ROLE OF PET/CT IN LIVER MALIGNANCY

ESSAY

SUBMITTED FOR FULFILLMENT OF MASTER DEGREE IN RADIODIAGNOSIS

BY:

Abdulkhaliq Mohammed Obaid

M.B.,B.Ch.

Aden University

Supervised By:

Dr. Hatem Hosney Sallam

Assistant Professor of Radiodiagnosis

Faculty of Medicine

Cairo University

Dr. Hazem Elkashef

Lecturer of Radiodiagnosis

Faculty of Medicine

Cairo University

Cairo University

2008

Acknowledgement

First and foremost, thanks to ***God****, to whom I relate any success in achieving any work in my life.*

I would like to express my deepest gratitude and extreme appreciation to ***Assistant Professor Dr. Hatem Hosney Sallam,*** *Professor of Radiodiagnosis, Faculty of Medicine, Cairo University for his kind supervision, kind advice constructive encouragement, generous help and guidance through the whole work which could not be a fact, without his guidance and kind help.*

I would like to express my great thanks to ***Dr. Hazem Elkashef,*** *Lecturer of Radiodiagnosis, Faculty of Medicine, Cairo University for his kind advice and help through the whole work.*

I would like to express my respect, appreciation and thanks for my ***parents*** *for their assistance encouragement and their pray for me.*

finally, great thanks to my ***wife*** *for her kind care and support throughout my life.*

Abdulkhaliq M Obaid

ABSTRACT

All the noninvasive techniques in current use are not sufficiently able to identify primary tumors and even unable to define the extent of metastatic spread.

Currently, positron emission tomography/computer tomography (PET/CT) are more and more widely available and their application with 18F-fluorodeoxyglucose (18F-FDG) in oncology has become one of the standard imaging modalities in diagnosing and staging of tumors, and monitoring the therapeutic efficacy in malignancies. PET/CT with 18F-FDG as a radiotracer may further enhance the hepatic malignancy diagnostic algorithm by accurate diagnosis, staging, restaging and evaluating its biological characteristics, which can benefit the patients suffering from hepatic metastases, hepatocellular carcinoma and cholangiocarcinoma.

Keyword liver malignancy - PET/CT

Table of Contents

Item	**Page Number**
List of Abbreviation	
List of tables	
List of figures	
Introduction and aim of the work	**1**
Pathology of malignant hepatic tumors	**5**
Classification of malignant tumors of the liver	5
Cellular classification of primary liver malignancy	7
Stage information	7
Hepatocellular carcinoma	9
Cholangiocarcinoma	12
Liver metastases	14
Fibrolamellar carcinoma	15
Hepatoblastoma	15
Positron Emission Tomography (PET)	**16**
What is PET?	16
Tumor Physiology and FDG Uptake	18
Positron emission	23
Hardware of PET	26
Radionuclides	28
– General principles of FDG production	28
– Production of F-18	28
– Synthesis of FDG	30
Clinical application of PET in oncology	31
– The American Board Classification of PET applications	32

– Indication of PET – Medicare Approved	33
Interpretation of PET scans	35
– Sites of physiological FDG uptake	35
– FDG uptake in the abdomen	37
– PET interpretation	46
PET/CT	**49**
Physical principles of PET/CT	49
Whole-Body PET/CT Imaging with 18F-FDG	54
Patient preparation	56
CT technique	58
– Protocol for CT imaging	58
PET technique	62
The PET/CT scanning process is as follows	64
Image interpretation	64
Standardized uptake value (SUV)	66
Reporting	68
Description of findings	68
Impression (conclusion or diagnosis)	69
Sources of error	69
– False positive FDG PET	69
– False negative FDG PET	70
Image artifacts	70
– Metallic implants	73
– Respiratory motion	74
– Contrast Media	76
Limitation of anatomic imaging methods for cancer assessment	77

Advantage of PET/CT	78
PET and PET/CT in evaluation of primary and metastatic liver malignancies	**79**
PET and PET/CT VS conventional imaging modalities	80
Evaluation of hepatic metastases	83
Evaluation of hepatocellular carcinoma (HCC)	91
Evaluation of chlangiocarcinoma (CC)	97
Evaluation of hepatic malignant biological characteristics	101
Selection of patients with hepatic colorectal metastases for hepatectomy	104
Monitoring the effect of systemic treatment	105
Viable tumors VS necrosis or fibrosis after treatment	106
Detecting residual disease after local treatment	107
Predictors of postoperative recurrence in asymptomatic patients	109
Evaluation of prognosis of hepatic malignancies	110
Role of PET/CT in identifies tumor growth or thrombosis in the portal vein with hepatocellular carcinoma	112
Summary and Conclusion	**118**
References	**120**
Arabic Summary	

List of Abbreviations

ACF	Attenuation Correction Factor
AC/AL	Attenuation correction/Alignment
AFP	AlphaFetoProtein
AJCC	American Joint Committee on Cancer
bFGF	basic Fibroblast Growth Factor
BGO	Bismuth Germinate
CC	Cholangiocarcinoma
CEA	Carcinoembryonic Antigen
cm	Centimeter
CMS	Centers for Medicare and Medicaid Services
CT	Computed Tomography
DNA	Deoxynucleic acid
ECT	Emission Computed Tomography
FDG	FluoroDeoxyGlucose
18FDG	^{18}F- FluoroDeoxyGlucose
FLT	F-18-3-Fluoro-3-deoxy-L-Thymidine
FDA	Food and Drug Administration
GLUT	Glucose Transporters
GSO	Gadolinium Silicate
H+	Hydrogen ion
HCC	Hepatocellular Carcinoma
HK	Hexokinase
HU	Hounsfield Unit
IV	Intravenous

KeV	Killo electron Volt
KV	Killo Volt
KVp	Killo Volt peak
LSO	Lutetium Oxyorthosilicate
MA	Milli Ampere
MAS	Milli Ampere Second
mCi	Micro Curies
MeV	Mega electron Volt
MRI	Magnetic Resonance Imaging
MDCT	Multi-Detector Computed Tomography
mRNA	messenger RNA
n sec	Nano second
PET	Positron Emission Tomography
PET/CT	Positron Emission Tomography/ Computed Tomography
PDGF	Platelet-Derived Growth Factor
PMTs	Photomultiplier Tubes
RFA	Radiofrequency Ablation
SPECT	Single Photon Emission Computed tomography
SUV	Standardized uptake value
TACE	Transcatheter Arterial Chemo-Embolization
TNM	Tumor Node Metastasis
VEGF	Vascular Endothelial Growth Factor
$ß^{+}$	Positron
ß-	Electron
γ	Gamma

List of tables

Table	Description	Page Number
Table 1	Classification of malignant tumors of the liver	6
Table 2	Risk factors of HCC	10
Table 3	High risk groups for developing hepatocellular carcinoma	10
Table 4	Radionuclides used in PET	28
Table 5	Characteristic of PET and PET/CT in detecting liver malignancies	82
Table 6	Comparison between PET/CT and conventional imaging modalities of their values in examination of liver malignancies	111

List of figures

Figure	Description	Page Number
Figure 1	Uptake of FDG	20
Figure 2	FDG Metabolism	21
Figure 3	Annihilation reaction	24
Figure 4	Mean positron range and annihilation angle blurring	25
Figure 5	Ring of multiple specialized crystals detects the "coincidence" 511-keV photons	27
Figure 6	Production of F-18. after acceleration in a cyclotron	30
Figure 7	Normal distribution of FDG	36
Figure 8	Physiologic diaphragmatic uptake in a 49-year-old woman with a history of abdominal lymphoma and severe chronic obstructive pulmonary disease who was referred for posttherapy follow-up	38
Figure 9	Recurrent disease in a 56-year-old man with esophageal carcinoma	39
Figure 10	Physiologic gastric uptake in a 52-year-old man with colorectal cancer who had undergone surgical tumor resection	40
Figure 11	Gastritis in a 47-year-old woman with a history of breast cancer	41
Figure 12	Newly diagnosed gastric cancer a 59-year-old woman who was referred for presurgical evaluation	41
Figure 13	Physiologic bowel uptake in a 36-year-old man with malignant thymoma who had undergone surgical tumor resection	42
Figure 14	Physiologic bowel uptake in a 44-year-old man with squamous cancer of the oropharynx who was referred for posttherapy evaluation	43
Figure 15	Primary carcinoid tumor of the bowel in a 47-year-old woman with a history of breast cancer and a recent diagnosis of metastatic carcinoid tumor in the lung	43

Figure 16	Adenocarcinoma of the cecum in a 77-year-old man with a cecal polyp that had recently been detected at colonoscopy	44
Figure 17	Chronic cholecystitis in a patient with papillary thyroid cancer who underwent thyroidectomy and radioiodine ablation	45
Figure 18	Liver metastasis in a 55-year-old man with rectal adenocarcinoma who was referred for posttherapy evaluation	46
Figure 19	Typical PET/CT	49
Figure 20	Current commercial PET/CT scanners	50
Figure 21	A schematic illustration of a PET/CT system	52
Figure 22	Typical scout image obtained during an FDG PET/CT study	60
Figure 23	Hybrid PET/CT scanner shows the PET (*P*) and CT (*C*) components	63
Figure 24	Screen of the syngo software platform	65
Figure 25	Metallic artifact	73
Figure 26	Respiratory artifact	75
Figure 27	Respiratory motion artifact	76
Figure 28	Patient status post left hemicolectomy for colon cancer without change in CEA level	84
Figure 29	Patient status post left hemicolectomy for colon cancer and increasing CEA level	87
Figure 30	33-year-old man under going ascending colon cancer resection tow years ago	88
Figure 31	Hepatocellular carcinoma (HCC).	92
Figure 32	68-year-old male undergoing HCC resection 28-month ago	94
Figure 33	Patient with left hepatic mass incidentally detected on ultrasound. PET/CT was requested for further assessment	95
Figure 34	Patient with poorly differentiated adenocarcinoma of unknown primary diagnosed on a biopsy from a left hepatic lobe mass	99

Figure 35	68-year-old female complaining of uncomfortable left upper abdomen for one month…………	102
Figure 36	Patient with metastasis from colonic primary in the anterior right hepatic lobe…………	108
Figure 37	Portal phase of contrast-enhanced CT demonstrating the left portal vein tumor thrombus	113
Figure 38	Integrated PET/CT image showing high FDG uptake by tumor thrombus in the left portal vein and a liver mass with a satellite lesion	114
Figure 39	MRI T2 imaging showing a thrombus in the left portal vein	115
Figure 40	Fused PET/CT imaging showing no hypermetabolism in the region of the left portal vein and in the region of previous hepatic resection	116

Introduction and Aim of the work

Cancer is one of the leading causes of morbidity and mortality even in developed countries. Complex clinical decisions about treatment of tumors are largely guided by imaging findings. Most radiological procedures map the anatomy and morphology of tumors with little or no information about their metabolism ***(Kappor et al., 2004).***

Cross sectional imaging modalities such as ultrasound, computed tomography (CT), magnetic resonance imaging (MRI), and positron emission tomography (PET) have benefited from rapid technical advances in recent years ***(Gaa et al., 2005).***

Because of the importance of the liver, and because it is one of the most common locales for spread of malignant disease, the liver is the abdominal organ of greatest interest for the use of imaging studies ***(Semelka . 2005).***

Modern cross sectional structural imaging techniques like ultrasonography, computed tomography (CT) and magnetic resonance imaging (MRI) provide high resolution images that aid in accurate detection, delineation and anatomic localization of liver malignancies. However, characterization of lesions into benign and malignant etiologies is often not possible from structural imaging techniques alone. Although functional imaging techniques like positron emission tomography (PET) with radiolabeled ^{18}F labeled 2-fluoro-2-deoxy-D-glucose (^{18}F-FDG) often provide critical information pertaining to a benign or malignant etiology, accurate anatomic localization of abnormal regions of uptake is often problematic due to inadequate spatial resolution. These circumstances make the combination of PET with CT appealing. It has the potential of offering a comprehensive ‘one-stop’ examination by providing information about lesion etiology based on functional activity on PET scanning along with precise anatomic localization and other morphological features of the abnormality with CT scanning ***(Wahl RL. 2004).***

Imaging of the liver is undertaken for the detection and characterization of suspected primary or secondary neoplasms, prior to planning a surgery or chemotherapy pump placement, for assessing treatment response, for evaluating biliary pathology, and for screening for liver neoplasms in high risk groups ***(Shani et al., 2004).***

PET now is widely applied in clinical oncology. The development of the resolution and sensitivity of PET have been improved by the availability of newer scanners with a larger field of view and introduction of integral PET and computer tomography (CT) systems in 2000 ***(Blodgett et al., 2007).***

The CT portion of PET/CT provides valuable anatomic and pathologic information to the functional information provided by PET and help improve the overall accuracy of the combined study ***(Kamel et al., 2004).***

Positron emission tomography (PET) is a functional imaging modality that has been documented to be useful in patient care. Oncologic PET imaging is used for a wide variety of neoplasms, mainly for staging and follow up, differentiation of equivocal morphologic findings, therapy stratification, and monitoring ***(Rosenbaum et al., 2006).***

Because PET imaging is based on the physiologically mediated distribution of the administrated tracer but not on anatomic information, the addition of computed tomography (CT) to PET may improve the interpretation of PET. Combined PET and CT offers several potential advantages over PET alone that may influence the clinical routine ***(Rosenbaum et al., 2006).***

FDG-PET is useful in the follow up of patients who underwent surgical procedures of the liver, since it is exquisitely sensitive in detecting residual or relapse malignancy in scarred liver tissue following both resection and local ablative techniques. For follow-up during systemic therapy, early FDG-PET appear predictive for response to therapy ***(Weiring et al., 2004).***

18F-FDG PET and PET/CT can provide added diagnostic information compared with conventional imaging in patients after radiofrequency ablation of liver metastases and can be useful in guiding repeat ablation procedures ***(Barker et al., 2005).***

Advances in imaging technology have improved our ability to detect, characterize, and stage metastatic liver disease. PET/CT therefore possibly proved superior to CT alone when assessing liver cancer ***(Veit et al., 2006).***