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Technical Resource

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High-frequency Multiphase 4DCT for the Detection of Parathyroid Adenomas: A Pictorial Essay

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Abbreviations: 4DCT, 4-dimensional computed tomography; HU, Hounsfield units; NECT, noncontrast enhanced computed tomography.

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Abstract

4-Dimensional computed tomography (4DCT) for the detection of (an) enlarged parathyroid(s) is a commonly performed examination in the management of primary hyperparathyroidism. In our center, we introduced a high-frequency multiphase 4DCT protocol obtaining 16 phases, including 11 different arterial phases. Exposure to this multiphase 4DCT technique is similar to that for classic helical 4DCT. In this pictorial essay we reconstructed our multiphase 4DCT series in the manner of a classic helical 4DCT and compare both techniques. We illustrate how multiphase 4DCT may aid in the detection of parathyroid adenomas. We found 17 out of 19 lesions demonstrating a type A pattern of enhancement, therefore suggesting this pattern could be more prevalent than previously thought. Some parathyroid adenomas may be mistaken for enlarged lymph nodes using classic 4DCT whereas high-frequency multiphase 4DCT can detect a temporary rise in enhancement, thus suggesting the lesions in question to be of parathyroid origin. Smaller lesions may prove more obvious as the difference in enhancement between parathyroid and thyroid can become more prominent.

Key Point

Using high-frequency multiphase 4DCT an arterial phase with maximum enhancement of parathyroid tissue can be defined. This phase may aid in the detection of parathyroid adenomas.

Key Words: Primary hyperparathyroidism, parathyroid adenoma, 4DCT, multiphase scanning

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The role of 4-dimensional computed tomography (4DCT) in the detection of parathyroid adenomas was first investigated by Rodgers et al. [1] in 2006. These authors made use of a 3-phasic approach including a noncontrast-enhanced computed tomography (NECT), an arterial phase at 25 seconds after start of contrast administration and a later venous phase. Over the years many different studies have been undertaken to investigate the use of 4DCT in the context of the detection of parathyroid adenomas. Regardless of different approaches in relation to the number of scanned phases and the timing of said phases, a mean sensitivity of 81.5% and a mean specificity of 86% is reported [2]. Typical parathyroid adenomas are hypoattenuating to thyroid tissue on NECT and lesions can demonstrate avid arterial enhancement during the arterial phase as well as rapid washout of contrast on the venous phase. The arterial phase is the most important phase, as adenomas can be visualized in this phase as hyperenhancing nodules in characteristic locations. Unfortunately for approximately one-third of adenomas, lesions are said to be isoattenuating to the thyroid on arterial and venous phases [3]. A study by Bahl et al. [4] in 2015 defined 3 different patterns of enhancement for parathyroid adenomas. A hypoattenuating lesion on the noncontrast-enhanced phase that demonstrates higher enhancement than the thyroid on the arterial phase is defined as a type A lesion. If the adenoma does not demonstrate arterial wash-in of contrast but instead demonstrates a lower enhancement on the venous phase when compared with thyroid tissue, this lesion is defined as a type B lesion. Type C lesions are those adenomas that demonstrate neither effect and are solely hypoattenuating on the noncontrast-enhanced phase.

A review of the existing protocols in the literature [2] found that only 3 out of 56 scanning protocols use bolus tracking to optimize the timing of the arterial phase. Most protocols obtain a single arterial phase 25 seconds after administration of contrast. This is also the case in the aforementioned study by Bahl et al. [4]. When scanning at absolute time intervals, no optimization of the arterial phase can be guaranteed, since variance in cardiac output exists and the visualization of arterial wash-in of contrast may prove to be a short-lived effect. As an alternative to bolus tracking, a high-frequency multiphase 4DCT protocol as previously investigated in our center now enables us to obtain 16 phases with 11 different arterial phases at a similar dose exposure when compared with classic 4DCT [5]. Using high-frequency multiphase 4DCT an optimal arterial phase can be defined; this is to say, the phase on which the suspected parathyroid adenoma demonstrates maximum arterial enhancement (HU max). This way, potential adenomas can be visually detected with more ease. Also, motion artefacts due to swallowing or other movement are less problematic, since more phases are available for analysis.

We scanned 21 patients presenting with a parathyroid adenoma prior to parathyroidectomy following this protocol; we found 18 true positive patients. In 3 patients with primary hyperparathyroidism, no lesion could be detected. This suggests a sensitivity of 86%, which is in accordance with the literature. Since we did not encounter false-positive cases in this small population, we cannot comment on the specificity of the protocol. Scanning is performed on a 256-slice Revolution CT (GE Healthcare, Waukesha, Wisconsin, USA). Wide beam axial scanning was used instead of helical scanning to limit the dose [6].

First, we obtained a nonenhanced scan (NECT). Simultaneously, contrast administration was initiated. After a delay of 20 seconds, 11 subsequent phases with a 2-second interphase delay were obtained (arterial phases). With a 10-second interphase delay, 4 more phases were obtained (venous phases).

The effective dose associated with our proposed 4DCT protocol has a mean value of 6.7 mSv and can be as low as 1.4 mSv. The effective dose of 4DCT protocols in the literature is situated between 10.4 mSv and 13.8 mSv [7, 8].

For use in this pictorial essay, we reconstructed all images as they would appear on a classic 4DCT and is the case for the study by Bahl et al. Their protocol included a NECT series, an arterial phase at a fixed time interval, and a venous phase. For the arterial phase we chose to include the phase at 24 seconds after administration of contrast, slightly earlier than the traditional 25-second delay. We however do not possess a phase at the 25-second timepoint. For the venous phase we find 80 seconds as used in the protocol by Bahl et al. to be late, we included an earlier venous phase at 60 seconds after administration of contrast. These 3 phases are labeled (A), (B), and (D) in Figs. 1–7. We also included a second arterial phase; this phase is defined as the phase on which a region of interest defined in the suspected adenoma presents the highest Hounsfield value (HU max). This phase is labeled as (C) in the figures.

One patient in our case series presented with 2 different parathyroid adenomas, so we then identified 19 parathyroid adenomas. All 19 parathyroid lesions demonstrate a lower enhancement on the NECT phase. For 18 out of 19 lesions, an optimized later arterial phase can be defined. In only 1 case, the standard arterial phase coincides with the maximum arterial enhancement of the lesion. In all other cases, a later arterial phase demonstrates maximum enhancement of the lesion. The mean timing for this optimized phase is 30.8 seconds after administration of contrast; however, peak enhancement of the parathyroid lesion can be as late as 40 seconds after administration of contrast.

When defining the pattern of enhancement based on the 3 phases of a classic 4DCT protocol, we found 13 lesions behaved as type A lesions (higher peak enhancement in the arterial phase than normal thyroid tissue). With the addition of more phases and thus the possibility to define HU max using an optimized time window, we found 4 more lesions for which elevated arterial peak enhancement could not be detected on the standard arterial phase. We then found 17 out of 19 lesions to behave as type A lesions, an effect Bahl et al. only described for 20% of lesions. Our sample size is smaller, but this small pilot study using multiphase 4DCT found 89% of parathyroid lesions demonstrate a type A pattern of enhancement. Only 2 cases did not demonstrate arterial wash-in; these lesions do show venous wash-out of contrast: type B pattern of enhancement. No type C lesions were found. Regardless of the arterial enhancement pattern, 12 out of 19 lesions (63%) demonstrated wash-out of contrast in the venous phases.

We present some illustrative cases to demonstrate the diagnostic capabilities of high-frequency multiphase 4DCT.

A 67-year-old man presented with a small lesion, posterior to the right lobe of the thyroid (Fig. 1). We can see a blush of contrast enhancement on both arterial phases. The enhancement at 28 seconds after administration of contrast is mildly more prominent than the early arterial phase. Both phases are capable of detecting the lesion and the enhancement type.

A 73-year-old woman presented with a large parathyroid adenoma inferior to the left thyroid lobe (Fig. 2). Maximum enhancement is reached at 26 seconds after administration of contrast, 2 seconds after the standard arterial phase. Again, the enhancement of the adenoma is moderately increased in the later arterial phase as opposed to the standard phase. No thyroid tissue is present at the depicted level, the reader in this case should consider the low density of the lesion on NECT and the venous wash-out to be hallmarks of a parathyroid adenoma. In a type A lesion, both phases are capable of detecting the lesion as well as the enhancement type.

A right-sided lesion was found in a 66-year-old female (Fig. 3). The cystic degeneration pattern is typically seen in large parathyroid adenomas and helps to confirm the diagnosis. An optimal enhancement is however only found at 32 seconds after administration of contrast. The cystic pattern is typical enough to allow an adequate diagnosis, even though the arterial enhancement of this type A lesion that does not demonstrate venous wash-out is significantly less pronounced on the standard arterial phase. Both phases are capable of detecting the lesion as well as the enhancement type.

A 61-year-old woman presented with a small lesion adjacent to the left common carotid artery (Fig. 4). This lesion demonstrates higher enhancement on the standard arterial phase; however, this effect may be difficult to observe to the naked eye. Thirty seconds after administration of contrast the difference in enhancement between parathyroid and thyroid tissue has increased to 128 HU, an effect that no longer needs to be measured in order for it to be ascertained. Type A lesion with venous wash-out of contrast on both early and optimized arterial phase; however, on the standard arterial phase the increase in arterial enhancement proved less conspicuous.

A large retropharyngeal lesion in a 78-year-old male did not enhance 24 seconds after contrast administration (Fig. 5). This is probably due to poor cardiac output. Forty seconds after contrast administration we can see a slightly higher enhancement. Since we can demonstrate a venous wash-out effect, we can then consider this to be a mediastinally located ectopic parathyroid adenoma. Only the optimized phase suggests a type A enhancement pattern; the lesion is unenhanced on the standard arterial phase. On classic 4DCT, this lesion

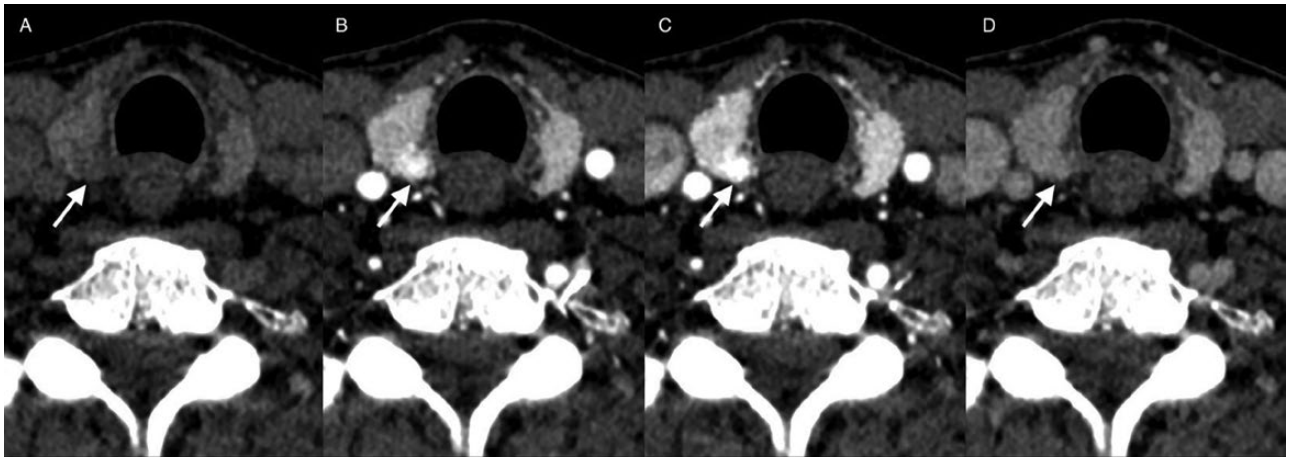

Figure 1. (A) NECT; (B) 24 seconds after contrast; (C) 28 seconds after contrast; (D) 60 seconds after contrast. Superior right-sided parathyroid adenoma. Contrast wash-in, no wash-out effect.

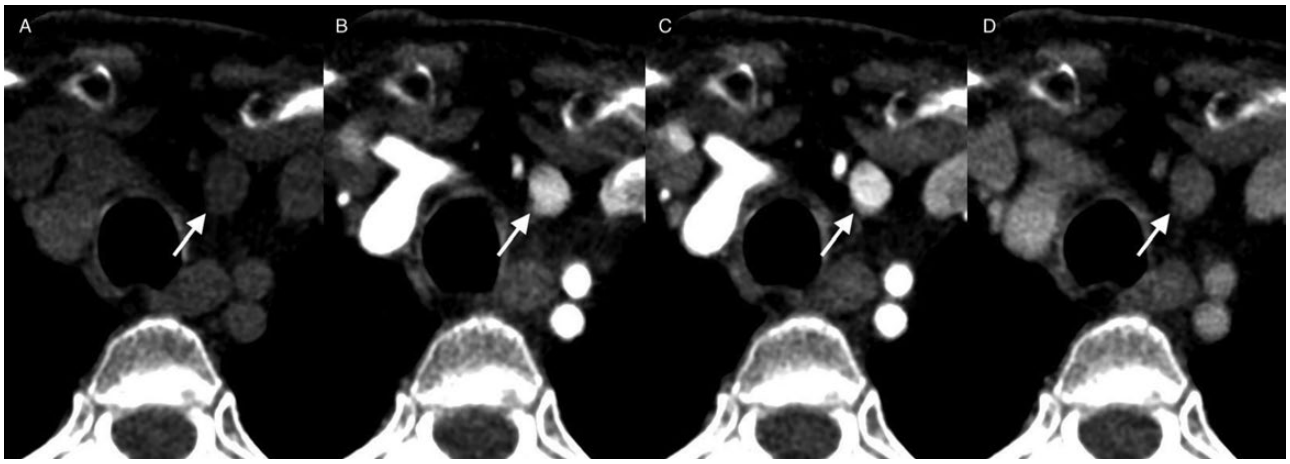

Figure 2. (A) NECT; (B) 24 seconds after contrast; (C) 26 seconds after contrast; (D) 60 seconds after contrast. Inferior left-sided parathyroid adenoma. Contrast wash-in and wash-out.

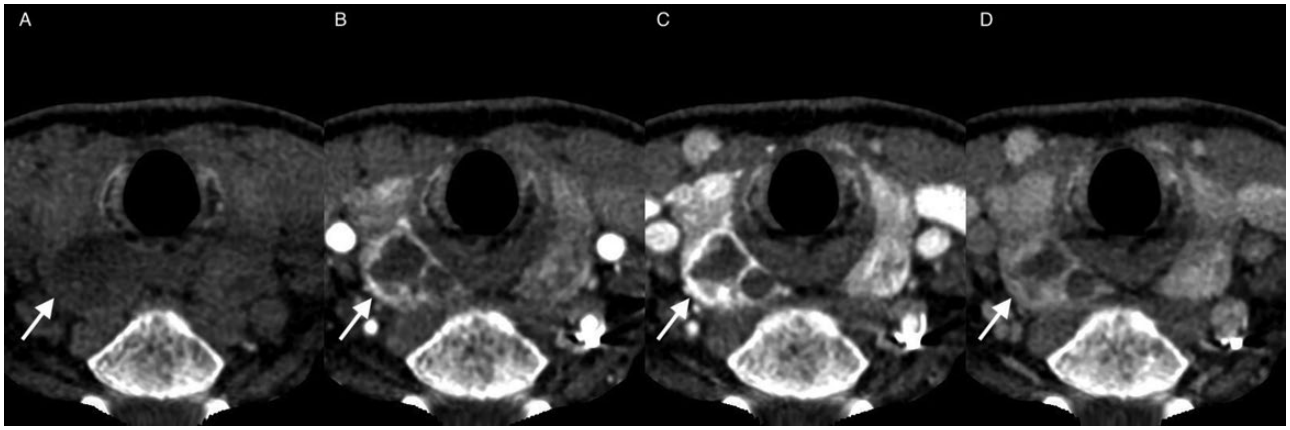

Figure 3. (A) NECT; (B) 24 seconds after contrast; (C) 32 seconds after contrast; (D) 60 seconds after contrast. Superior right-sided parathyroid adenoma. Contrast wash-in, no wash-out effect.

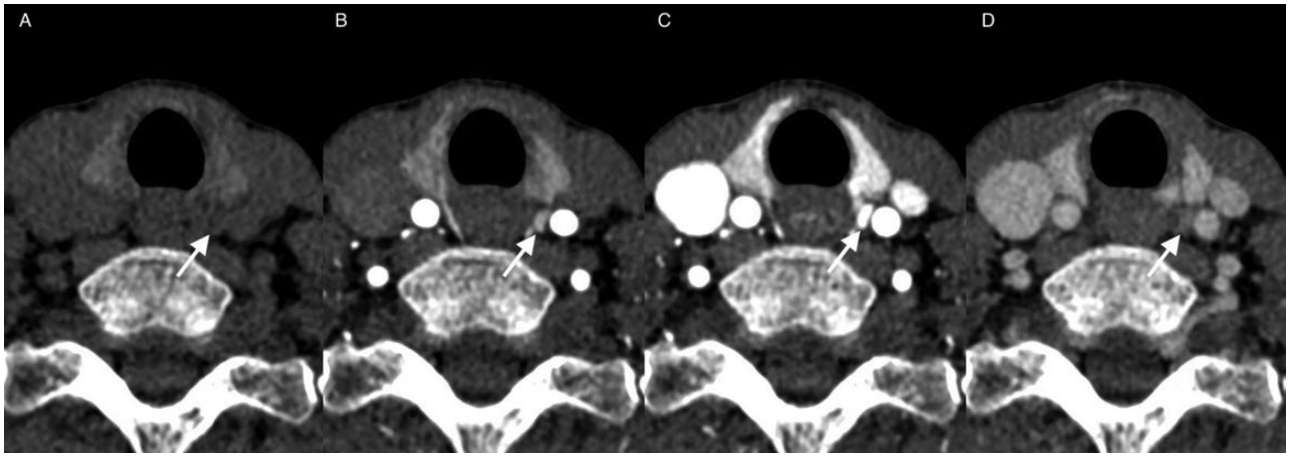

Figure 4. (A) NECT; (B) 24 seconds after contrast; (C) 30 seconds after contrast; (D) 60 seconds after contrast. Superior left-sided parathyroid adenoma. Contrast wash-in unclear at 24 seconds but evident at 30 seconds after contrast administration. Contrast wash-out.

might have gone undetected since it could have been mistaken for an enlarged lymph node.

In the same patient as Fig. 5, we also demonstrated a second enlarged parathyroid, posterior to the left thyroid lobe (Fig. 6). Again, arterial enhancement on the standard arterial phase is nonexistent. Forty seconds after contrast administration we see enhancement of the lesion but less intense than the thyroid. Type B lesion with wash-out of

contrast on the venous phase. On classic 4DCT this lesion probably would have also been mistaken for an enlarged lymph node.

The last example in this pictorial essay is a 70-year-old male (Fig. 7). This lesion posterior to the right thyroid lobe would have to be considered as a type C lesion on a classic

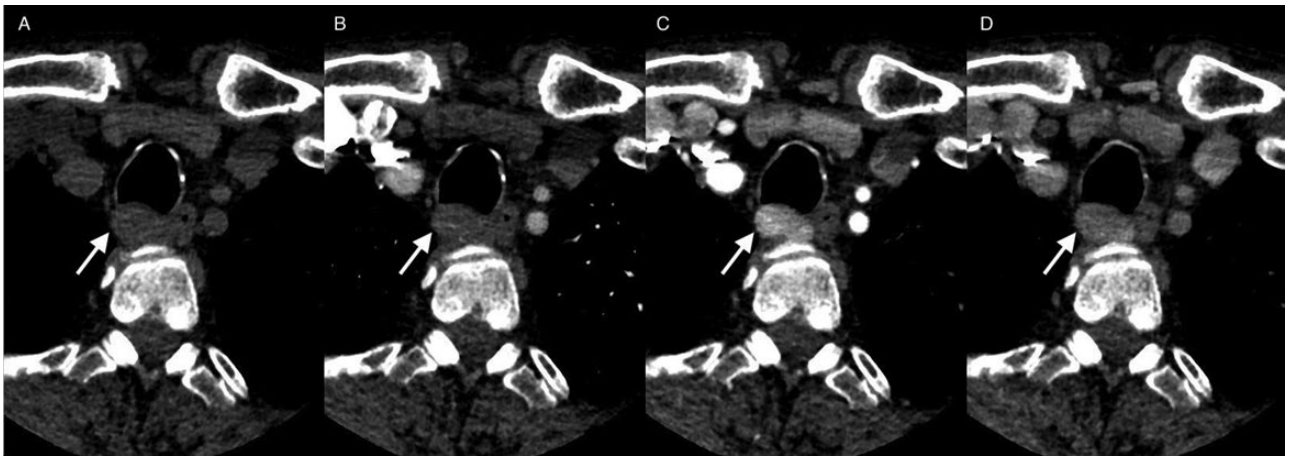

Figure 5. (A) NECT; (B) 24 seconds after contrast; (C) 40 seconds after contrast; (D) 60 seconds after contrast. Ectopic retropharyngeal situated parathyroid adenoma. No contrast wash-in at 24 seconds, discrete wash-in at 40 seconds after contrast administration. Contrast wash-out.

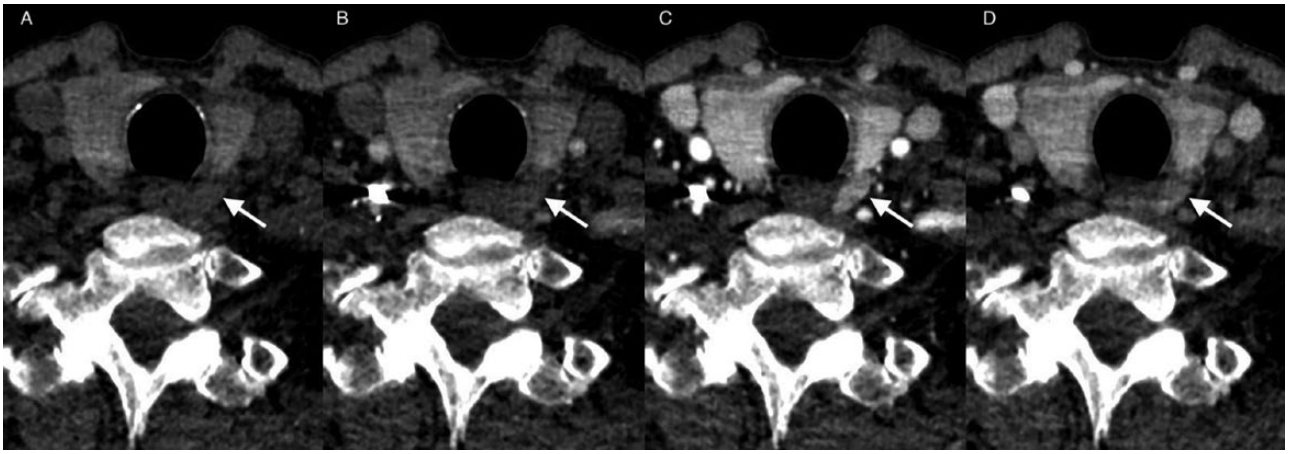

Figure 6. (A) NECT; (B) 24 seconds after contrast; (C) 40 seconds after contrast; (D) 60 seconds after contrast. Inferior left-sided parathyroid adenoma. No enhancement at 24 seconds, discrete enhancement at 40 seconds after contrast administration but no wash-in effect. Contrast wash-out.

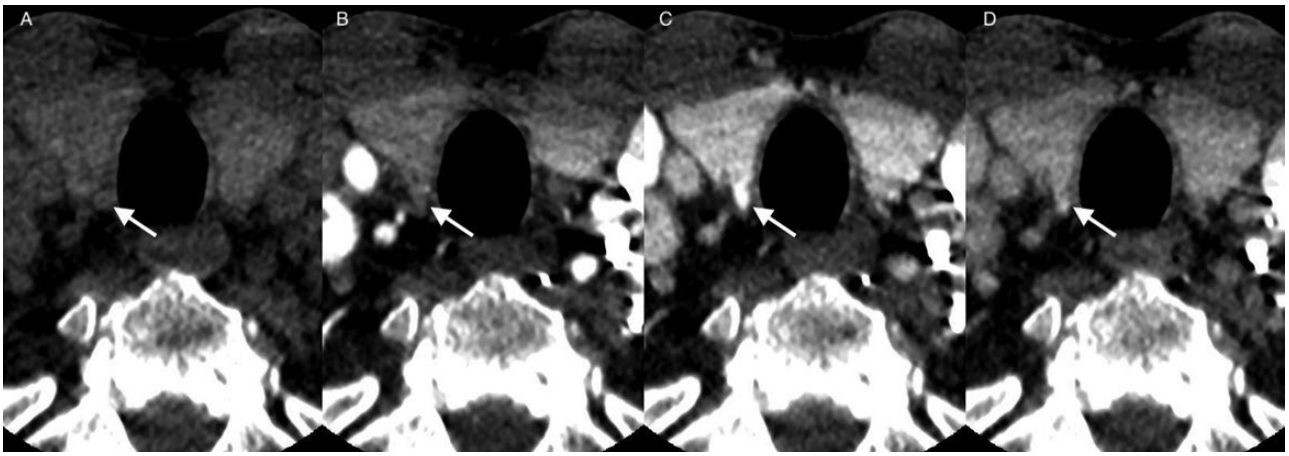

Figure 7. (A) NECT; (B) 24 seconds after contrast; (C) 38 seconds after contrast; (D) 60 seconds after contrast.

4DCT, if it were detected at all. It does not enhance in the standard arterial phase, neither does the lesion demonstrate venous wash-out. Our attention was only drawn to this lesion in the later arterial phases, where we could confirm an arterial wash-in of contrast. An absolute difference of 142 HU in enhancement between thyroid and parathyroid can be measured 38 seconds after administration of contrast. For this case only multiphase 4DCT was capable of detecting the lesion, as a detection of this small lesion based solely on the NECT images of a classic 4DCT protocol seems unlikely.

In conclusion, we can demonstrate an added value of high-frequency multiphase 4DCT in the detection of parathyroid lesions. More data are available for analysis at a similar dose exposure when compared with classic 4DCT. The mean timing for the optimized arterial window is 30.8 seconds after administration of contrast; however, peak enhancement of the parathyroid lesion can be as late as 40 seconds after administration of contrast. We found 17 out of 19 lesions demonstrating a type A pattern of enhancement, suggesting this pattern could be more prevalent than previously thought. Some parathyroid adenomas may be mistaken for enlarged lymph nodes using classic 4DCT whereas high-frequency multiphase 4DCT can detect a temporary rise in enhancement during the arterial phases, thus suggesting the lesions in question to be of parathyroid origin. Smaller lesions may prove more obvious as the difference in enhancement between parathyroid and thyroid becomes more prominent.

Acknowledgments

Conflict of Interest: No conflict of interest declared.

Informed Consent: All procedures followed were in accordance with the ethical standards of the responsible institutional committee on human experimentation. Informed consent was obtained from all patients for being included in the study.

Additional Information

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Data Availability: The data analyzed during the current study are included within the article. The different sets of CT images are not publicly available due to medical confidentiality.

References

1. Rodgers SE, Hunter GJ, Hamberg LM, et al. Improved preoperative planning for directed parathyroidectomy with 4-dimensional computed tomography. *Surgery*. 2006;**140**(6):932-940; discussion 940.
2. Raeymaeckers S, Tosi M, De Mey J. 4DCT scanning technique for primary hyperparathyroidism: a scoping review. *Radiol Res Pract*. 2021;**2021**:6614406.
3. Vijayasarathi A, Karnezis S, Azizyan A, Salamon N, Sepahdari A. 4D CT parathyroid for the general radiologist: a pictorial essay of illustrative cases. *Curr Probl Diagn Radiol*. 2020;S0363-0188(20)30046-3. doi: 10.1067/j.cpradiol.2020.02.012
4. Bahl M, Sepahdari AR, Sosa JA, Hoang JK. Parathyroid adenomas and hyperplasia on four-dimensional CT scans: three patterns of enhancement relative to the thyroid gland justify a three-phase protocol. *Radiology*. 2015;**277**(2):454-462.
5. Raeymaeckers S, De Brucker Y, Vanderhasselt T, Buls N, De Mey J. Detection of parathyroid adenomas with multiphase 4DCT: towards a true four-dimensional technique. *BMC Med Imaging*. 2021;**21**(1):64.
6. Lambert JW, Phillips ED, Villanueva-Meyer JE, Nardo L, Facchetti L, Gould RG. Axial or helical? Considerations for wide collimation CT scanners capable of volumetric imaging in both modes. *Med Phys*. 2017;**44**(11):5718-5725.
7. Hinson AM, Lee DR, Hobbs BA, Fitzgerald RT, Bodenner DL, Stack BC Jr. Preoperative 4D CT localization of nonlocalizing parathyroid adenomas by ultrasound and SPECT-CT. *Otolaryngol Head Neck Surg*. 2015;**153**(5):775-778.
8. Mahajan A, Starker LF, Ghita M, Udelsman R, Brink JA, Carling T. Parathyroid four-dimensional computed tomography: evaluation of radiation dose exposure during preoperative localization of parathyroid tumors in primary hyperparathyroidism. *World J Surg*. 2012;**36**(6):1335-1339.