

# Management of Incidental Pituitary Findings on CT, MRI, and <sup>18</sup>F-Fluorodeoxyglucose PET: A White Paper of the ACR Incidental Findings Committee

**EC:** Editor's Choice

**SA-CME**

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## Abstract

The ACR Incidental Findings Committee presents recommendations for managing pituitary findings that are incidentally detected on CT, MRI and <sup>18</sup>F-fluorodeoxyglucose PET. The Pituitary Subcommittee, which included radiologists practicing neuroradiology and an endocrinologist, developed this algorithm. The recommendations draw from published evidence and expert opinion and were finalized by informal iterative consensus. Algorithm branches successively categorize pituitary findings on the basis of imaging features. They terminate with an ascertainment of an indolent lesion (with sufficient confidence to discontinue follow-up) or a management recommendation. The algorithm addresses most, but not all, pathologies and clinical scenarios. The goal is to improve the quality of care by providing guidance on how to manage incidentally detected pituitary findings.

**Key Words:** pituitary lesion, Rathke's cleft cyst, incidental, pituitary adenoma

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## OVERVIEW OF THE ACR INCIDENTAL FINDINGS PROJECT

The core objectives of the incidental findings project are to (1) develop consensus on patient characteristics and

imaging features that are required to characterize an incidental finding, (2) provide guidance to manage such findings in ways that balance the risks and benefits to patients, (3) recommend reporting terms that reflect the

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This study was approved by the institutional review board of the institution that provided the sonograms. Dr Hoffman is a consultant to Ascendis, Ono, GeneScience, Genexine, Sandoz, and Versartis. Dr Wintermark is a member of the advisory board of GE-BFL and holds equity in More Health and Magnetic Insight. Dr Pandharipande received research funding from the Medical Imaging and Technology Alliance, outside the submitted work. Dr Berland receives consulting fees from Nuance Communications. Dr Seidenwurm is a consultant for RASMG Medical Group, The Alliance, HSAG, the National Quality Forum, ACR. All other authors have no conflicts of interest related to the material discussed in this article.

level of confidence regarding a finding, and (4) focus future research by proposing a generalizable management framework across practice settings.

## THE CONSENSUS PROCESS: MANAGEMENT OF INCIDENTAL PITUITARY FINDINGS

The current report presents the ACR Incidental Findings Committee's (IFC) recommendations regarding incidental pituitary findings detected on CT, MRI, or <sup>18</sup>F-fluorodeoxyglucose (FDG) PET. The process of developing this algorithm included naming a subcommittee chair, who appointed four radiologists (who interpret neuroimaging examinations) and an endocrinologist to the Pituitary Subcommittee. The subcommittee then developed and gained consensus on preliminary recommendations. The subcommittee used published evidence as its primary source. When evidence was not available, the subcommittee invoked the collective expertise of the team. The preliminary algorithm underwent review by additional members within the IFC, including the Body Commission chair and the IFC chair. The revised algorithm and corresponding white paper draft were submitted to additional ACR stakeholders to gain input and feedback. Consensus was obtained iteratively after successive reviews and revisions. After completion of this process, the algorithm and white paper were finalized.

The IFC's consensus processes meet policy standards of the ACR. However, they do not meet any specific, formal national standards. This algorithm and set of recommendations does not represent policy of the ACR Practice Guidelines or the ACR Appropriateness Criteria. Our consensus may be termed "guidance" and "recommendations" rather than "guidelines," which has a more formal definition.

## ELEMENTS OF THE FLOWCHARTS: COLOR CODING

The algorithm is summarized in two flowcharts. Within each flowchart, yellow boxes indicate using or acquiring clinical data (eg, lesion size), green boxes describe recommendations for action (eg, follow-up imaging), and red boxes indicate that imaging workup or follow-up may be terminated. To minimize complexity, each algorithm addresses most, but not all, imaging appearances and clinical scenarios. Radiologists should feel comfortable deviating from the algorithm in circumstances that are not represented in the algorithm, on the basis of the specific imaging appearance of the finding in question and patient characteristics: the algorithm content must be

viewed as recommendations and should not be considered as "standard of care."

## NATURE AND SCOPE OF THE PROBLEM

Incidental pituitary lesions are common, estimated to occur in 11% to 23% of the population in postmortem studies [1-3]. The observed prevalence depends on the imaging protocol. They are detected in 0.1% to 1.2% of patients undergoing MRI head examinations [4-6] and in 10% of normal subjects on MRI pituitary examinations [7].

The two most common pathologies responsible for incidental pituitary lesions are Rathke's cleft cysts and pituitary adenomas. Other diagnoses are rare and include pituitary metastases, infarctions, hemorrhage, epidermoid cysts, and abscesses. In addition, pituitary glands can be heterogeneous on imaging, resulting in small "pseudolesions" [8-12]. Suprasellar and parasellar masses, such as craniopharyngioma and meningioma, may mimic pituitary lesions when large. The literature includes a combination of studies that encompass all these diagnoses (pituitary incidentalomas) or focus specifically on solid lesions that are assumed to be pituitary adenomas. Lesions are categorized as macro- versus microadenomas (or incidentalomas) using a 10-mm size threshold.

Macroincidentalomas of the pituitary gland that are large enough to cause compression and invasion of surrounding structures require endocrine or neurosurgical consultation. However, they are rarely incidentally detected. In consecutive postmortem cohorts, fewer than 1% of incidental pituitary lesions were >10 mm [3]. Incidental pituitary lesions are usually small at imaging. In 100 normal patients, a total of 10 incidental pituitary lesions were detected on MRI pituitary examinations, all measuring 3 to 6 mm [7]. In retrospective surgical cohorts, the proportion of pituitary macroincidentalomas will be higher, reflecting referral bias.

When left untreated, a small percentage of patients will have pituitary adenomas that grow or hemorrhage. This can lead to hypopituitarism or visual field deficits (from compression of optic nerves or chiasm) or ophthalmoplegia (from invasion into the cavernous sinus or orbital apex). Even fewer will have subclinical hypersecreting pituitary adenomas that could result in morbidity if left undiagnosed in the long term. Misperceptions about the likelihood of these rare outcomes commonly prompt unnecessary and repeated examinations for patients with incidental pituitary lesions, leaving them vulnerable to anxiety, avoidable medical expenses, and risks associated with unnecessary treatment.

The Endocrine Society published guidelines on following incidental pituitary lesions in 2011 [13]. They recommended that patients with pituitary incidentalomas of any size undergo clinical evaluation that includes laboratory evaluation and screening for hormone hypersecretion and for hypopituitarism. Patients with normal pituitary function are recommended to undergo follow-up (MRI pituitary examination) at 6 months for lesions >10 mm and at 1 year for ≤10-mm lesions and thereafter progressively less frequently if the adenoma is unchanged in size. Here, we present an algorithm for incidental pituitary lesions detected on imaging and recommendations based on a review of new literature and expert consensus.

### Implications and Risks of Incidental Pituitary Lesions Detected on CT or MRI

Several surgical series with mean follow-up ranging from 3 to 10 years showed that 20% to 50% of pituitary adenomas can grow [14-17]. However, the majority of growth occurred in macroadenomas, and none occurred in adenomas <5 mm [14]. Furthermore, growth resulting in new compressive symptoms is uncommon. Only 8% of patients with incidental pituitary lesions >10 mm developed new visual field abnormalities when followed over time [13]. There are no cases of a microadenoma that enlarged over time to cause compression or invasion. Rathke's cleft cysts, of any size, will rarely grow.

Hemorrhage into a large pituitary adenoma (ie, pituitary apoplexy) can cause acute onset of compressive symptoms. The risk for pituitary apoplexy is low overall and negligible in patients with microadenomas. A retrospective study of 574 patients with pituitary adenomas found apoplexy in 42 patients (7.3%); all had macroadenomas [18]. A smaller study of 42 pituitary adenomas focused on incidental nonfunctioning pituitary adenomas [16]. After a mean follow-up period of 62 months, 4 patients (9.5%) developed pituitary apoplexy, but initial tumor sizes were 18 to 24 mm. The only large series showing hemorrhage in microadenomas was a study of 368 patients with prolactinomas that found hemorrhage in 3% of microadenomas compared with 20% of macroadenomas [19]. However, classical pituitary apoplexy with compressive symptoms occurred in only three cases, all macroadenomas. The rest of the patients with new pituitary hemorrhage were asymptomatic, and the hemorrhage resolved on imaging over 2 years.

Another reason for the workup of incidental pituitary lesions is to diagnose clinically occult abnormal endocrine function. In a surgical retrospective series of 46 patients with pituitary incidentalomas, 29 patients (63%) had

pituitary macroincidentalomas, and 17 (37%) had microincidentalomas. In total, 66% of macroincidentalomas demonstrated pituitary insufficiency from mass effect on the normal pituitary gland, leading most frequently to secondary hypogonadism, followed by hypothyroidism and hypoadrenalism [20]. Suprasellar extension of nonsecreting macroincidentalomas resulted in complications of hyperprolactinemia from presumed stalk compression and decreased dopamine secretion in 34%. A total of 17 patients underwent surgery during a mean follow-up time of 3.2 years, revealing 16 pituitary adenomas and 1 case of craniopharyngioma. None of the patients with microincidentalomas required surgery.

Secretory pituitary adenomas lead to abnormal endocrine function, which can occur in pituitary adenomas of any size. However, secreting pituitary adenomas are rare, with a prevalence of fewer than 1 in 2,000 individuals [21]. In patients presenting with symptoms, prolactin hypersecretion is the most common, occurring in 57% of adults and 76% of women [22] with pituitary adenomas. Adrenocorticotropic hormone (ACTH)-hypersecreting adenomas (resulting in Cushing's disease) and growth hormone-hypersecreting adenomas (resulting in acromegaly) represent 11% and 2% of symptomatic adenomas, respectively [22]. There are typically overt symptoms of these diseases, but a secreting pituitary adenoma, especially a growth hormone-secreting tumor [23], may be clinically occult in its early stages. A long duration of active disease in patients with secreting pituitary adenomas is associated with an increased risk for comorbidities, such as osteoporosis, hypertension, cardiovascular disease, obesity, and diabetes [21].

In incidental pituitary adenomas, the risk for pituitary hypersecretion is much lower. The strongest evidence comes from a study of 334 pituitary adenomas detected post-mortem. Immunohistochemistry was positive for prolactin in 40% of the tumors and for ACTH in 14% of the tumors, and the rest were said to be nonfunctioning cell types [3]; many nonfunctioning tumors will stain positive for gonadotropins. However, positive immunohistochemistry does not necessarily indicate clinical expression. Retrospective review of medical records showed that some patients had hypertension, diabetes, hyperthyroidism, and hypothyroidism, but these are common diseases in the general population, and there was no correlation between clinical data and adenoma type. None of the patients with prolactin and ACTH staining had symptoms of adeno-hypophyseal hormone hypersecretion.

A single clinical study followed outcomes in 46 patients with incidental pituitary lesions in which only

37% of the lesions were microadenomas, reflecting referral bias [20]. Hypopituitarism was present in 41% of the patients (all of whom had macroadenomas). In total, 22% had hyperprolactinemia, but there were no cases of elevated ACTH or growth hormone [20]. Immunohistochemical staining of 13 surgical specimens showed two tumors with positive growth hormone staining, but neither patient had elevated serum growth hormone or clinical signs of acromegaly.

### Incidental Pituitary Lesions on FDG PET

Incidental pituitary FDG uptake was a very rare finding, occurring in 0.07% to 0.08% of FDG PET studies [24-26]. Incidental pituitary FDG uptake represents pituitary adenomas in more than 50% of cases [24-26]. Other causes of incidental pituitary FDG uptake include metastases, Langerhans cell histiocytosis, inflammatory lymphocytic hypophysitis, and, rarely, benign physiologic uptake without any corresponding lesion [24]. Standardized uptake values do not distinguish reliably among these entities [24].

## REPORTING CONSIDERATIONS

### Management of Incidental Pituitary Lesions Detected on MRI and CT

The following elements must be reported when an incidental pituitary finding is detected on CT and MRI:

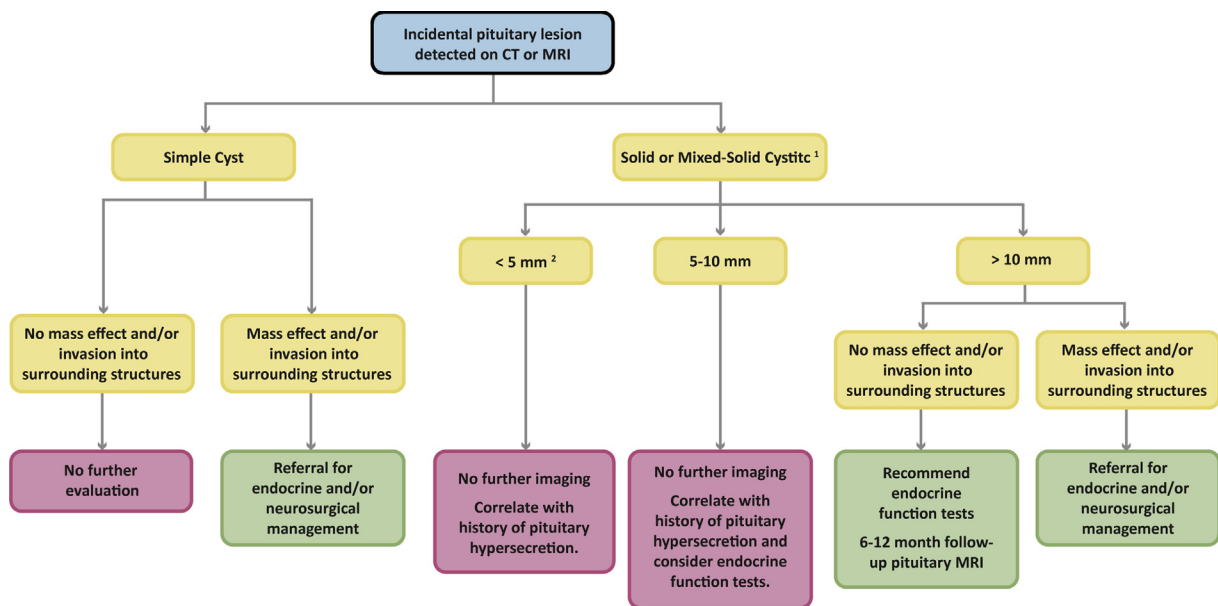
1. Composition of cystic, solid, and mixed solid-cystic
2. Size of lesion
3. Mass effect and/or invasion into surrounding structures such as the optic chiasm, optic nerve, and cavernous sinus

### Management of Incidental Pituitary Lesions Detected on FDG PET

If the FDG PET study is part of a PET/CT or a PET/MRI study, the FDG avidity and the three elements listed previously should be reported. The absolute standardized uptake value need not be reported because it does not distinguish reliably among diagnoses [24].

## INCLUSION AND EXCLUSION CRITERIA FOR USE OF THE ALGORITHM

Our algorithm consists of two flowcharts (Figs. 1 and 2). These should be applied to incidentally detected pituitary lesions only if the patient is  $\geq 18$  years of age, asymptomatic, and referred to imaging for a reason that is unrelated to potential pituitary pathology. Although the algorithm is intended to manage most encountered scenarios, the decision to evaluate further should also take into account the patient's life expectancy, based primarily on age and comorbidities. In addition, if there are symptoms of pituitary dysfunction on targeted history stimulated by imaging findings, endocrine



<sup>1</sup>If the composition of the lesion cannot be determined, it should be managed as if solid.

<sup>2</sup>Consider the possibility of a pseudolesion given the lesion's size. Pseudolesions require no further management.

Fig 1. Flowchart for incidental pituitary lesions detected on CT or MRI.

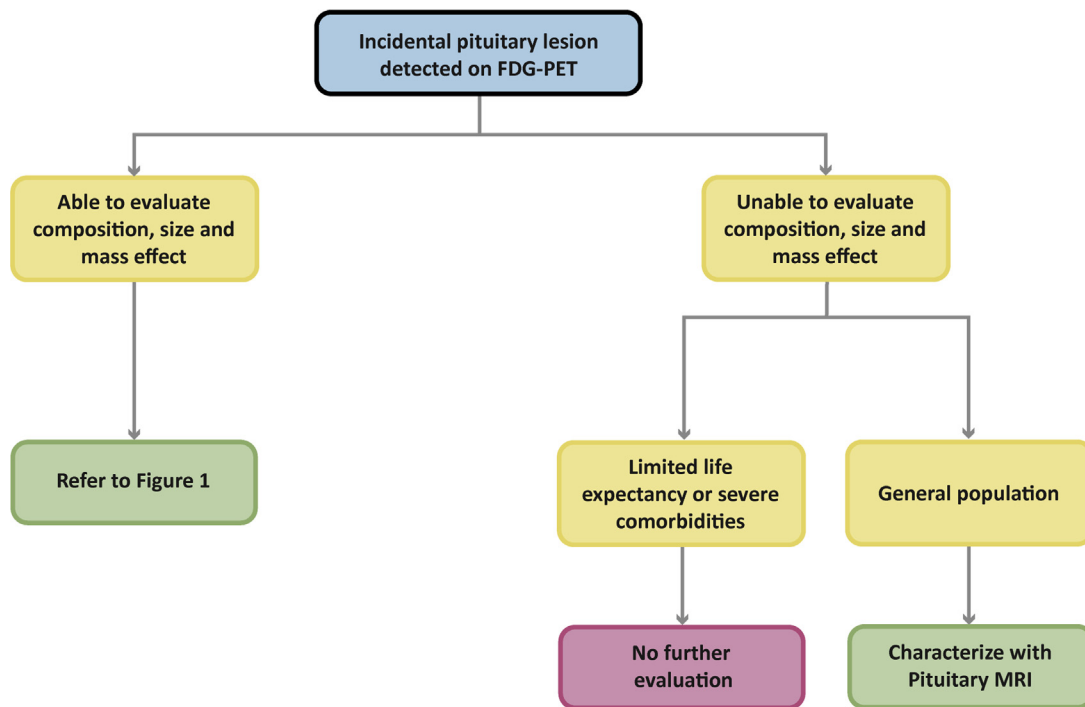


Fig 2. Flowchart for incidental pituitary lesions detected on FDG PET, regardless of metabolic activity.

testing should be performed regardless of imaging findings.

## IMPLICATIONS OF IMAGING AND CLINICAL FEATURES

### Five Common Principles of our Algorithm

1. An incidental pituitary lesion that is a simple cyst should be considered to be a Rathke's cleft cyst; no further workup is needed unless it has mass effect or invasion into surrounding structures.
2. An incidental pituitary lesion <5 mm does not require imaging follow-up to monitor growth.
3. If an incidental pituitary lesion is solid (or mixed solid-cystic) and 5 to 10 mm, the report may include a statement regarding correlation with clinical history for endocrine dysfunction. If the tumor is determined to be nonsecretory and there is no evidence of hypopituitarism, further imaging may not be required to monitor growth.
4. If an incidental pituitary lesion is solid (or mixed solid-cystic) and >10 mm, endocrine function tests are advised to evaluate for pituitary hypersecretion or insufficiency, and a follow-up MRI pituitary examination should be performed after 6 to 12 months to monitor growth.

5. An incidental pituitary lesion of any composition with mass effect and/or invasion requires endocrine and/or neurosurgical consultation.

## OVERVIEW OF THE ALGORITHM

### Management of Incidental Pituitary Lesions Detected on CT and MRI

Chart 1 (Fig. 1) addresses patients with incidental pituitary findings on CT and MRI.

**Simple Cyst.** If an incidental pituitary lesion is a simple cyst with no enhancing solid component, it should be considered to be a Rathke's cleft cyst. A cyst can have uniform signal similar to cerebrospinal fluid or higher attenuation on CT and T1 hyperintensity on MRI because of increased protein content.

Rathke's cleft cysts do not require follow-up imaging because they very rarely grow. An endocrine or neurosurgical referral should be considered in cases of a very large cyst with mass effect and/or invasion into surrounding structures.

If the composition of the lesion cannot be determined, it should be categorized as mixed solid-cystic; as described later, the recommended management for such lesions is the same as for solid lesions. If the lesion has more complex signal characteristics

indicative of blood products or necrosis, it may represent other entities, such as a pituitary adenoma or craniopharyngioma.

**Solid (or Mixed Solid-Cystic) Pituitary Lesion, <5 mm.** When an incidental pituitary lesion in this category is <5 mm, the first step is to determine whether the lesion is a true lesion. Many are not adenomas but rather pseudolesions related to gland heterogeneity or imaging technique. Pseudolesions can be nodular hyperplasia, cell clumping, cyst formation, or fibrous tissue or can be related to imaging techniques and artifacts [8-12]. Imaging noise causing apparent gland heterogeneity may be exacerbated by the thin slices and small field of view (FOV) typically used in pituitary protocols. The small size of the gland and its proximity to the carotid arteries and cavernous sinuses together make it particularly vulnerable to partial volume artifacts, particularly along the lateral aspect of the gland. Proximity to bone and sinus gas may produce susceptibility artifacts inferiorly.

If the lesion is a true lesion, the report may include a statement regarding correlation with clinical history for pituitary hypersecretion, but it does not require imaging follow-up for evaluation of growth. A pituitary adenoma at a size of <5 mm is unlikely to ever hemorrhage or grow to a size at which surgery is required. The risk that the patient will have an asymptomatic secreting pituitary adenoma is low [3].

**Solid (or Mixed Solid-Cystic) Pituitary Lesion, 5 to 10 mm.** When an incidental pituitary lesion in this category is 5 to 10 mm, the report may include a statement regarding correlation with clinical history for pituitary hypersecretion. If there is concern for a hypersecreting pituitary adenoma, endocrine function tests should be performed. Imaging follow-up for growth may not be necessary because these lesions are unlikely to hemorrhage or grow to the size at which surgery is required. The risk that the patient will have an asymptomatic secreting pituitary adenoma is low [3].

**Solid (or Mixed Solid-Cystic) Pituitary Lesion, >10 mm.** If an incidental pituitary lesion is solid and >10 mm, a basic workup should include endocrine function tests and an MRI pituitary examination after 6 to 12 months to evaluate for growth.

If there is mass effect on surrounding structures, early referral to an endocrinologist and/or neurosurgeon is generally required.

## Management of Incidental Pituitary Lesions Detected on FDG to PET

Chart 2 (Fig. 2) addresses patients with incidental pituitary findings on FDG PET. If composition, size, and mass effect cannot reliably be evaluated, further workup and characterization with an MRI pituitary examination should be performed. However, because many patients undergoing FDG PET have a primary malignancy, the recommendation should consider the life expectancy of the patient. For example, if the patient has widely metastatic disease, significant intracranial pathology, or severe comorbidities, the workup of a small pituitary lesion without mass effect on surrounding structures, and without associated clinical symptoms, is unlikely to alter quality of life or life expectancy.

## IMAGING PROTOCOL OPTIMIZATION

An MRI examination is considered the imaging modality of choice for the diagnosis of pituitary disorders because of its superior soft-tissue contrast relative to CT. The protocol should include 3 mm or less coronal and sagittal T1-weighted images with and without contrast, with a small FOV centered on the pituitary gland. Sagittal images show the anterior and posterior lobes and the stalk. The coronal images show the pituitary gland with a midline stalk between the cavernous sinuses.

A CT pituitary examination with thin slices and a small FOV is an option in patients who cannot undergo MRI, but it is less sensitive for evaluation of lesion composition and invasion of local structures relative to MRI.

## TAKE-HOME POINTS

- Incidental pituitary lesions occur in almost one-quarter of the population on postmortem studies. The incidence on imaging studies is lower and depends on the imaging modality and its resolution.
- The two most common pathologies responsible for incidental pituitary lesions are Rathke's cleft cysts and pituitary adenomas.
- Pituitary adenomas are benign, but macroadenomas have a higher risk for pituitary insufficiency and growth than microadenomas.
- Recommendations for incidental pituitary lesions detected on MRI and CT depend on composition, size, and presence of mass effect and/or invasion.

- Recommendations for incidental pituitary lesions detected on FDG PET should follow the CT and MRI algorithm when possible, but if lesion features cannot be determined and the patient has normal life expectancy, an MRI pituitary examination should be performed.

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