Fluorine-18 2-fluoro-2-deoxy-D-glucose (18F-FDG) positron emission tomography (PET) has been used extensively for the diagnosis of various malignancies with high rates of sensitivity and specificity (1). This imaging technique is based on the identification of the increased glycolysis that occurs in malignant cells. FDG is preferentially concentrated in the malignant cells due to an increase in the number of membrane glucose transporter proteins known as the GLUT transporters in the tumor cells.

In a mechanism similar to glucose, FDG is subsequently phosphorylated by hexokinase to FDG 6-phosphate. FDG 6-phosphate is not efficiently metabolized, and therefore is trapped within the cell (2). Because of increased metabolic activity, most lung malignancies have a threshold standardized uptake value of 2.5, representing a much greater FDG uptake than found in normal tissues (2). According to a recent meta-analysis, the estimated sensitivity of PET for identifying a malignant pulmonary lesion is 96.8% and its specificity is 77.8% (3).

However, increased FDG uptake is not always limited to malignant tissues, and it is well recognized that inflammation may lead to FDG accumulation of macrophages and other activated inflammatory cells. Moreover, the development of the PET/CT scanner allows for the simultaneous acquisition of both anatomic and functional data and reassessment of biological distribution patterns of physiological tracers. Thus, PET/CT can improve image interpretation and can have an impact on the diagnostic and therapeutic aspects of patient management (4).

In this report, we demonstrate the physiological FDG uptake of normal structures in the thorax using PET/CT imaging and illustrate many benign pathological conditions with standardized uptake values greater than 2.5.

Index words: Positron emission tomography (PET) Thorax

Fluorine-18 2-fluoro-2-deoxy-D-glucose (18F-FDG) positron emission tomography (PET) has been used exclusively to diagnose malignancies. However, increased FDG uptake is not always limited to malignant tissue. Many false positive findings for PET have been reported. Moreover, the use of PET/CT may allow the reassessment of previously recognized patterns of physiological bio-distribution of a tracer. In this report we demonstrate the physiological FDG uptake of normal structures in the thorax using PET/CT imaging and illustrate many benign pathological conditions with standardized uptake values greater than 2.5.
Normal whole body FDG distribution

For whole body PET examinations, performed between 1 and 2 hours after IV administration of FDG, the brain, heart and urinary tract are the most prominent sites of tracer accumulation. The brain, an obligate user of glucose, typically shows high uptake of FDG in the cortices, thalami and basal ganglia. Cortical activity may be reduced in patients under sedation or general anesthetic. The myocardium has similar FDG avidity in the fed state as the brain. FDG follows the urinary excretory route and it will be present in the bladder and to varying degrees in the upper urinary tract (5).

Elsewhere, tracer activity is distributed at low levels in recognizable anatomic structures on attenuation-cor-

Fig. 1. Normal whole body FDG distribution. The brain, heart and urinary tract are the most prominent sites of tracer accumulation, one hour after IV administration of FDG.

Fig. 2. Uptake in the supraclavicular area fat (“USA-fat”). A 35-year old woman with breast cancer was evaluated after a mastectomy and chemotherapy. (A and B) PET/CT (A) and non-contrast CT (B) clearly reveal the location of the bilateral FDG uptake to be the fatty tissue of the supraclavicular regions, and not the lymph nodes (peak-SUV 3.7, arrows).

Fig. 3. FDG uptake in brown adipose tissue in a 42-year-old woman with breast cancer after breast conserving surgery. (A and B) Axial images of PET/CT (A), and non-contrast CT (B) obtained at the level of the aortic arch show increased FDG uptake in the right prevascular space of the mediastinum (peak-SUV 4.5, arrow), localized to the adipose tissue.
rected images. In the neck, it is common to see moderate symmetrical activity in the tonsillar tissues. The adenoidal tissue is not usually perceptible in adults but may show noticeable uptake in children. FDG activity associated with the laryngeal musculature or thyroid tissue is frequently seen. In the chest, there is variation in the lung regions, being greater in the inferior and posterior segments. In the abdomen, homogeneous, low-grade accumulations are seen in the liver and spleen. Small and large bowel activities are quiet variable. The bone marrow is normally associated with FDG accumulation at levels higher than blood pool activity, and vertebral bodies are therefore consistently identified, as well as other major marrow containing skeletal structures such as the pelvis, hips and sternum [6].

The normal distribution of FDG is shown in Figure 1.

![Figure 1](image1.png)

**Fig. 1.** Normal distribution of FDG uptake. (A and B) Axial images of PET/CT (A) and non-contrast CT (B) show an inverted V-shaped area of anterior mediastinal uptake (peak SUV 2.7, arrows), corresponding to the thymus. In young patients, the thymus is normally associated with moderate FDG uptake. Given the morphological features, this finding is typical of normal thymic uptake.

![Figure 4](image2.png)

**Fig. 4.** Normal FDG uptake in the thymus of a 16-year-old boy. (A and B) Axial images of PET/CT (A) and non-contrast CT (B) show an inverted V-shaped area of anterior mediastinal uptake (peak SUV 2.7, arrows), corresponding to the thymus. In young patients, the thymus is normally associated with moderate FDG uptake. Given the morphological features, this finding is typical of normal thymic uptake.

![Figure 5](image3.png)

**Fig. 5.** Muscle uptake of FDG in a 14-year-old girl. (A) A coronal PET image shows a bilateral symmetric pattern of FDG uptake in both supraclavicular regions, similar to that for USA-fat (arrowheads). (B) An axial PET/CT scan obtained at the level of the thyroid shows increased FDG uptake localized to the anterior scalene muscles (peak SUV 2.2, arrowheads), and not to the adipose fat.
Normal Variant FDG Distribution in the Thorax

FDG uptake depicts tissue glucose metabolism. Hence, in addition to the abnormal glucose metabolism associated with a malignant neoplasm, FDG PET/CT reveals normal variations in glucose metabolism. Some of the normal variations may mimic pathological processes (5, 6).

Brown Adipose Tissue

Increased FDG uptake in the supraclavicular regions is well known, and is called “USA-fat”. It was thought to be attributed to muscular uptake. However, PET/CT images subsequently proved that these foci of FDG uptake were localized to adipose tissues rather than to muscles (Fig. 2). Increased FDG uptake by fat is visible in the paraspinal area, mediastinum, and upper abdomen as well as the neck (Fig. 3). This FDG uptake can be explained by non-shivering thermoregulation that involves a direct increase in glucose uptake by brown adipose tissue caused by increased sympathetic nervous system activity and the need for glucose continuing the process of lipolysis (7).

Thymus

An increase in FDG uptake can be seen in normal thymic tissue in pediatric and adult patients, and the degree of FDG uptake by the thymus overlaps the values of thymic hyperplasia and neoplasia (8). The characteristic shape [an inverted V or Y], facilitates the differentiation from other anterior mediastinal tumors (Fig. 4) (6).

Skeletal Muscle

At rest, skeletal muscles rely on fatty acid oxidative metabolism for energy. However, with increased energy demand, glycolysis becomes the major source of energy for the skeletal muscles. Skeletal muscles in active contraction and tension demonstrate elevated FDG accumulation (Fig. 5). Additionally, insulin increases muscle uptake of glucose (Fig. 6) (5).

Non-malignant Pathological Uptake in the Thorax

Inflammatory cells such as lymphocytes, neutrophils, and macrophages have increased glucose utilization, and increased FDG uptake has been reported in various inflammatory and infectious lesions (9).

Although FDG uptake in infectious and inflammatory lesions can increase the number of false-positive results and reduce the specificity of PET that is performed for oncology examinations, conversely FDG PET can be exploited for detection and assessment of infectious and

![Fig. 6. Diffuse muscular FDG uptake in a 70-year-old man with diabetes mellitus. Insulin increases muscle uptake of glucose.](image)

![Fig. 7. Tuberculosis in a 71-year-old woman, proven by a percutaneous needle biopsy of the consolidation. An axial PET/CT scan at the level of the subcarina shows diffuse FDG uptake in the triangular consolidation of the right upper lobe (peak SUV 3.6, thin arrows) and the peribronchial regions (peak SUV 4.0, arrow).](image)
inflammatory lesion activities, especially in the management of the patients with fever of unknown origin (9).

**Granulomatous Disorder**

Active granulomatous processes such as tuberculosis, fungal infections and sarcoidosis have been reported to accumulate FDG and cause false-positive results for a malignancy on PET scans. Moreover, Goo et al. (10) reported that 90% of tuberculomas were falsely thought to be positive as malignant nodules when using 2.5 as the threshold SUV.

Granulomatous lesions are characterized by cellular infiltrates, granuloma formation and macrophage proliferation. Activated inflammatory cells have markedly increased glycolysis. Uptake of FDG is more rapid in the inflammatory cells and as a rule, inflammatory tissues demonstrate avid FDG uptake, in which the uptake is predominantly in the cellular component. In tuberculosis, the cellular infiltrate is composed of lymphocytes and macrophages (Fig. 7) (10). FDG uptake by sarcoid granulomas is also common, which appears typically as active lymph nodes in the mediastinum and hilar regions (Fig. 8) (9).

**Non-tuberculous Infection**

FDG rapidly accumulates at sites of bacterial infection and in the reactive lymph nodes, resulting in a high contrast between the affected and non-involved tissues. In addition to the increased glycolytic activity, the FDG accumulation in activated inflammatory cells is attributed to the increased expression of the glucose. Moreover, it is possible that glucose metabolism and FDG uptake in inflammatory cells is more complicated than in malignant cells. For example, there is evidence that numerous cytokines and growth factors, levels of which are often increased during infection, may dramatically affect glucose uptake by the inflammatory cells (9).

Pyogenic infections such as abscess and pneumonia typically cause diffuse relatively uniform FDG activity. However, with cavitation or necrosis the appearance can be indistinguishable from certain neoplasms with cavities and necrotic centers (9).
Non-infectious Non-granulomatous Benign Conditions

Normal wound healing is associated with an inflammatory response and thus with modest FDG uptake (Fig. 9). Similarly, a resolving hematoma or thrombus results in modest FDG uptake since leukocytic infiltration is present in the granulation tissue. Recent surgery can result in spuriously increased FDG uptake in areas of resolving inflammation. Sternotomy sites will show modest FDG uptake as well (Fig. 10) [9].

Focal FDG uptake is also seen at the insertion sites of uncomplicated indwelling percutaneous tubes or lines and permanent venous ports (Fig. 11) [5, 6].

Major arteries complicated by advanced atheromatous disease will often be unexpectedly conspicuous due to FDG uptake by the arterial walls (Fig. 12). Atherosclerosis is an inflammatory disease, characterized by subendothelial lipid accumulation, monocyte/macrophage accrual, and vascular calcification. Macrophage aggregation results in FDG uptake. As aortic aneurysm is characterized by transmural inflammation with lymphocyte and macrophage aggregation, FDG PET can image the aneurysmal wall [5].

Degenerative or inflammatory joint disease can give rise to elevated FDG uptake. Elevated tracer uptake in sternoclavicular joints, and to a lesser extent in the acromioclavicular joints that are frequently demonstrated on bone scans, are seen far less frequently on a FDG PET scan (Fig. 13) [5].

The FDG uptake associated with radiation therapy can be seen even months after the therapy and the up-
take is usually slightly greater than blood pool activity. Radiation pneumonitis, however, can be intense and difficult to differentiate from an active infection or neoplasm [Fig. 14] (7).

Certain benign tumors and non-infectious inflammatory conditions have increased FDG uptake, and they can have an intensity that is entirely within the range of a malignant neoplasm [Fig. 15] (7). Yet, benign tumors of the lung with FDG uptake have rarely been reported.

Summary

FDG PET plays an important role in the evaluation of cancer. Although highly sensitive for the detection of a malignancy, FDG uptake in physiological and benign processes is also well documented. Recognition of the unusual patterns of FDG bio-distribution is important in order to avoid misinterpretation of the PET images. PET/CT provides accurate information regarding both the morphological and metabolic aspects, enabling precise localization of FDG uptake within distinct structures and improving the diagnostic interpretation. Moreover, the utility of PET/CT in the detection and characterization of infectious diseases is promising.

References

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18F-FDG uptake는 PET/CT의 정상적 적용을 위한 중요한 표지자입니다. PET/CT는
FDG uptake의 정상적인 분포를 모니터링하는데 중요한 역할을 합니다. PET/CT는
FDG uptake가 정상적인 경우를 확인하는 데 도움이 됩니다. FDG uptake가 정상
일 때, PET/CT는 정상적인 결과를 나타내며, FDG uptake가 이상일 때, PET/CT는
이상한 결과를 나타냅니다.