# PHYSIOLOGICAL UPTAKE OF 18F-FLUORODEOXYGLUCOSE IN PET/CT IMAGING: A FREQUENT DIAGNOSTIC PITFALL

# PET/BT GÖRÜNTÜLEMEDE FIZYOLOJIK 18F-FLORODEOKSIGLUKOZ TUTULUMU: SIK GÖRÜLEN BIR TANISAL TUZAK

PHYSIOLOGICAL FDG UPTAKE IN PET/CT

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**Öz**

Normal fizyolojik durumlar bile vücutta beyin, kalp, iskelet kası, üriner sistem, gastrointestinal sistem, kahverengi yağ, lenf dokusu, karaciğer, dalak, tiroid bezi, timus, tükrük bezleri, meme dokusu, gonadlar, uterus ve kemik iliği gibi çok sayıda lokalizasyonda artmış flor-18 florodeoksiglukoz (FDG) tutulumuna neden olabilir. Pozitron emisyon tomografi/bilgisayarlı tomografi görüntülerinin doğru değerlendirilmesi ve yalancı pozitif tanıdan kaçınılması için fizyolojik FDG tutulumu ile ilgili ayrıntılı bilgiye sahip olunması elzemdir. Fizyolojik FDG tutulumunu olabildiğince azaltmak için doğru önlemler alınmalıdır.

**Anahtar Kelimeler**

Fluorodeoksiglukoz F18; Pozitron-Emisyon Tomografi/Bilgisayarlı Tomografi; Fizyolojik Olaylar

**Abstract**

Even normal physiological conditions can cause elevated fluorine-18 fluorodeoxyglucose (FDG) uptake in several locations, such as the brain, heart, skeletal muscle, urinary system, gastrointestinal system, brown fat, lymphatic tissue, liver, spleen, thyroid gland, thymus, tongue, salivary glands, breast tissue, gonads, uterus, and bone marrow. Detailed knowledge of physiological FDG uptake is crucial for correct evaluation of positron emission tomography/computed tomography images and for avoiding false-positive diagnoses. Proper measures should be taken to decrease physiological FDG uptake as much as possible.

**Keywords**

Fluorodeoxyglucose F18; Positron-Emission Tomography/Computed Tomography; Physiological Phenomena

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## Introduction

During the last decade, fluorine-18 fluorodeoxyglucose (FDG)-positron emission tomography/computed tomography (PET/CT) has gained a crucial role in oncological imaging [1, 2]. The image interpreter should be aware of the diagnostic pitfalls in PET/CT practice such as physiological FDG uptake. Even normal physiological conditions can cause elevated FDG uptake in several locations [3] including the intestines, lymphatic tissue, muscle tissue, and brown adipose tissue (BAT) [4], though such non-pathological distribution of FDG is dependent on many factors [5]. Increased FDG in non-relevant organs or anatomical sites may be confusing; for instance high concentrations of FDG in normal cerebral cortex restricts its use in diseases of these regions [4, 6]. In daily practice, FDG-PET/CT is usually not utilized for primary imaging of cerebral metastases [6]. In this review, main organs and tissues that demonstrate physiological FDG uptake are included and the measures to be taken for prevention of the adverse effects of normal FDG uptake on image interpretation, are discussed.

### *Common locations of physiological FDG uptake*

After its intravenous administration, FDG can normally accumulate in the heart, brain (particularly cerebral cortex), and the urinary system (kidneys, ureters, urinary bladder filled with urine), whereas elevated FDG uptake may also be detected in normal individuals in the skeletal muscle after exercise, in the gastrointestinal system including the stomach, esophagus, and the intestines including terminal ileum and cecum [6, 7]. Hyperventilation and crying in children can cause increased uptake of the diaphragm [8]. FDG uptake in the normal esophagus, stomach, small intestine, and colon is very variable and can be mild, moderate, or intense with a localized or diffuse pattern. Mild esophageal uptake may be demonstrated on sagittal images. A crescent shaped, diffuse, but mild uptake can usually be seen in the stomach wall. Small bowel uptake is changeable and, if present, it is generally mild. FDG uptake of the colon is very variable and may be locally or diffusely intense [8, 9]. Other commonly encountered organs or tissues in which physiological FDG uptake may cause false-positive results are as follows: liver, thyroid gland, thymus in the pediatric age group, tongue, salivary glands, Waldeyer's ring (adenoids, palatine, and lingual tonsils), soft palate, breasts, gonads, uterus, bone marrow (not the bone itself), and spleen [6, 8–11]. In pediatric patients, an increased uptake of Waldeyer's ring is most prominent between ages 6–8, is usually symmetrical, and shows a decrease during the following years [9]. Despite the fact that the thyroid gland shows various types of FDG uptake, mild diffuse uptake can be seen within normal glands of some patients as a normal variation, though some benign causes such as thyroiditis or goiter can also demonstrate such a diffuse uptake. In normal individuals, salivary glands symmetrically show mild to moderate physiological FDG uptake. Skeletal muscles of the neck including sternocleidomastoid muscles, facial muscles, the inferior obliquus capitis muscle, or prevertebral muscles often demonstrate focal uptake patterns rather than being symmetric, usually representing the myotendinous junctions and insertions, that causes difficulty in distinguishing them from pathological lymph nodes. Several muscles of the pharynx, including pterygoid muscles and the muscles of the mouthfloor, such as the mylohyoid muscle, show symmetric uptake, but in cases of an asymmetric uptake, it can be difficult to differentiate these focal areas from malignancy. Diffuse and focally symmetric FDG uptake of the tongue is also frequent. Increased uptake of laryngeal muscles during talking or coughing is a frequent finding. The cricopharyngeus muscle may be depicted as an area of locally increased activity. Coughing also causes increased activity in the pharyngeal constrictor muscles during the uptake phase [11]. Extraocular muscles such as medial and lateral rectus muscles can also demonstrate increased uptake, that is usually bilateral. In normal children, the thymus is commonly depicted as a bilobed structure similar to an inverted "V" on coronal images, representing homogeneous uptake [8]. After meals, elevated blood glucose and insulin can result in increased cardiac uptake [8, 9]. Because of the glandular structures, moderate uptake can be demonstrated in normal breasts [12]. A much increased FDG activity may be seen in adolescent females who have dense breast tissue [9] and in lactating women [13]. Normally, both testes may symmetrically demonstrate a moderate and a diffuse uptake pattern. Ovaries may show increased uptake during ovulation and endometrial uptake may be variable depending on the menstrual cycle phase; menstruation or corpus luteum cysts can cause false-positive results [10]. Bone marrow uptake less than hepatic uptake is normal, usually homogeneous, and more extensive in pediatric patients compared to adults. Though no FDG uptake can be demonstrated in normal bone, bilateral linear activity can be seen in long bone physes of children [9]. The normal spleen displays faint FDG uptake [8].

### *The role of brown fat*

Prominent FDG uptake within BAT, present for heat production in the cervical region, axillas, mediasten, and paravertebral locations, particularly in children, can be confusing during evaluation of malignant tumours and lymph nodes on PET/CT images [9, 14, 15]. Younger age, female gender, a lower body mass index, and a low environmental temperature are predisposing factors for more BAT with increased FDG uptake [14, 16]. Focal FDG uptake by BAT may be confused with the skeletal muscles because they usually look alike on PET/CT images. However, anatomically, FDG uptake within BAT shows no correlation with a certain skeletal muscle of that location [11] that tends to be bilateral and symmetrical [9].

### *Measures to be taken*

While evaluating an anatomical location with a high FDG uptake, an image interpreter should obtain the patient's current clinical data and medical background, evaluate the features of FDG uptake (i.e. bilaterality), take the anatomical properties into account, use reconstructed PET/CT images, and check the radiological images yielded by other modalities, in order to discriminate a physiological uptake from a malignant one [6]. In physiological processes, there is generally symmetrical or bilateral uptake of FDG. But since symmetry alone cannot rule out malignancy or indicate the presence of physiologic processes [11], all of the above mentioned data and factors should be taken into consideration. Prominently asymmetric uptake by sternocleidomastoid muscle can be differentiated from malignant lymph node uptake by checking reconstructed PET/CT images that depict the linearity of the muscle. Additionally, the outermost location of paraspinal muscles frequently helps to identify the reason for increased FDG uptake [11]. Since the increased FDG uptake of normal brain tissue limits the use of FDG in diagnosis of these areas, most scans are of the patient's torso, starting from the base of the skull and ending mid thigh [4]. Increased muscle activities such as exercise should be avoided

or minimized 1–2 days before FDG-PET/CT scanning [17, 18]. Avoiding repeated movements, such as hyperventilation, crying of a child, persistant coughing, fidgeting, or mastication, is also necessary [17, 19]. Fasting for about 4–6 hours before oncological FDG-PET/CT imaging decreases unnecessary myocardial uptake [9]. After the injection of FDG, the patient should rest on a comfortable sitting apparatus or bed in a silent room with low interior light, without talking or making unnecessary movements to help reduce muscle uptake as much as possible [6, 20]. In some patients, administration of medications such as diazepam before FDG injection may be necessary to reduce the tension in the muscles [19]. For minimizing the FDG uptake of BAT, cold exposure should be avoided before the scanning and the patients should wear warm clothes. A warm temperature is necessary, and if needed or desired, more blankets should be provided [6]. In individuals with increased FDG uptake in their BAT, oral β-blockers can be administered 1 hour before the injection of FDG, if their heart rates and blood pressures are controlled [17]. To differentiate locally increased activity in the neck and upper thorax from that of the muscles or pathological lymph nodes, the attenuation has to be measured on plain CT images so that fat density (-50 to -150 Hounsfield units) can help in the diagnosis [11]. To avoid the artifacts resulting from FDG-filled urinary bladders, patients should be told to go to the toilet to urinate before the scanning. In some patients, catheterization of the urinary bladder may be needed to better evaluate lesions in the pelvic region. For such patients, scanning should start from the pelvis and continue to the cranium. If the examination involves the neck and the esophagus, drinking or rinsing the mouth with water will help reduce the FDG accumulated in saliva [19]. Subcutaneous injection of FDG into the soft tissues of the arm should be avoided because of the possibility of depositing FDG into axillary or supraclavicular lymph nodes. In such situations, follow-up scans after a couple of weeks can demonstrate that there is no persistent nodal uptake [11]. The site of FDG injection should be recorded for the interpreters of the images [19].

### *Conclusion*

A thorough knowledge of physiological FDG uptake is necessary for correct interpretation of PET/CT images and to avoid making false-positive diagnoses. Proper measures before and during PET/CT imaging should be taken to decrease physiological FDG uptake as much as possible.

### *Competing interests*

The authors declare that they have no competing interests.

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