1.01
RT hilar LN	4.31	0.724
Splenic hilar	4.52	0.784
RT cervical LN	4.41	0.56
Nasopharyngeal	11.76	0.84
LT axillary	6.27	0.7
Abdominal LN	8.08	0.76

Table 4.4-B**:** Comparison between SUV and ADC values for different lesions crossing whole body for 33-oncology patient.

Anatomical Region	**SUV**	***ADC**
LT infra clavicular	9.97	0.626
Sub carinal	13.1	0.901
Retro peritoneum	19.36	0.486
Tensor fascia lata muscle	8.8	0.82
RT sacral bone	5.44	0.425
LT thyroid nodule	8.63	0.92
RT cervical LN	5.3	0.94
RT hilar LN	11.08	0.852
RT lamina L4	8.37	0.48
Cervical LN	2.74	0.96
Posterior aspect of the lung base	7.76	0.438
LT adrenal gland	4.13	0.736
Lower oesophagus	11.3	1.06
Pleural-based nodules	3.24	1
RT Lung upper lobe	4.84	0.841
Jejunum	7.49	0.891
LT supraclavicular LN	14.77	0.54

***(ADC value) x10^{-3} mm^2/s**

Chapter 5: Discussion

It is important to realize which methods are much more suitable to represent our results in this study. The nature of data that extracted in this thesis are quantities, the first group is comparison between numbers of lesions for each body zone with confirmation for the presence of the same lesions that detected in PET previously on MRI later on. The extra lesions for the same body zone that had been recorded for MRI are subcentimetric lesions that didn't make any metabolic activity on PET scan, or considered to be less than capability of PET regarding resolution, since their size is less than one centimetre. The second group of variables are data that represents the values of comparison between SUV and ADC for the different anatomical regions, which extracted by PET reports in a total of 45 lesion with their actual SUV and measured ADC by the reporting radiologists.

5.1 Clinical Analysis

As mentioned previously in chapter 4, it has been managed to quantify and sort whole body lesions for 33 oncology patient according to their related anatomical zone on both modalities. The first step was to count regions that contain positive lesions regardless the number of lesions in addition to the number of regions that represent a negative findings on both modalities, to be sure of correct output of our result. The total anatomical zone for 33 patient is 132 region; the amount of positive lesions was only confirmed hypermetabolic malignancies by PET radiologist.

On MRI; lesions that behave as a restricted diffusion which show a hyperintense signal on DWI image b=800 and show a drop in signal in ADC was treated as malignancy. ADC was measured for each restricted lesion to confirm it as a true restriction, ADC values less than or equal $1.1x10^{-3}mm^2/s$ was within our criteria. Any ADC value above this value was neglected by the research team, after that, lesions which confirmed in anatomical zone to be malignant in both modalities in addition to be identical also have been counted.

By looking to (table 5.1) below a variation in the net count of lesions will be noted, this variation came from MRI sensitivity to restricted lymph nodes less than one cm in size, it is important to mention that most of lesions that had been detected by PET has showed a true restricted diffusion on MRI.

Table 5.1: The total lesion count for different anatomical whole body zone.

Anatomical zone	**PET scan lesions**	**MRI WB-DWI/STIR lesions**
Head-Neck	17	59
Chest	70	72
Abdomen-Pelvis	69	101
MSK	25	19
Total	**181**	**251**

The total sum of body regions is classified into positive and negative regions, the region of chest shows an identical results in both modalities, MSK show an almost similarities between PET and MRI.

It has been noticed a large variation in the results in area of head-neck and abdomen-pelvis due to nature of anatomical area of being containing a large amount of lymph node which highly represented in WB-DWI, (table 5.2) clarify the amount of positive and negative regions in PET and MRI.

Table 5.2**:** The amount of positive and negative regions in PET and MRI.

Body zone	**No of –(ive) regions PET**	**No of -(ive) regions MRI**
Head Neck	23	13
Chest	18	18
Abdomen-Pelvis	17	12
MSK	27	28
Total	**85**	**71**

Body zone	**No of +(ive) Regions PET**	**No of +(ive) Regions MRI**
Head Neck	10	20
Chest	15	15
Abdomen-Pelvis	16	21
MSK	6	5
Total	**47**	**61**

The lesions appearance on DWI sequences is attractive due to projection of signal intensity for lesions with suppression of background tissue that has a normal diffusion of their water molecules; (figures 5.1, 5.2) below are an examples for lesions projection on both modalities in addition to detailed SUV and ADC with maximum intensity projection for DWI with background suppression.

SUV values had been limited during the process of review for PET-CT reports, it has been only found around 45-lesion distributed through the whole body zones for the 33 patients. It was noted that all mentioned SUV are more than 2.5, which indicates a status of hypermetabolism for these lesions to be correlated later with their ADC values.

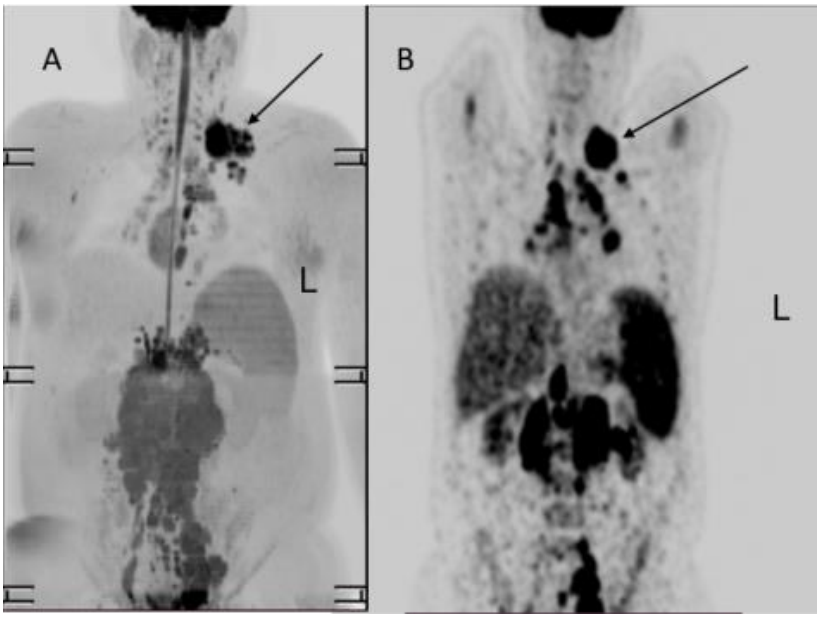

Figure 5.1: 37 years old male, a case of Non-Hodgkin lymphoma, image A: left supraclavicular DWIBS lymphoma, image B: PET scan (^{18}F-FDG) hypermetabolic left cervical supraclavicular lymphoma (black arrow)

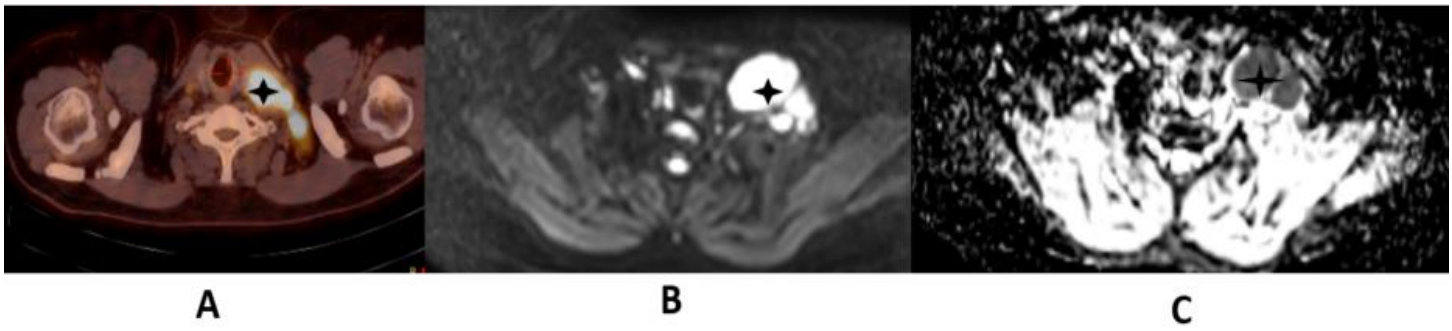

Figure 5.2: 37 years old male, a case of Non-Hodgkin lymphoma, different views for the supraclavicular lymphoma (black star) SUVmax=14.77, ADC = 0.54 x10^{-3} mm^2/s on PET (image A), DWI b=800 s/mm^{-2} (image B) and ADC mapping (image C).

5.2 Statistical Analysis

Regarding to our values for both variables groups to each body zone based in the number of lesions in PET-CT and WB-DWI MRI, the analysis process had to split data for two

different groups, the idea of correlation measurement is the main key to evaluate if there is association between each variable.

Therefore, Microsoft Excel software used to evaluate the strength and direction of correlation between extracted quantities for the number of lesions in each zone by PET-CT and WB-DWI MRI, SUV and ADC, test of normality for data distribution shows a significant value (sig. > 0.05), which is statistically significant.

Lesion counts for each zone for PET and MRI had been applied on a matrix to be processed, statistical results with charts of clustered columns to compare values in a cross multi categories, Also a plot of correlation direction as fitted line was done by MS EXCEL.

Our analysis result shows a significant positive correlation between number of detected lesions on PET and MRI using WB-DWI for each body zone at p value < 0.05 and R-values = 0.178, 0.434, 0.606 and 0.840 for head-neck, chest, abdomen-pelvis and musculoskeletal respectively, with a mean R value for the whole body = 0.520.

Figures (5.3), (5.4), (5.5), and (5.6) below are showing the nature of positive correlation between number of detected lesions for each zone using PET-CT and WB-DWI MRI.

It has been noticed that most hypermetabolic lesion cross the body (SUV>2.5) has ADC mapping value < 1.1 $x10^{-3}$ mm^2/s. also noticed that there is a negative correlation between SUV and ADC. Each lesion that has larger SUV, it has a smaller ADC value, that means the amount of restriction of extracellular water molecules is larger for lesions that have more cellular activity. Our statistical test for correlation between SUV and ADC shows a significant negative correlation between them at p value < 0.05 and R-value= -0.3073, (figure 5.7) explains the nature of negative correlation between SUV and ADC.

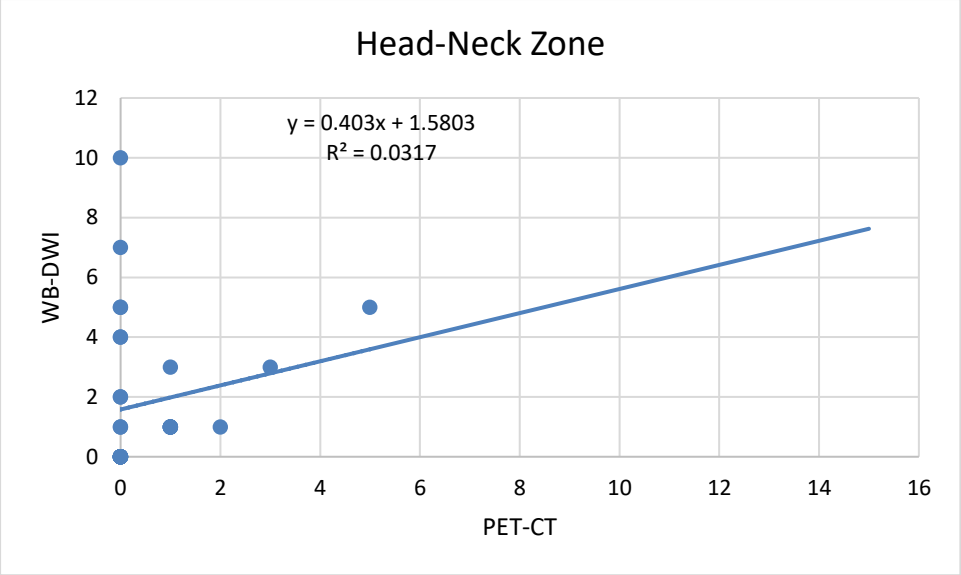

Figure 5.3: The nature of positive result correlation between number of detected lesions in head-neck using PET and WB-DWI MRI.

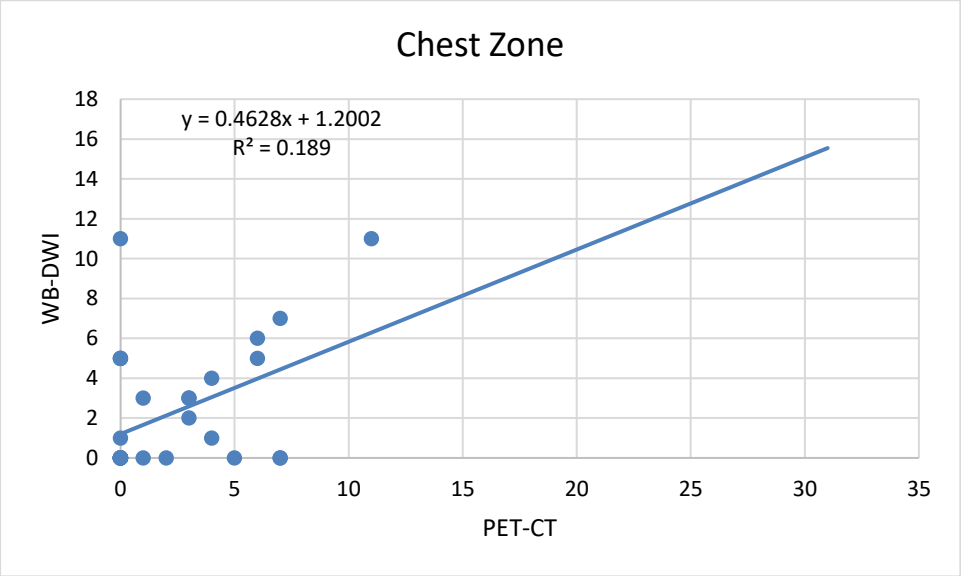

Figure 5.4: The nature of positive result correlation between number of detected lesions in chest using PET and WB-DWI MRI.

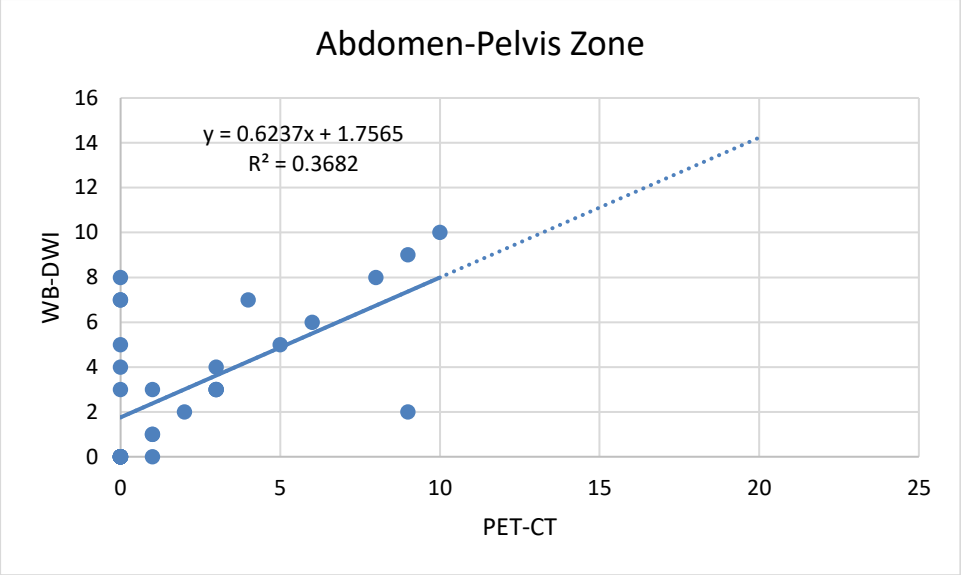

Figure 5.5: The nature of positive result correlation between number of detected lesions in abdomen-pelvis using PET and WB-DWI MRI.

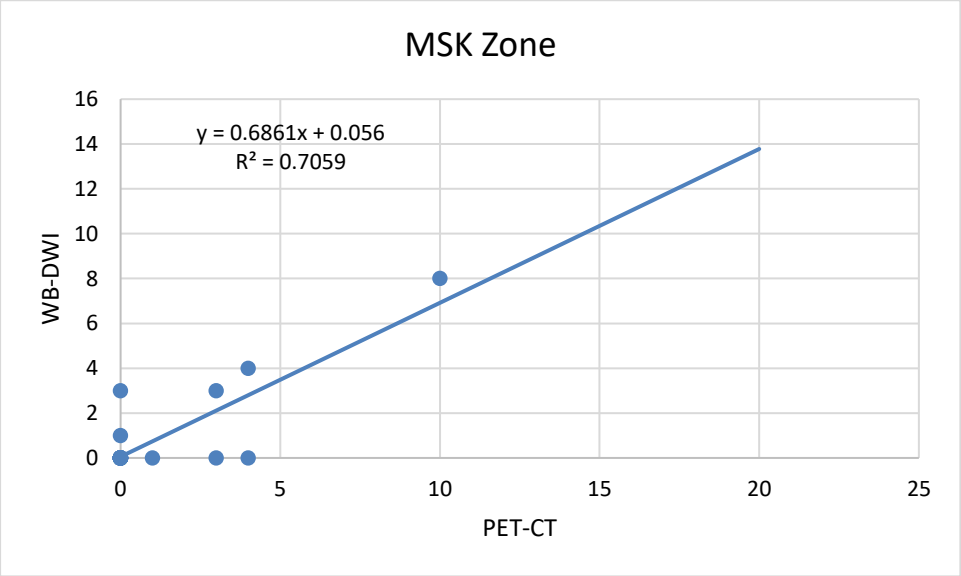

Figure 5.6: The nature of positive result correlation between number of detected lesions in musculoskeletal using PET and WB-DWI MRI.

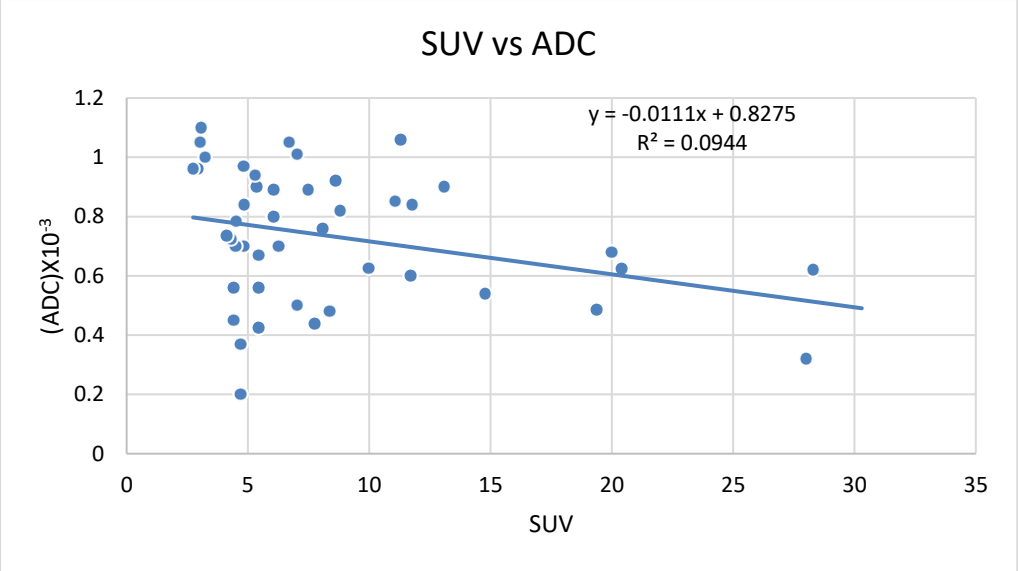

Figure 5.7: The nature of negative result correlation between SUV and ADC.

Chapter 6: Conclusions

This chapter is concluding the final opinion of the researcher about the findings and results, below there is three sections, section 6.1conclusions, section 6.2 limitations and section 6.3 recommendations.

6.1 Limitations

The main limitations in the process of data collection, there is no clear system in our region that creates a definite policies for facilitation new fields researches. The time for proceeding the target of this research was limited also, financial issues, dealing with patients to convince them to participate in researches on their pathological cases makes them feel scared, coordination and official correspondence are too complicated either. Number of interested samples and number of lesion that has a quantified metabolic SUV in PET reports to correlate them with measured ADC either, all of these mentioned conditions created a limitations for as to enhance our findings regarding our research hypothesis.

Obstacles are expected in any research, many difficulties have been faced during planning to proceed this study, and most of these difficulties had been overcome, but there was some that made limitations for us. Our vision was the target of whole oncology centers in Palestine to increase the validity of our result, practically it is not easy to perform that, we had to be enough with subjects from An Najah Hospital due to ease of access to the related data. Moreover, the funding issues consumed a lot of time; we applied within five months to more than eleven sponsors, only one company for medical drugs trading took care of 70% of the total expenses, the principal investigator paid the remainder of the expenses in order to not more delaying of research procedures.

6.2 Conclusions

After finishing all previous works, coordination with oncologists, getting financial funding, connecting with interested patients, retrieving their medical history in data collection and finally modifying a sequence for MRI imaging to analyse the findings, WB-DWI MRI shows a fault in some lesions that showed positive in PET scan.
There is a very weak statistical correlation in the area of head-neck zone ($R < 0.3$), slightly weak correlation in the area of chest zone ($0.3 < R < 0.5$), moderate correlation in the area of abdomen-pelvis zone ($0.5 < R < 0.7$) and strong correlation in the MSK zone ($R > 0.7$).

On other hand, most of lesions that showed by MRI are already presented by PET; statistics for findings are good indication for us that there is an actual significant correlation between hypermetabolism and diffusion.

WB-DWI MRI can be used as an alternative for PET-CT in Palestine to support oncology team in following up their patients in case they might face any obstacles in the process of booking for PET scanning sessions for their patients.

Radiologist's opinions regarding WB-DWI: WB-DWI MRI can be used in lymphoma cases for follow up as an alternative to PET scan in case if there is no access is available for PET imaging. DWI can be used also for localized tumors follow up to monitor the response for treatment after chemotherapy or radiotherapy either post-surgical resection for any remnant cancer tissues.

In chapter 1, two hypothetical questions has been made, the answer of the first questions is ready, the second question that is talking about if there is any relation between SUV and water molecules diffusion, there is a negative correlation between hypermetabolic lesions and water diffusion in the same lesion since it has been approved previously. The relation between ADC and SUV, each lesion shows a restricted diffusion with low ADC value when its SUV is high due to high metabolic and cellular activity rate.

Each lesion seen in PET and confirmed in WB-DWI has a high SUV and low ADC mapping value, there is a relation especially when describing an area that contains a very large amount of high metabolic activity cells within a small tissue volume relatively.

The extracellular space absolutely will be affected, as a result, the present fluids or water molecules will occupy a less area in size by the same volume of extracellular fluid, water molecules motion and diffusion will be affected in some way causing diffusion restriction in MRI WB-DWI sequence.

6.3 Recommendations

First addressing radiology technologists to not tolerate with any parametric modification on their exam settings in medical imaging in general and in MRI in more specific, every set of parametric modification is able to change a lot of resultant output especially when it comes to the issue of dealing with physiological changes at cellular and tissue levels. Therefore, they must be aware to the principles of imaging techniques to enhance their clinical findings.

The radiologists also have a major role in guiding the technologists for what to roll out in any radiological examination, technical and clinical issues are responsibility of both to get as much as possible perfect medical results.

Diffusion sequence in MRI is not a simple imaging technique; it is a powerful technology, which is under research in a many known international medical and biological research center. Its actual ability is not discovered totally, many studies are published every year to unveil their actual ability in the whole world due to its main principle, which depends mainly on the function of water molecules diffusion that coexists in the most of living body tissues.

Also recommend others who are interested in this field to reduce slice thickness in the area of head-neck, using saturation band for signals outside the field of view in the same phase direction, mainly in feet-head for axial plan, it may increase the scan time but will increase the quality of the images. STIR sequence is better in axial transverse plane for better anatomical correlation for radiologists, parenchymal signal suppression is better in b-value range (140-800) s/mm^2 as used in this research to detect lesions and to suppress the signal from normal diffusion and not to be affected by microperfusion from visceral capillaries also.

It has been managed to look for an alternative to help our patients and serving humanity to find a healthy, safe, available and least expensive way to monitor and follow up their health and medical conditions.

Oncologists also need to enrich their background about MRI sequences and diffusion sequence specifically for its role in detection and differentiation for many oncological cases. The results had been well received by the oncologists and radiologists who participated in this research, later on, they will decide the protocol of activation for patient's categories and cases that will be compatible to be followed up using WB-DWI MRI. Moreover, they recommend inserting diffusion sequence in each MRI study for oncology patients in order to assure the idea of diffusion restriction for follow up studies.

The findings extracted depended only on a simple analysis stations and tools. It is important in the future to reach a method that uses artificial intelligence and machine learning to analyze the images of diffusion at voxel level to investigate how really tumor cells react and behave inside the voxel with ability of defining the real tumor apart of its surrounding effect like edema, fibroses and necrosis.

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Appendices

Appendix A

Table 4.1: Demonstrates the values of findings on PET scan using FDG isotope and MRI using WB-DWI and STIR for all participants.

				PET	MRI	PET	MRI	PET	MRI	PET	MRI
Pt No	**Weight**	**Gender**	**Age**	**Head, Neck**	**Head, Neck**	**Chest**	**Chest**	**Abdomen Pelvis**	**Abdomen Pelvis**	**MSK**	**MSK**
1	70	M	21	0	0	0	1	0	3	0	0
2	79	M	50	0	2	5	0	5	5	0	0
3	96	M	59	0	0	0	0	3	3	0	0
4	65	F	65	1	3	6	5	8	8	0	0
5	63	F	60	1	1	0	5	3	4	0	0
6	78	M	18	2	1	3	2	1	1	1	0
7	75	M	68	0	4	0	5	3	3	10	8
8	125	F	37	3	3	0	0	0	5	0	0
9	114	M	30	1	1	0	0	0	0	0	0
10	74	M	57	0	0	0	0	0	0	0	0
11	62	M	47	1	1	11	11	10	10	3	3
12	61	F	55	0	5	4	1	0	7	0	3
13	85	M	43	0	7	3	3	0	4	3	0
14	117	F	58	0	5	0	5	0	0	0	0

15	87	M	74	0	4	1	3	4	7	0	0
16	105	M	37	5	5	6	6	9	9	0	0
17	56	M	28	0	0	2	0	1	0	0	0
18	77	M	43	0	1	1	0	9	2	0	0
19	58	F	32	1	1	0	0	3	3	0	0
20	60	F	54	1	1	7	7	0	0	0	0
21	68	M	51	0	10	0	11	1	3	0	1
22	95	M	32	0	0	4	4	2	2	4	4
23	85	M	58	0	0	0	0	0	0	0	0
24	92	M	51	0	0	3	3	1	1	0	0
25	112	F	46	1	1	7	0	6	6	0	0
26	81	F	68	0	1	7	0	0	8	4	0
27	70	M	45	0	0	0	0	0	0	0	0
28	68	M	47	0	0	0	0	0	0	0	0
29	84	F	60	0	0	0	0	0	0	0	0
30	102	M	40	0	0	0	0	0	0	0	0
31	100	F	33	0	0	0	0	0	0	0	0
32	80	F	53	0	0	0	0	0	0	0	0
33	104	F	52	0	2	0	0	0	7	0	0

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إعداد: أحمد محمد أحمد أبوعلي.

إشراف: د. محمد حجوج.

ملخص

فكرة وجود وحدة طب نووي متكاملة تتكون من جهاز ماسح مع مصدر للنظائر المشعة مثل المسارع النووي الدائري للعمل بكفاءة في فلسطين يكاد يكون مستحيلًا بسبب العديد من القضايا التي تبدأ من القضايا السياسية وتنتهي بالقضايا المالية بسبب الإحتلال الإسرائيلي.

الهدف من هذه الدراسة هو إيجاد طريقة آمنة وصالحة ومتاحة على نطاق واسع كبديل للتصوير البوزيتروني الطبقي لمساعدة أطباء الأورام وكذلك المرضى ، اقترحنا بروتوكول نموذجي معدل للرنين المغناطيسي لتصوير الجسم بالكامل (WB–DWI MRI) لاستغلال خاصية الإنتشار من جزيئات الماء داخل انسجة الجسم.

شارك 33 مريضًا من مرضى الأورام بهذه الدراسة ، 60٪ ذكور (20) و 40٪ إناث (13) ، تتراوح أعمارهم بين 18–74 عامًا بمتوسط عمري 48 عامًا ومتوسط وزن جسم 83 كجم .

تم تشخيص إصابة المشاركين بالفعل بأورام أولية بما في ذلك سرطان الغدد الليمفاوية اللاهودجكين،و سرطان الغدد الليمفاوية هودجكين ، سرطان الرحم ، والبروستات ، والبنكرياس ، والمعدة ، والغدة الدرقية ، والكسور المرضية ، والكُتل الجلدية.

أظهرت نتائجنا أن التصوير المقطعي بالإصدار البوزيتروني أظهر 181 كتلة ذات نشاط حيوي عالي في المناطق الأربع (الرأس والعنق، الصدر، البطن والحوض، والجهاز العضلي الهيكلي) لجميع المرضى ، تم اكتشاف نفس الكتل بواسطة

WB–DWI MRI الذي يُظهر معظم الكتل نفسها مقيدة في الانتشار بالإضافة لكتل لمفاوية ذات حجم أقل من 1سم بعدد إجمالي 251 كتلة مع مقارنة بين حجم الامتصاص القياسي (SUV) ومعامل الانتشار الظاهر ADC حيث تبين أن الكتل ذات حجم الإمتصاص القياسي (SUV> 2.5) كان معامل الإنتشار الظاهر لها ADC أقل من 1.1×10^{-3} مم ^{2} / ث.

يُظهر التحليل الكمي الإحصائي ارتباطًا إيجابيًا معنويًا بين عدد الكتل المكتشفة باستخدم الرنين المغناطيسي والتصوير البوزيتروني في نفس المنطقة لكل مريض بدلالات إحصائية موزعة كالتالي:

0.178 و 0.434 و 0.606 و 0.840 للرأس والعنق والصدر والبطن والحوض والجهاز العضلي الهيكلي على التوالي ، ويظهر الارتباط المقارن بين ADC و SUV وجود ارتباط سلبي بقيمة $p < 0.05$ وقيمة $R = -0.3073$. يمكن أن يحل التصوير بالرنين المغناطيسي WB–DWI محل التصوير المقطعي بالإصدار البوزيتروني في حالات سرطان الغدد الليمفاوية ومتابعة الأورام لمراقبة الاستجابة للعلاج بعد العلاج الكيميائي أو العلاج الإشعاعي وكذلك الأمر بعد عمليات الإستئصال الجراحي.