Role of Fluorine-18-Fluorodeoxyglucose(F-18-FDG) Positron Emission Tomography (PET) in Management of Gastrointestinal Malignancy

Essay
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Abstract

FDG is used because it is taken up by many types of tumors and produces images of good contrast. PET has been found to assist in diagnosis, staging, monitoring therapy response and assessing recurrence in patients with different tumors**,** PET using F-18-FDG is more accurate than CT or other conventional imaging modalities for diagnosis of previously unknown recurrent or metastatic malignant foci, focal colonic F-18-FDG uptake has a high 70-80% probability of showing corresponding abnormal histopathological Finding**.**

Key Words :

Alfa-fetoprotein – Endosongraphy – Flurothymidine .

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Table of Contents

List of Figures

List of Abbreviations

5-Fu	5-Flurouracil
ACS	American cancer society
AFP	Alfa-fetoprotein
BE	Barium enema
CEA	Carcinoembryonic antigen
CT	Computed tomography
DCBE	Double contrast barium enema
DNA	Deoxyribonucleic acid
DOI	Depth of interaction
DRE	Digital rectal examination
ERCP	Endoscopic retrograde cholangeopancreatography
EUS	Endosongraphy
F18	Flourine 18
FDA	Food and Drug Association
FDG	FluoroDeoxyGlucose
FLT	Flurothymidine
IMC	International Medical Center
FOV	Field of vision
FWHM	Full width at half maximum
GCSF	Growth colony stimulating factort
GI	Gastrointestinal
GIST	Gastrointestinal stromal tumours
GIT	Gastrointestinal tract
HBV	Hepatitis B virus
HCC	Hepatocellular carcinoma
HCV	Hepatitis C virus
HDV	Hepatitis D virus
HGV	Hepatitis G virus
HIDAC	High density avalanche chamber
HPLC	High performance liquid chromoatography
LaBr3	Lanthanum bromide
LOR	Line of response
LSO	Lutetium orthosilicate
LYSO	Lutetium yttrium orthosilicate
MALT	Mucosal associated lymphoid tissue
MRI	Magnetic resonance imaging
PET	Positron Emission Tomography
PMT	Photo Multiplier Tube
SUV	Standard uptake volume

Introduction

Positron emission tomography (PET) is one of the fastest growing areas in nuclear medicine, and oncologic imaging is the most rapidly expanding use of PET.

Conventional diagnostic imaging such as magnetic resonance imaging (MRI), computed tomography (CT) and ultrasound reveal structural abnormalities. However, limitations of conventional imaging are well known in differentiating residual lesions or recurrent malignant tumors from post-therapy fibrosis***(Peter et al., 2005)***.

A number of tracers have been developed for PET, however F-18 fluorodeoxyglucose (FDG) accounts for most of the routine clinical use of PET in oncology at present. FDG is used because it is taken up by many types of tumors and produces images of good contrast. FDG is also retained in a number of normal organs, such as the heart, bowel, kidneys and bladder, this is easily recognized by physician as normal biodistribution. PET has been found to assist in diagnosis, staging, monitoring response and assessing recurrence in patients with different tumors ***(Peter et al., 2005)*.**

PET using F-18-FDG is more accurate than CT or other conventional imaging modalities for diagnosis of previously unknown recurrent or metastatic malignant foci, focal colonic F-18-FDG uptake has a high 70-80% probability of showing corresponding abnormal histopathological Finding ***(Agress et al., 2004)*.**

Integration of PET and CT can provide synergistic benefit regardless of the technique applied. Hybrid PET/CT is more expensive than software fusion, but it delivers a fast, logistically easy and more reliable image correlation. While software image fusion is likely to result in suboptimal results. The true benefit of integrated PET/CT not only depends on integration of images, but also on the integration of expert opinions. Therefore, it is strongly advised that joint reading sessions take place with the radiologist and nuclear medicine physician with the appropriate clinical input from clinical oncologists and/or surgeons ***(Veit et al., 2005)*.**

Aim of the work:

The goal of this study is to focus light on the role of fluorine-18-fluorodeoxyglucose positron emission tomography in diagnosis, staging and follow up of gastrointestinal malignancy.

Histopathology of GIT cancers

Gastrointestinal (GI) tumors is commonly seen in the esophagus, stomach,, colon, rectum, liver, pancreas and less likely in gallbladder and biliary system ***(Catalano et al., 2001)*.**

Predisposing causes in GIT cancers:

Dietary, environmental and genetic factors contribute to the etiology, pathogenesis and risk for gastrointestinal cancers. Measurements of cell proliferation and differentiation further identify abnormal cellular properties associated with increased susceptibility to gastrointestinal cancer. Genetic alterations of cancer-related genes and molecules are involved in the course of the development and progression of gastrointestinal cancers. These include genetic instability, abnormalities of oncogenes, tumor suppressor genes, cell cycle regulators, cell adhesion molecules and DNA repair genes ***(Yasuku et al., 2006)*.**

The exact cause of **esophageal cancer** is unknown, although many investigators believe that chronic irritation of the esophagus is a major culprit. Most of the identified risk factors represent a form of chronic irritation. However, the wide variance in the distribution of esophageal cancer among different demographic groups raises the possibility that genetic factors also play a role ***(Heitmiller et al., 2000)*.**

Several risk factors are associated with esophageal cancer, tobacco and alcohol consumption are the major risk factors, especially for squamous cell carcinoma, they increase the risk of

squamous cell carcinoma by five-fold. The effects of the two are synergistic, in that the combination of smoking and alcohol increases the risk by 25- to 100-fold ***(Martin et al., 2000)*.**

In some cases of gastroesophageal reflux, the chronic exposure to acid causes the inner lining of the lower esophagus to change from squamous cells to glandular cells. This is called Barrett's esophagus. Patients with Barrett's esophagus are roughly 30 to 40 times more likely than the general population to develop adenocarcinoma of the esophagus.

A diet low in fruits, vegetables, zinc, riboflavin, and other vitamins can increase risk of developing to esophageal cancer ***(Heitmiller et al., 2000)*.**

The exact cause for **stomach cancer** has not been identified, several potential factors have lead to increased numbers of individuals developing the disease and therefore, significant risk has been associated. Diet, work environment and a history of stomach disorders such as ulcers or polyps are believed to be risk factors. Studies have shown that eating foods with high quantities of salt and nitrites increases the risk of stomach cancer. A high risk for developing stomach cancers has been linked to certain industries especially persons who work in coal mining and those who work processing timber, nickel, and rubber. Several studies have identified Helicobacter pylori that cause chronic inflammation in the inner lining of the stomach which may lead to development of MALT lymphomas in the stomach. Another rare risk factor is the

development of polyps, benign growths in the lining of the stomach ***(Braunwald et al., 2001).***

The exact cause of primary **liver cancer** is still unknown. In adults, however, certain factors are known as higher risk of developing liver cancer. These factors include male sex, age over 60 years, Asian-Americans with cirrhosis have four times as great a chance of developing liver cancer in younger age than African-American, exposure to carcinogens in the environment as aflatoxins, thorium dioxide and vinyl chloride. Cigarette smoking and the use of oral estrogens for birth control also believed to predispose to liver cancer. Hereditary hemochromatosis often develops into cirrhosis and it is estimated that a patient with cirrhosis has 40 times the chance of developing a hepatoma than a person with a healthy liver. Exposure to hepatitis viruses: hepatitis B(HBV), Hepatitis C (HCV), Hepatitis D (HDV), or hepatitis G (HGV). It is estimated that 80% of worldwide HCC is associated with chronic HBV infection ***(Beers et al., 2002).***

Gallstones are the most significant risk factor for the development of **gallbladder cancer**. Roughly 75 to 90 percent of patients with gallbladder cancer also have gallstones. Larger gallstones are associated with a higher chance of developing gallbladder cancer. Chronic inflammation of the gallbladder from infection also increases the risk for gallbladder cancer ***(Ahrendt et al., 2001).***

Risk factors for **colon cancer** often are environmental in sporadic cases (80%) and sometimes genetic (20%). Since malignant

cells have a changed genetic makeup, this means that in 80% of cases, colon cancer is more common in industrialized nations. Diets high in fat, red meat, total calories, and alcohol seem to predispose people to colon cancer whereas high-fiber diets may help to decrease exposure of the colon lining to carcinogens from the environment, as the transit time through the bowel is faster with a high-fiber diet than it is with a low fiber diet. Age plays a definite role in the predisposition to colon cancer as two-thirds of all cases occur after the age of 50 years. There is also a slight increase risk for colon cancer in the individual who smokes. Patients who suffer from inflammatory diseases of the colon known as ulcerative colitis and Crohn's colitis are also at increased risk ***(Golden et al., 2003)*.**

Histopathology of GIT cancers :

Esophageal cancer usually develops in the inner layer cells and grows outward. There are two major types of esophageal cancer. The first occurs in the cells found in the lining of the esophagus, and the cancer is called squamous cell carcinoma(Fig 1). It can develop anywhere along the entire length of the esophagus and represents approximately half of all reported esophageal cancers. The second type of cancer known to occur in the lower third of the esophagus is an adenocarcinoma, which may be associated with a condition known as Barrett's esophagus(Fig 2). ***(Nishida et al., 2000)*.**

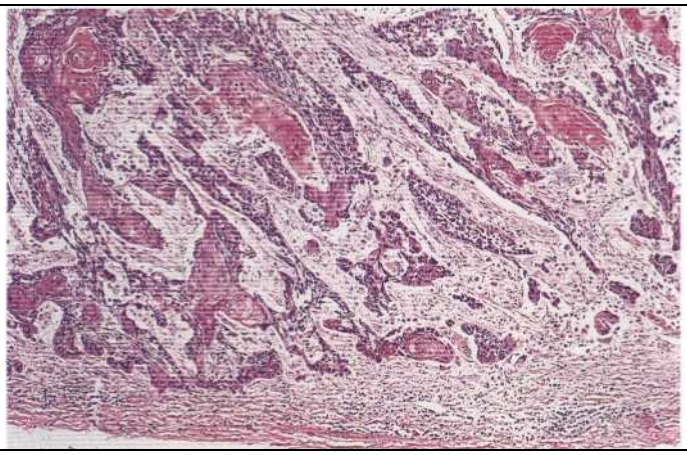

Figure 1: Invasive well-differentiated keratinizing squamous cell carcinoma of the esophagus.(Bytzer et al,2000).

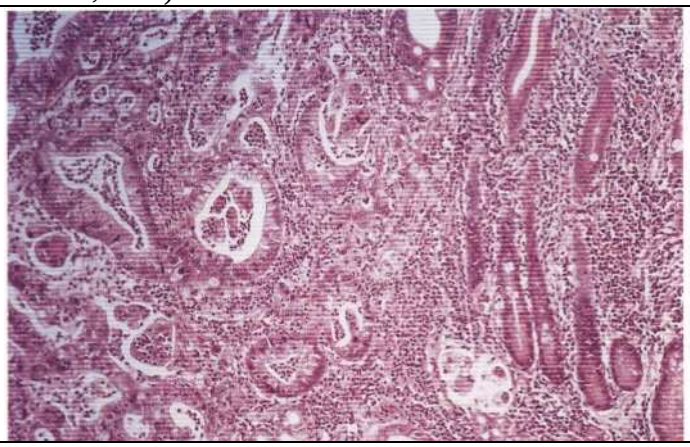

Figure 2: Adenocarcinoma arising from Barrett' esophagus..(Bytzer et al,2000).

In cancer of the stomach it may grow along the stomach wall into other organs such as the esophagus or small intestine. Or it may go through the stomach wall and invade the nearby lymph nodes or organs such as the liver, pancreas, and colon. It may also spread to more distant organs, such as the lungs, the lymph nodes and the ovaries. The major type of stomach cancer is adenocarcinoma (90%)(Fig 3) ***(Feczko et al., 2000)*.**

Other less common types of stomach cancers are the gastric carcinoma with lymphoid stroma (medullary carcinoma), gastric carcinoma with extensive neutrophilic infiltration and adenosqamous and squamous cell carcinoma ***(Campbell et al., 2006)*.**

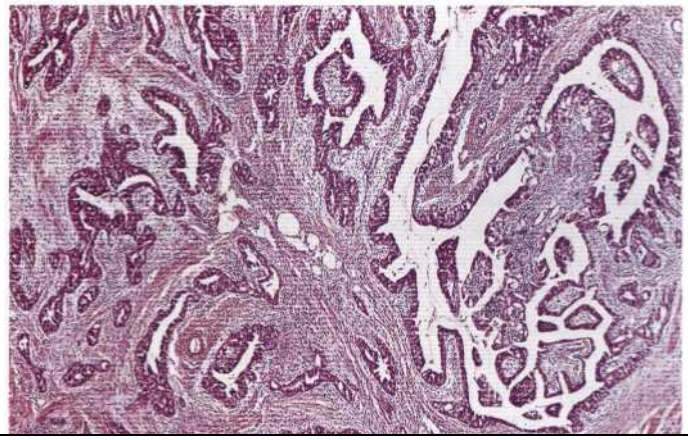

Figure 3: Well-differentiated gastric adenocarcinoma of mixed papillary and tubular types.(Habermann et al,2004).

Liver cancers can be classified into two types. They are either primary, when the cancer starts in the liver itself, or metastatic, when the cancer has spread to the liver from some other part of the body. About 80% to 90% of primary liver cancers are hepatomas. One type of primary liver cancer, called a hepatoblastoma , usually occurs in children younger than four years of age and between the ages of 12 and 15. Unlike liver cancers in adults, hepatoblastomas have a good chance of being treated successfully. Approximately 70% of children with hepatoblastomas experience complete cures. If the tumor is detected early, the survival rate is over 90%(Fig 4) ***(Zock et al., 2001)*.**

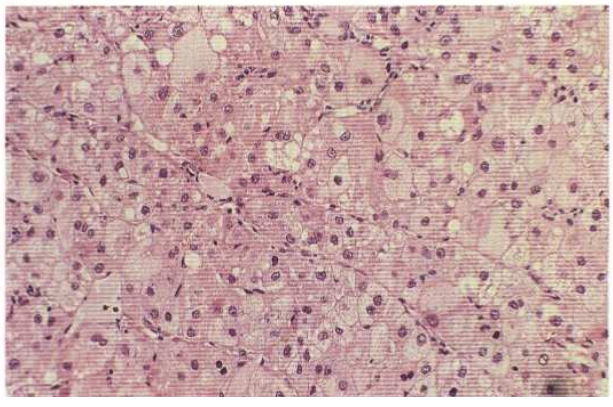

Figure 4: Well-differentiated liver cell carcinoma with compressed liver cell plates and visible endothelial lining of sinusoids(Beers et al,2002).

The second major category of liver cancer is metastatic liver cancer it is about 20 times more common than primary liver cancer. Primary cancers in the colon, stomach, pancreas, rectum, esophagus, breast, lung, are the most likely to metastasize to the liver. It is not unusual for the metastatic cancer in the liver to be the first noticeable sign of a cancer that started in another organ ***(Harrison et al., 2004).***

Several types of cancer can occur in **gall bladder**, such as adenocarcinoma, squamous cell carcinoma, carcinosarcoma and small cell (oat cell) carcinoma, all of them are uncommon ***(Catalano et al., 2001).***

In **pancreatic cancer**, the cancer can develop either exocrine pancreatic cancer which is much more common as adenocarcinoma or less common endocrine tumors as Insulinoma, Gastrinoma, Glucagonoma, Vipoma and Somatostinoma ***(Feczko et al., 2000).***

Colorectal cancers usually start in the inner most layer and can grow through some or all of the other layers. Colorectal cancers are common, and occur more frequently in people over the age of 50 years. Over 95% of colorectal cancers are adenocarcinomas(Fig 5). Other, less common types of colorectal cancers are: carcinoid tumors, and gastrointestinal stromal tumors ***(Royce et al., 2000).***