Role of Fluorine 18 fluorodeoxy glucose (FDG) Positron Emission Tomography (PET) / Computed Tomography (CT) in Pediatric Lymphoma

Thesis

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DEDICATION

To my Mum and Dad,

Who gave me roots,

And gave me wings.

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ABSTRACT

Malignant pediatric lymphoma accounts for 10–15% of all pediatric cancers, (representing 2–3% of all malignancies), with a peak incidence between 5–9 years. Chemotherapy is usually the first and most common mode of treatment. The choice of treatment and prediction of prognosis depend on the histological type of tumor, initial staging, evaluating treatment response, and detection of early recurrence. Conventional imaging modalities have many limitations. Compared to CT, PET/CT has much higher sensitivity and specificity in the initial diagnosis, assessment of response to therapy and routine surveillance of pediatric lymphoma patients.

KEYWORDS

PET/CT-CT-pediatric lymphoma-initial staging-response assessment-routine surveillance

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LIST OF ABBREVIATIONS

2D: Two dimensional

3D: Three dimensional

AC: Attenuation Corrected

CHL: Classic Hodgkin Lymphoma

CR: Complete Remission

CT: Computed Tomography

CTV: Clinical Tumor Volume

DLBCL: Diffuse Large B-cell Lymphoma

EBV: Epstein Barr Virus

FDG: Fluoro-Deoxy-D-Glucose

FNA: Fine Needle Aspiration

GTV: Gross Tumor Volume

HD: Hodgkin Disease

HIV: Human Immunodeficiency Virus

HRS: Hodgkin Reed Stenberg

IMRT: Intensity Modulated Radiotherapy

IV: Intravenous

IWC: International Workshop Criteria

LDCHL: Lymphocyte-depleted Hodgkin Lymphoma

LRCHL: Lymphocyte-rich classic Hodgkin Lymphoma

MCCHL: Mixed cellularity Hodgkin Lymphoma

MIP: Maximum Intensity Projection

MRI: Magnetic Resonance Imaging

NSCHL: Nodular sclerosis classical Hodgkin Lymphoma

NAC: Non Attenuation Corrected

NHL: Non Hodgkin Lymphoma

NLPHL: Nodular lymphocyte predominant Hodgkin Lymphoma

NPV: Negative Predictive Value

OS: Overall Survival

OSEM: Ordered-Subsets Expectation Maximization Algorithm

PET/CT: Positron Emission Tomography and Computed Tomography

PET: Positron Emission Tomography

PHA: Pulse Height Analyzer

PMT: Photomultiplier Tube

PPV: Positive Predictive Value

PTV: Planning Target Volume

REAL: Revised European American Lymphoma

ROI: Region Of Interest

RTP: Radiotherapy Planning

SPECT: Single Photon Emission Computed Tomography

SPD: Sum of Products of greatest Diameters

SUV max: Maximum Standarized Uptake Value

SUV: Standarized Uptake Value

WHO: World Health Organization

INTRODUCTION

Malignant lymphoma accounts for 10–15% of pediatric cancers (representing 2–3% of all malignancies) **(Riad et al, 2010).** Conventional imaging methods such as computed tomography (CT), magnetic resonance imaging (MRI) and ultrasonography (US) are commonly used in the evaluation of pediatric lymphomas, along with physical examination and bone marrow biopsy. Physical examinations are obviously limited by the location of the disease but are of primary importance for peripheral lymph node staging. All imaging techniques have significant limitations. CT diagnostic criteria are mainly based on size. As a result, CT neither identifies malignant involvement in normal-size lymph nodes nor characterizes enlargement due to other causes. In addition, CT performs rather poorly in detecting spleen and liver involvement. MRI is the procedure of choice in assessing bone marrow and central nervous system infiltration, but it is not convenient for the routine imaging of the entire bone marrow. Some of these limitations are most evident in post-treatment evaluation, in which anatomical imaging methods are unable to differentiate residual tumor from fibrosis or to detect early recurrence **(Zinzani et al, 2005)**.

During the last decade, hybrid imaging has revolutionized nuclear medicine. Multimodal camera systems, integrating positron emission tomography (PET) or single photon emission computed tomography (SPECT) with computed tomography (CT) now combine the contrast provided by tumor-avid radioactive drugs with the anatomic precision of CT **(Biermann et al, 2013).**

18F fluorodeoxyglucose (18F-FDG) is a glucose analogue that provides unique information about glucose metabolism of normal and abnormal tissues, in particular in malignant diseases. Although adult lymphomas have been widely

investigated with 18F-FDG positron emission tomography (PET), the literature concerning children is limited and the number of patients studied in reported articles are small **(Hudson et al, 2004)**. Currently, in adult oncology imaging, there is a transition phase from stand-alone PET to PET-computed tomography (CT), with PET-CT most likely becoming the accepted international standard in pediatric cancer imaging **(Stauss et al, 2008)**. 2-[18F]fluoro-2-deoxy-D-glucose positron emission tomography (18F-FDG PET)/CT is a relatively new, integrated imaging technique, which provides both functional metabolic data from18F-FDG PET and structural anatomic information from CT in one examination. The combination of the high sensitivity and specificity of 18F-FDG PET with the high anatomical resolution of CT is expected to improve the diagnostic accuracy for the detection of primary tumors as well as regional and distant metastases. For instance, the metabolic information obtained from 18F-FDG PET may help to differentiate normal and metastatic lymph nodes with a size of less than 1 cm. On the other hand, the anatomical information obtained from CT images may aid to detect even small pulmonary metastases, with a size that might be below the detection limit of an isolated 18F-FDG PET study **(Kleis et al, 2009).**

The number of clinical applications for 18F-FDG PET/CT in oncology has grown rapidly during the last few years. Several studies in adults have shown, that patients benefit from the use of integrated 18F-FDG PET/CT because of its superior diagnostic accuracy over 18F-FDG PET or CT alone **(Paul et al, 2007).**

Limited information is available on the use of positron emission tomography (PET) in paediatric oncology especially pediatric lymphoma.

AIM OF WORK

The aim of this study is to evaluate the performance of 18F-FDG PET/CT in pediatric lymphomas for the purpose of initial staging, evaluating treatment response and for long-term follow-up. We also aimed to compare the 18F-FDG PET/CT results with those of CT.

PET/CT Physics and Instrumentation

Positron emission tomography *(*PET*)* is a molecular imaging technique based on the detection of the two annihilation photons produced when a positron is emitted from a radionuclide tagged tracer molecule. The latter is biologically active and follows a certain metabolic pathway within the body. Hence, with this technique real qualitative and quantitative information about a certain biological function can be obtained. During the last 2 decades, great improvement of the diagnostic accuracy of PET has been achieved through the development of new data acquisition/ processing systems and the use of new positron emitting radiopharmaceuticals. Most recently, the combination of PET and CT has been strongly advocated representing as a unique imaging modality that adds the advantage of anatomical information on a single scanner with nearly perfect image co-registration **(Poeppel et al, 2009)**.

I. Positron Decay

In positron decay one of the protons (P) in the nucleus changes to a neutron (N), and a positron (β+) and a neutrino (ν) are emitted (fig.1). Positrons are the antimatter counterparts of electrons, having the same mass as (511 keV/c^2, where c is the speed of light) and the opposite charge of the electron. The positron then leaves the decay site, gradually losing its kinetic energy in the surrounding tissue through ionization and excitation of nearby atoms. Its path length depends on its initial energy which is particular for each radionuclide (less than 1mm for 18F). Once most of its energy is lost, the positron annihilates with a nearby electron producing two photons (γ) having two important features: they have energy of 511 keV and they leave the annihilation site in opposite directions **(Jadvar and Parker, 2005)**.