18F-FDG PET/CT of Adrenal Lesions

**OBJECTIVE.** The purpose of this review is to describe FDG uptake characteristics of adrenal lesions, which can show increased FDG uptake on PET/CT.

**CONCLUSION.** Both benign and malignant adrenal lesions can show increased FDG uptake. Knowledge of the uptake characteristics of these lesions is helpful for increasing diagnostic accuracy and expanding the differential diagnosis for adrenal lesions.

**fluorine-18-FDG PET/CT** is a useful imaging technique in characterizing adrenal masses [1–4]. However, false-positive interpretations may result from benign lesions. It may be difficult to differentiate some benign lesions from malignant ones without careful correlation with the patients’ histories, laboratory test results, and other imaging findings. The purpose of this article is to describe the FDG uptake characteristics of adrenal lesions, which can show increased FDG uptake on PET/CT.

**Adrenal Hyperplasia**

Cushing syndrome is the clinical manifestation of hypercortisolism and is caused by an excess of either exogenous (most frequently) or endogenous glucocorticoids. Endogenous Cushing syndrome is a relatively rare disease and may be adrenocorticotrophic hormone (ACTH) dependent (80–85% of cases) or ACTH independent (15–20% of cases) [5]. ACTH-dependent Cushing syndrome is caused by an ACTH-secreting pituitary adenoma (Cushing disease) (80–85% of cases) or an ectopic ACTH-secreting tumor (10–15% of cases) [6]. ACTH-independent Cushing syndrome is always caused by primary adrenal disease secreting cortisol. It is mainly due to an adenoma or carcinoma. On rare occasions, it may be caused by other diseases, including primary pigmented nodular adrenal dysplasia and ACTH-independent macronodular adrenal hyperplasia [5]. On CT, about 70% of patients with ACTH-dependent Cushing syndrome have enlarged adrenal glands. The mean width of the adrenal limbs positively correlates with the circulating cortisol and ACTH levels. However, having normal-sized adrenal glands (30% of the cases) does not exclude the diagnosis [6]. In primary pigmented nodular adrenal dysplasia, multiple tiny (2–5 mm) nodules can be visible bilaterally, with no overall glandular enlargement and normal intervening adrenal tissue. In ACTH-independent macronodular adrenal hyperplasia, both glands are grossly enlarged and contain nodules up to 3 cm in diameter [5]. On FDG PET/CT, ACTH-dependent Cushing syndrome caused by Cushing disease (Fig. 1) or ectopic ACTH-secreting tumor and ACTH-independent Cushing syndrome caused by ACTH-independent macronodular adrenal hyperplasia can show bilateral adrenal diffuse or nodular enlargement because of adrenal hyperplasia, with bilateral symmetric increased adrenal FDG uptake [7–11]. Cheng et al. [12] reported a case of pulmonary carcinoid tumor showing increased activity at the bilateral adrenal glands. Repeat FDG PET/CT after resection of the tumor showed complete metabolic resolution of the bilateral adrenal glands.

**Adrenal Tuberculosis**

A resurgence of tuberculosis has been observed recently owing to the increasing number of people with suppression of the immune system, the development of drug-resistant strains of *Mycobacterium tuberculosis*, aging population demographics, and an increase in the number of health care workers exposed to the disease [13]. Adrenal tu-
Hemorrhage appears as a thin-walled pseudocyst or one or both adrenal glands. Chronic hemorrhages are nonspecific and can vary widely depending on the degree and rate of hemorrhage are nonspecific and can vary widely depending on the degree and rate of hemorrhage. Acute hemorrhage is characterized by a thin-walled pseudocyst or atrophy [19]. Calcification can develop several months after acute adrenal hemorrhage. Both acute and chronic adrenal hemorrhage can show increased activity on FDG PET, which may result from an inflammatory reaction due to fat necrosis [23–25]. An underlying hemorrhagic tumor must always be considered as a possible cause of adrenal hemorrhage, especially in a patient with a history of malignancy and without discernible risk factors of hemorrhage. It may be difficult to differentiate neoplastic from nonneoplastic adrenal hemorrhage on imaging. Imaging findings that may indicate underlying tumor include intralesional calcification and an enhancing mass with increased FDG uptake [19]. Although nonneoplastic adrenal hemorrhage can show increased FDG uptake, it shows no enhancement on CT. Intralesional calcification is helpful for differentiating neoplastic from nonneoplastic acute adrenal hemorrhage but cannot exclude chronic adrenal hemorrhage.

Adenoma

Adrenal adenomas are common benign adrenal cortical tumors and may be functional or nonfunctional. Adrenal masses are found in approximately 5% of patients imaged with CT. Adenomas represent 75% of all adrenal tumors in patients with no known malignancy [26]. About 20% of adenomas are bilateral [27].

Many studies have confirmed the usefulness of attenuation measurement, at both unenhanced and delayed contrast-enhanced CT, in the differentiation of adenomas from nonadenomas. Around 70% of the adenomas showed lower attenuation (< 10 HU) on unenhanced CT because they contain intracytoplasmic fat [28]. Therefore, most adenomas can be diagnosed with use of an unenhanced CT attenuation threshold of less than 10 HU. However, approximately 30% of adenomas are lipid poor and show attenuation more than 10 HU on unenhanced CT, making them indeterminate [28]. On delayed contrast-enhanced CT, adenomas usually show a higher washout rate than the nonadenomas. Therefore, the washout rate on delayed contrast-enhanced CT is useful for characterizing lipid-poor adrenal masses [29]. CT or MRI cannot differentiate hyperfunctioning adenomas from nonhyperfunctioning adenomas [30]. Most adenomas show FDG uptake less than 3.1 [31]. On visual PET analysis, adenoma usually shows FDG uptake less than that of the liver background [32]. There is no difference in standardized uptake value (SUV) between lipid-rich and -poor adenomas [12]. Hypermetabolic adenomas are rare [31–33] (Fig. 3). About 3% of arterial benign lesions show FDG uptake greater than that of the liver background [32]. The functional state of an adenoma may be related to the FDG uptake degree [33]. The secreting adenomas have a higher mean maximum SUV (SUV_max) than do the nonsecreting ones [1].

Myelolipoma

Myelolipoma is a benign tumor consisting of mature fat interspersed with hematopoietic cells resembling bone marrow. Myelolipoma represents 6% of all adrenal tumors in patients with no known malignancy [26]. It is most often encountered in the adrenal gland but may rarely occur in extraadrenal sites. Myelolipoma manifests in four distinct clinicopathologic patterns, including isolated adrenal myelolipoma, adrenal myelolipoma with hemorrhage, extraadrenal myelolipoma, and myelolipoma associated with other adrenal disease [34].

On CT, a well-defined adrenal mass with a pseudocapsule and the admixture of fatty and higher-attenuation contents are the imaging features of myelolipoma [34]. Myelolipoma with hemorrhage is identified in 11–12% of the patients with myelolipoma [34, 35]. CT is a useful method for detecting the hyperdense hemorrhage in myelolipoma. Myelolipomas with hemorrhage usually are larger than those without hemorrhage. Most of the myelolipomas with hemorrhage are predominantly fat. About 24% of adrenal myelolipomas have calcifications, which usually are small and punctuate [35]. On PET, myelolipomas typically show FDG uptake lower than that of the liver background [36, 37]. Rarely, myelolipoma with extensive adenomatous and hematopoietic elements can show high FDG uptake [38].

Ganglioneuroma

Ganglioneuroma is a rare benign neoplasm and consists of a variable mixture of mature ganglion cells, mature Schwann cells, and nerve fibers [39]. Cellular atypia, mitotic activity, and necrosis are not features of ganglioneuroma. Ganglioneuromas may arise anywhere along the paravertebral sympathetic plexus and, occasionally, from the adrenal medulla, with the retroperitoneum and posterior mediastinum being the most common sites of involvement [39]. Ganglioneuromas tend to occur in adolescents and young adults [39, 40]. The prognosis is excellent, and recurrence is rare after surgical resection. Ganglioneuromas are often asymptomatic even if they are large. About 39% of the patients have
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Adrenocortical Carcinoma

Adrenocortical carcinoma (ACC) is a rare and aggressive malignant neoplasm. ACCs account for only 0.05–0.2% of all cancers or one to two patients per 1 million population per year [52]. The increased use of cross-sectional imaging for unrelated reasons has led to a greater number of ACCs being detected incidentally at an earlier stage [52]. The median survival time is 14.5 months, and the 5-year survival rate is 22%. Age over 40 years and the presence of metastases at the time of diagnosis were the factors recognized as indicating a poor prognosis. At the time of diagnosis, about 68% of patients have endocrine symptoms, most frequently Cushings syndrome with or without virilization, and 30% have distant metastases. About 79% of the tumors are functional [53].

The typical appearance of ACC on unenhanced CT is of a large inhomogeneous but well-defined suprarenal mass that displaces adjacent structures as it grows. After the IV administration of contrast material, there is inhomogeneous enhancement of the tumor, typically with greater enhancement seen peripherally and relatively little enhancement seen centrally, because of central necrosis [52]. There are only a few studies evaluating the role of FDG PET in the management of patients with a diagnosis of ACC in the literature [54]. ACC usually is an FDG-avid tumor. FDG PET or PET/CT can reveal the primary tumor, local recurrence, and distant metastases [55, 56] (Fig. 6). Lebouleux et al. [55] reported that the mitotic rate of ACC was significantly associated with FDG uptake. The FDG uptake degree of \( \text{SUV}_{\text{max}} > 10 \) and the volume of FDG uptake (\( > 150 \text{ mL} \)), which was representative of tumor burden, were related to the prognosis [55]. Fifty-four percent of the patients with an \( \text{SUV}_{\text{max}} \) above 10 died within 6 months after PET/CT examination, whereas none of the patients with an \( \text{SUV}_{\text{max}} \) lower than 10 died. Fifty-five percent of the patients with an FDG uptake volume of more than 150 mL but only 14% of the patients with an FDG uptake volume of less than 150 mL died within 6 months after PET/CT examination [55].

Lymphoma

Occasionally, non-Hodgkin lymphoma (NHL) can involve the adrenal glands. It can be either primary or secondary, with the secondary form being more common. Primary adrenal NHL is very rare, accounting for less than 1% of all NHLs [57]. Primary adrenal NHL commonly occurs in older people (mean age, 68 years), with bilateral adrenal involvement in 60%, and predominantly diffuse large cell histology with B cell immunophenotype. Adrenal insufficiency is present in two thirds of the patients at diagnosis [57]. Secondary adrenal NHL accounts for about 4% of all NHLs [58]. The adrenal gland can be involved at the time of presentation or a site of tumor recurrence after therapy.

Like most lymphomas elsewhere, adrenal lymphoma shows FDG activity [59–61]. In early disease, adrenal lymphoma may present as adrenal enlargement and thickening, maintaining the triangular shape of the adrenal gland (Fig. 7) because of the diffuse infiltration of lymphoid cells [61]. This feature is similar to the appearance of adrenal hyperplasia. Clinical presentations and laboratory tests are useful for differentiating adrenal lymphoma from adrenal hyperplasia. The adrenal cortical function of adrenal lymphoma is normal or insufficient, as opposed to those of Cushings syndrome [62]. In progressive disease, more nodular enlargement is noted. Extensive retroperitoneal tumor may engulf the entire gland (Fig. 8). After successful treatment, decreased FDG avidity is seen in adrenal lesions and other metastatic foci, and the involved adrenal glands will often return to their original size and configuration.

Metastasis

The adrenal glands are common sites of remote metastatic disease. A study of 464 patients with metastatic disease in the adrenal glands has shown that the lung is the most common primary tumor site (35%), followed by the stomach (14%), the esophagus (12%), and the liver and bile ducts (10%) [63]. Adrenal metastases are bilateral in approximately half of patients. They are often asymptomatic and are detected as part of multorgan metastases. Only 4% of adrenal metastases are symptomatic [63]. Patients with surgically removed adrenal metastases have slightly better survival rates than those without surgical resection.

Characterization of adrenal lesions in patients with cancer is essential to predict prognosis of the primary disease, to assess staging, and to direct therapy. FDG PET and PET/CT are accurate methods for differentiating benign from malignant adrenal masses in patients with cancer [2, 64, 65] (Fig. 9). Adrenal metastasis usually shows FDG uptake higher than that of the liver background. Kumar et al. [65] reported that about 90% of adrenal metastases from lung cancers show FDG uptake significantly higher than that of the liver. Ad-
renal metastases from renal cancer, neuroendocrine tumor, early metastases, and necrotic or hemorrhagic metastases may cause false-negative results [1, 64, 65]. Occasionally, benign lesions do show increased FDG uptake compared with that of the liver and may mimic some malignant lesions. Some authors recommend that, in the case of a positive PET scan, incorporation of delayed contrast-enhanced CT for washout analysis may be a useful diagnostic adjunct when determination of the nature of the adrenal disease is essential for patient treatment [2, 32].

**Other Rare Adrenal Tumors**

Other rare benign and malignant tumors can occur in the adrenal gland. FDG PET/CT findings of adrenal hemangioma [66], solitary fibrous tumor [67], angiosarcoma [68], leiomyosarcoma [69], and small cell carcinoma [70] have been reported. The benign adrenal hemangioma and solitary fibrous tumor can show increased FDG uptake mimicking malignancies [66, 67]. For unusual adrenal malignancies, FDG PET/CT is helpful for detecting the primary tumors and distant metastases [68–70] (Fig. 10).

Collision adrenal tumor is a rare entity in which coexistent but histologically different neoplasms exist separately in the same adrenal gland. It usually includes a benign entity and a malignant metastasis. Coexisting benign and malignant tumors, although rare, should be considered as a possibility in patients with known malignancy. One case report described a collision adrenal tumor that appeared as an enlarging and hypermetabolic adrenal mass previously characterized as an adenoma [71]. Another case report showed the role of FDG PET/CT in distinguishing an adenoma from a metastasis in a collision adrenal tumor. The adenoma showed an attenuation of 4 HU on CT and no significant FDG uptake on PET, whereas the metastasis showed higher attenuation on CT and intensely increased FDG uptake on PET [72].

**Conclusion**

Both benign and malignant adrenal lesions can show increased FDG uptake on FDG PET/CT. Knowledge of the uptake characteristics of these lesions is helpful for accurate reading of FDG PET/CT and expanding the differential diagnosis for adrenal lesions.

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### References


28. Caoili EM, Korobkin M, Francis IR, Cohan RH, Dong et al.
FDG PET/CT of Adrenal Lesions

Dunnick NR. Delayed enhanced CT of lipid-poor adrenal adenomas. AJR 2000; 175:1411–1415


Fig. 1—47-year-old man with bilateral adrenal hyperplasia caused by pituitary tumor. 
A, Transverse CT image shows slight enlargement of bilateral adrenal glands (arrow). 
B, Fused FDG PET/CT image shows increased FDG uptake of bilateral adrenal glands (maximum standardized uptake values, 4.1 and 4.4 for right and left adrenal glands, respectively).

Fig. 2—71-year-old man with bilateral adrenal tuberculosis. 
A, Transverse CT image shows enlargement of bilateral adrenal glands (arrow). 
B, Fused FDG PET/CT image shows increased FDG uptake of bilateral adrenal glands (maximum standardized uptake values, 20.1 and 20.9 for right and left adrenal glands, respectively).

Fig. 3—28-year-old woman with virilizing syndrome caused by bilateral secreting adrenal adenomas. 
A, Transverse contrast-enhanced CT image shows enhancing nodule (arrow) in right adrenal gland. 
B, Transverse contrast-enhanced CT image also shows enhancing nodule (arrow) in left adrenal gland. 
C, Fused FDG PET/CT image shows increased FDG uptake of right adrenal nodule (maximum standardized uptake value [SUV_{max}], 4.9). 
D, Fused FDG PET/CT image shows increased FDG uptake of left adrenal nodule (SUV_{max}, 4.2).
Fig. 4—14-year-old boy with right adrenal ganglioneuroma.
A, Transverse enhanced MR image shows tumor (arrow) in right adrenal gland with inhomogeneous enhancement.
B, Fused FDG PET/CT image shows inhomogeneous FDG uptake of tumor (maximum standardized uptake value, 4.2).

Fig. 5—42-year-old woman with right adrenal pheochromocytoma.
A, Transverse enhanced MR image shows tumor (arrow) in right adrenal gland with inhomogeneous enhancement.
B, Fused FDG PET/CT image shows increased FDG uptake of tumor (maximum standardized uptake value, 6.1).

Fig. 6—35-year-old man with right adrenal adrenocortical carcinoma.
A, Transverse contrast-enhanced CT image shows tumor (arrow) in right adrenal gland with inhomogeneous enhancement.
B, Fused FDG PET/CT image shows increased FDG uptake of tumor (maximum standardized uptake value, 33.8) and retroperitoneal metastatic lymph node (arrowhead).

Fig. 7—68-year-old man with bilateral secondary adrenal lymphomas.
A, Maximum-intensity-projection PET image shows increased FDG uptake in bilateral adrenal glands (arrows).
B, Transverse CT shows enlargement of bilateral adrenal glands (arrows) with preservation of adrenal contours.
C, Fused FDG PET/CT image shows increased FDG uptake of bilateral adrenal lesions (maximum standardized uptake values, 31.4 and 33.8 for right and left adrenal lesions, respectively).
Fig. 8—22-year-old woman with lymphomatous involvement of left adrenal gland. 
A, Transverse contrast-enhanced CT image shows hypodense areas (arrow) around enhancing adrenal gland (arrowhead).
B, Fused FDG PET/CT image shows extensive retroperitoneal hypermetabolic lesions (arrow) engulfing entire left adrenal gland (maximum standardized uptake value, 7.1).
C, Follow-up contrast-enhanced CT image (1 month after initiation of chemotherapy) shows normal adrenal gland (arrowhead), indicating successfully treated lymphomatous involvement of adrenal gland.

Fig. 9—65-year-old man with left adrenal metastasis from hepatocellular carcinoma. 
A, Transverse contrast-enhanced CT image shows nodule (arrow) in left adrenal gland with inhomogeneous enhancement.
B, Fused FDG PET/CT image shows increased FDG uptake of nodule (maximum standardized uptake value, 6.9).

Fig. 10—57-year-old man with left adrenal small cell carcinoma. 
A, Transverse contrast-enhanced CT image shows inhomogeneously enhanced tumor (arrow) in left adrenal gland.
B, Fused FDG PET/CT image shows increased FDG uptake of tumor (maximum standardized uptake value, 8.3).

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