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# Back to the Future: Dynamic Contrast Enhanced Photon Counting Detector CT for the Detection of Pituitary Adenoma in Cushing Disease

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## ABSTRACT

Historically, MRI has been unable to detect a pituitary adenoma in up to half of patients with Cushing disease. This is problematic, as the standard of care treatment is surgical resection, and its success is correlated with finding the tumor on imaging. Photon counting detector CT (PCD-CT) is a recent advancement that has multiple benefits over conventional energy integrating detector CT. We present the use of dynamic contrast enhanced imaging using PCD-CT for detection of pituitary adenoma in patients with Cushing disease.

**ABBREVIATIONS:** PCD-CT = Photon Counting Detector CT; EID =Energy-integrating detector; VMI = Virtual monochromatic imaging.

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## INTRODUCTION

MRI is the primary imaging modality to evaluate pituitary lesions.[1] Post-contrast dynamic imaging of the pituitary has been shown to be helpful for the identification of pituitary lesions, especially for small lesions.[1,2] MRI of the sella remains extremely challenging predominantly due to the small size of the pituitary as well as artifacts related to the skull base and sphenoid sinus aeration patterns. Historically, MRI has been unable to detect a pituitary adenoma in up to half of patients with Cushing disease.[3] This is problematic, as the identification of the adenoma is an imperative step in successful surgical resection. Photon counting detector CT (PCD-CT) is a new technique with increased spatial and contrast resolution relative to conventional energy-integrating detector (EID) CT.[4] The purpose of this report is to describe our dynamic contrast enhanced PCD-CT technique for pituitary microadenoma identification in Cushing disease.

### PCD-CT Technique

A dynamic contrast-enhanced CT protocol was developed on a PCD-CT scanner (Naeotom Alpha, Siemens Healthineers) for imaging patients with Cushing disease. Our institutional practice is to obtain a pre-operative skull base CTA to assist surgeons with operative planning. The protocol consists of a skull base CTA scan (120 kV, CAREkeV IQ level of 230) followed by 4 delayed scans of the sella (effective mAs of 260), spaced 20 seconds apart. All scans used a high-resolution mode with a detector collimation of 120x0.2 mm. The CTA scan is triggered using contrast bolus tracking with a region of interest over the ascending aorta and a trigger threshold of 175 HU at 90 kV. For the 4 scans over the sella, images were reconstructed at both 0.2 mm and 0.6 mm slice thickness using a smooth kernel of Hr40 (with quantum iterative reconstruction strength setting of 3). Virtual monochromatic imaging (VMI) at 70 keV and low energy threshold (T3D) were used for the 0.6 mm and 0.2 mm reconstructions, respectively. We performed a preliminary evaluation on multiple VMI energies: 40, 50, 60, and 70 keV, and found out that the 70 keV images had the optimal balance between contrast enhancement and noise. Lower keV did increase the contrast between a microadenoma and pituitary tissue, but the increased noise degraded the image quality. 70 keV had the best the visual image quality. Per our CTA protocol, contrast dose for patients under 136 kg included Iohexol 350 (Omnipaque-350; GE HealthCare; Waukesha, WI) 100 mL at 4 mL/second, followed by 35 mL 0.9% NaCL at 4 mL/second. The CTDIvol was 44.6 mGy for each delayed scan of the sella.

### Cases

We present three patients who were diagnosed with Cushing disease after a workup with endocrinology. These patients were defined endocrinologically to have pituitary tumors. Each patient was scheduled to undergo a pre-operative skull base CTA to help guide our




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surgical team. The clinically indicated CTA was then augmented with 4 delayed imaging passes of the sella as described above. In all three patients, we identified discrete hypoenhancing lesions, compatible with a pituitary adenoma. These adenomas were most conspicuous on different delayed sequences in each patient. In two cases, the CT-identified lesions were not seen with certainty on the comparison MRI.

*Patient 1*

67-year-old female with osteoporosis, muscle weakness, and progressive weight gain was diagnosed with Cushing disease. Pre-operative 1.5T MRI including dynamic contrast enhanced images reported heterogenous enhancement in the right pituitary without a clear lesion. PCD-CT (Fig 1) found two clear hypoenhancing lesions (measuring 7 mm and 4 mm) in the right aspect of the pituitary on the 3rd dynamic series. The patient underwent transsphenoidal resection of these lesions, and pathology examination confirmed corticotroph adenomas.

*Patient 2*

57-year-old female who presented with uncontrolled diabetes mellitus type 2 and hypertension was diagnosed with Cushing disease. Pre-operative 1.5T MRI demonstrated a 2-3 mm area of T2 hyperintense signal (Fig 2) in the left superior aspect of the pituitary with heterogeneous enhancement on the dynamic contrast enhanced series. PCD-CT demonstrated a hypoenhancing lesion in the same location, best seen on the 1st PCD-CT series of the pituitary. Intra-operatively, a whitish fluid-filled lesion was seen and felt by the neurosurgical team to be consistent with a tumor but given the liquidous consistency it did not generate sufficient material to yield a pathological diagnosis of corticotroph adenoma. However, biochemical remission was documented post-operatively, as the patient developed post-operative adrenal insufficiency.

Patient 3

68-year-old male presented with osteoporotic vertebral body compression fractures, with subsequent workup demonstrating Cushing disease. His pre-operative 3T MRI with dynamic post contrast imaging was severely motion degraded and non-diagnostic. PCD-CT identified a 4 mm hypoenhancing lesion in the right aspect of the pituitary that involved the cavernous sinus, best seen on the 4th series (Fig 3). Intra-operatively, this imaging finding corresponded with a firm lesion that contained a pseudocapsule. Pathology examination of resected lesion confirmed a corticotroph adenoma.

## DISCUSSION

In this report, we describe an imaging protocol for dynamic post contrast imaging of the pituitary on PCD-CT. Pituitary lesions were identified on PCD-CT in three patients with Cushing disease.

Traditional EID-CT converts x-ray photons to visible light, then subsequently converts the light to electrical signals. PCD-CT, on the other hand, simplifies this process by directly converting each photon to electrical signal and recording its energy information. PCD-CT has shown an advantage for increased spatial resolution compared to both typical clinical protocols on MRI and EID-CT.[5] In addition to improved spatial resolution and the potential to lower radiation dose, PCD-CT has higher iodine signal than EID-CT due to higher weighting of low-energy photons during photon detection, which increases conspicuity of iodine-enhanced soft tissue structures.[6] While a new application only receiving FDA approval in 2021, PCD-CT has already been shown to have multiple useful applications including evaluation of multiple myeloma involving the spine[7], CSF-venous fistula[8], and temporal bone[9] amongst many other applications. None of these, however, have been applied to pituitary imaging.

Dynamic contrast enhanced EID-CT imaging of the sella was previously described in the 1980's[10] and 1990's[10,11]. A study published in 2015 including patients imaged beginning in 2004 found that dynamic EID-CT was more effective than MRI without dynamic contrast enhanced imaging.[12] Modern imaging, however, has abandoned CT in favor of MRI.[1] Neuroimaging of the pituitary gland in patients with Cushing disease continues to serve an imperative function in the diagnosis and management. Cushing disease is caused by a pituitary adenoma that secretes corticotropin, subsequently leading to an increase in the production of cortisol from adrenal cortex. Hypercortisolism leads to development of features of overt Cushing syndrome on exam (skin fragility, bruising, striae, supraclavicular and dorsocervical pads, facial rounding, proximal myopathy), comorbidities, such as hypertension, diabetes, obesity, fractures, infections, and pulmonary embolism, and increase in mortality.[13] While inferior petrosal sinus sampling can help to distinguish Cushing disease from ectopic Cushing syndrome, it has not shown to reliably localize a lesion within the pituitary.[14] This is particularly important as surgical resection is the standard of care treatment for Cushing disease. If MRI is unable to locate an adenoma, surgical resection is associated with a higher rate of complications and decreased cure rates.[13]

Our experience does not advocate for PCD-CT as a replacement for MRI, however there are several situations in which CT has advantages over MRI. CT tables generally have higher weight limits than MRI tables to accommodate larger patients, and the larger bore size of CT could help patients who cannot tolerate MRI due to claustrophobia. As shown in patient 3, the faster acquisition time of CT can be helpful in patients who are unable to lay still long enough for diagnostic quality MR images to be acquired. Additionally, PCD-CT could help in patients who are unable to undergo an MRI secondary to metal safety concerns, non-conditional implants, or gadolinium-based contrast reactions. Finally, in cases where patients have over-pneumatized sphenoid sinuses that produce significant artifact over sella on MRI, CT image quality is not confounded by this problem. Specific to PCD-CT, imaging technique allows for thin sub-millimeter slice thickness. In our experience, the primary benefit is outlining the peripheral margin of the adenoma relative to the normal pituitary, which allows for greater confidence in identifying a hypoenhancing lesion as an adenoma.

At our institution, patients scheduled for pituitary surgery undergo a pre-operative skull base CTA to help with surgical planning. Thus, as is the case with all CT, this technique increases the radiation dose to the patient. Further work studying a larger number of patients could further refine the imaging technique to decrease the number of imaging passes of the sella and help decrease radiation dose. Given

the clear advantages of PCD-CT over EID-CT, and the significant importance of pre-operative adenoma identification in Cushing disease patients, we believe that this technique should be thoroughly studied and will continue to use it as our institutional preference.

## CONCLUSION

We provide the first description of dynamic contrast enhanced imaging on PCD-CT for evaluation of pituitary adenomas in Cushing disease. Given the importance of pre-operative tumor localization of pituitary microadenomas to patient outcomes, this technique may potentially serve as an adjunct for MRI negative cases.

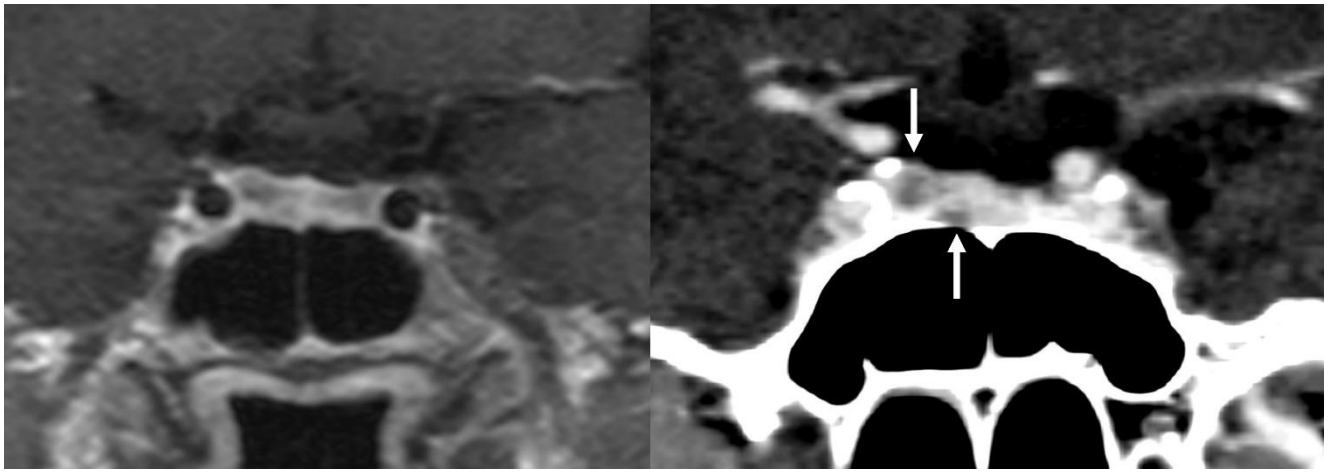

**FIG 1.** Patient 1, a 67-year-old female with Cushing disease. Her pre-operative dynamic post contrast T1-weighted image (left) shows heterogeneous enhancement in the right pituitary without a definite lesion. Dynamic contrast enhanced PCD-CT (right) showing the 3rd imaging series of the sella with 0.6 mm slice thickness shows two distinct hypoenhancing lesions (arrows) in the right pituitary, found to be pathology proven adenomas.

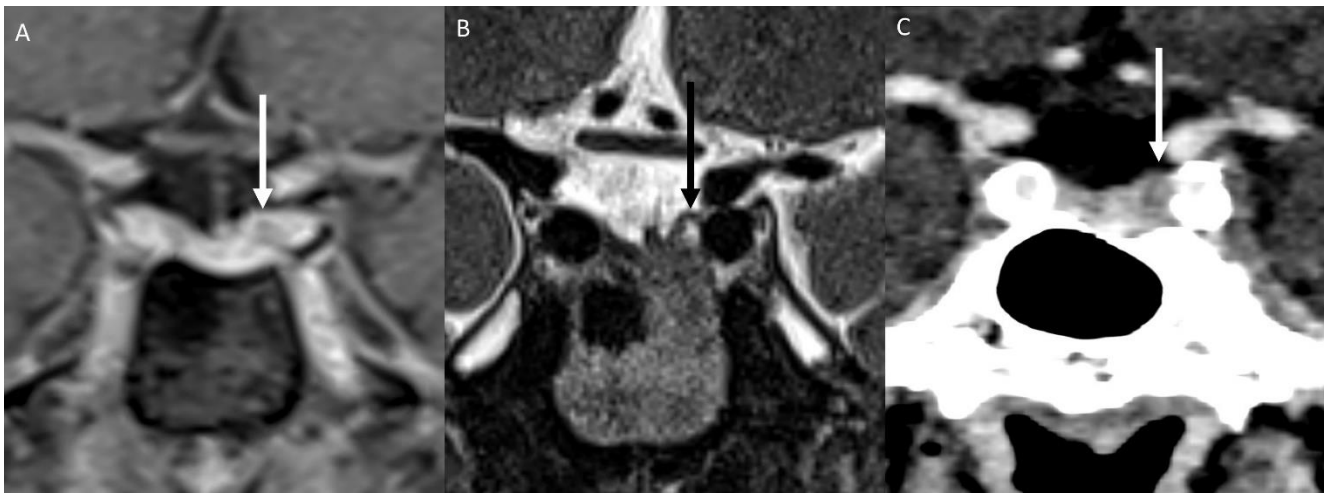


**FIG 2.** Patient 2, 57-year-old female with Cushing disease. Coronal dynamic contrast enhanced MRI (A, white arrow) shows a small hypoenhancing lesion in the left superior aspect of the pituitary with corresponding T2 hyperintense signal (B, black arrow). PCD-CT (C, white arrow) shows corresponding hypoenhancement on the 1st series of the sella seen as a coronal reconstruction at 0.6 mm slice thickness.

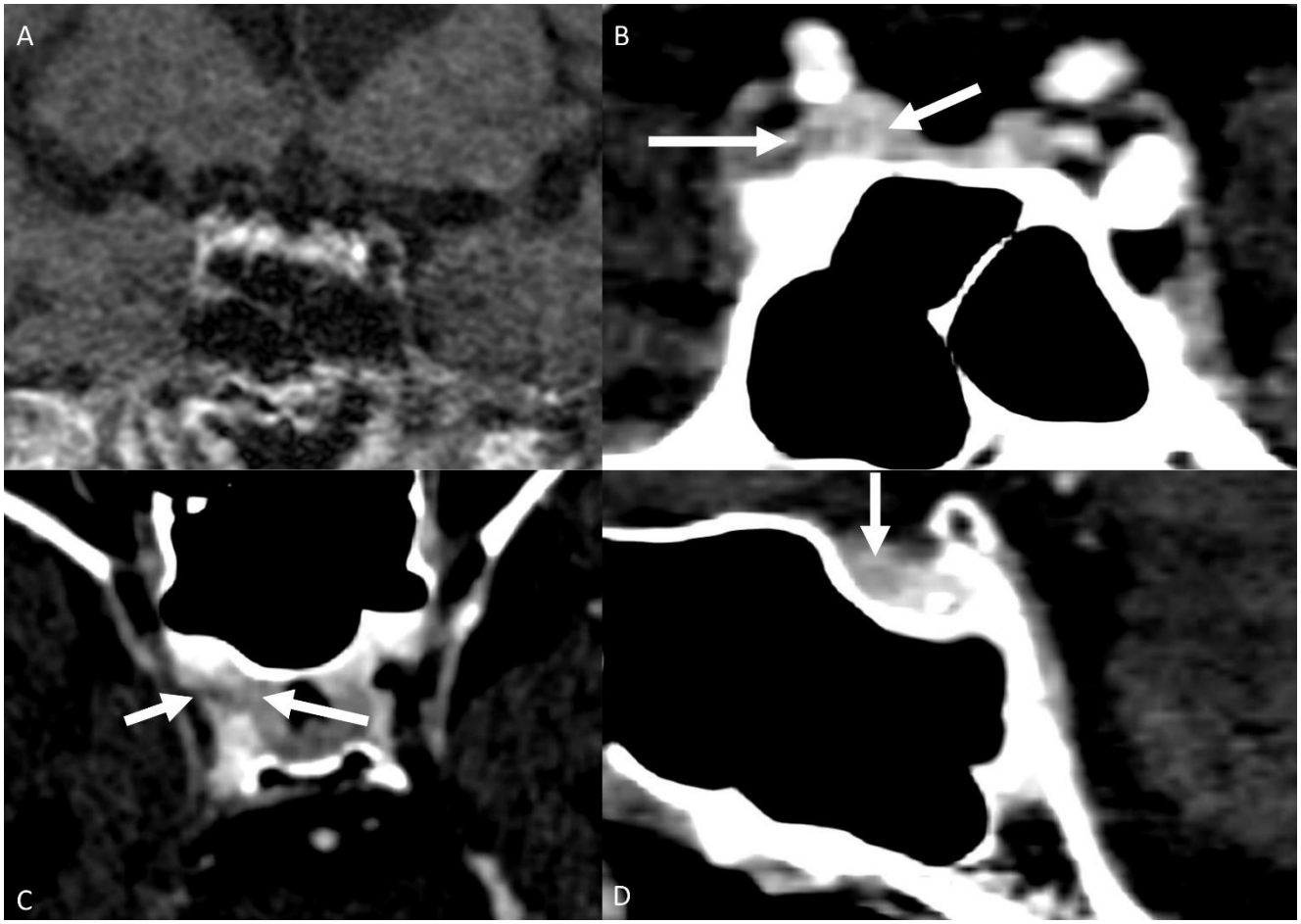


**FIG 3.** Patient 3, 68-year-old male with Cushing disease. His pre-operative MRI (A) was non-diagnostic secondary to motion. Coronal (B), axial (C), and sagittal (D) images from the 4th sequence of a dynamic contrast enhanced PCD-CT shows a hypoenhancing lesion (arrows) in the right aspect of the pituitary that involves the cavernous sinus. This was a pathology proven adenoma.

Disclosure forms provided by the authors are available with the full text and PDF of this article at www.ajnr.org.

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