Supplement

Supplement 1: The reasons for the application of dual-energy computed tomography (DECT) in patients with papillary thyroid carcinoma (PTC)

In the Chinese Society of Clinical Oncology (CSCO) diagnosis and treatment guidelines for persistent/recurrent and metastatic differentiated thyroid cancer (version 2018) (1), when there are suspected local lesions, neck ultrasound, enhanced CT or contrast MRI are juxtaposed as a level I-2A recommendation. And in National Comprehensive Cancer Network (NCCN) guidelines (version 2018), for papillary carcinoma or suspicious for papillary carcinoma, CT/MRI with contrast was suggested to use for fixed, bulky, or substernal lesions. This support that enhanced CT is not a contraindication for patients with PTC. Moreover, CT examination can more accurately determine the extent of lymph node metastasis (LNM), which plays a vital role in the plan of surgical procedures.

In the current study, the patient suspected of thyroid malignant lesion by ultrasound (US) firstly, and then confirmed by US-guided biopsy or US-guided fine-needle aspiration (US-FNA) as PTC. DECT was performed to rule out or confirmed the presence of LNM.

The reason for using DECT in the current study as following. First, its radiation dose (total dose-length product, DLP) was 5 - 6 times lower than ordinary enhanced CT (2). Second, significantly lower kVp and tube current with better image quality was achieved with DECT. Third, DECT realizes multi-parameter imaging, such as single-energy images, energy spectrum curves, base material images, and the

quantitative concentration values and effective atomic numbers of corresponding base materials. The biggest advantage of DECT is not only to show morphological changes but also to provide many quantitative indicators that reflect the essential characteristics of the lesion (3). The current study looked forward to applying DECT to predict ipsilateral lateral cervical lymph node metastasis (ipsi-LLNM) in patients with PTC before the operation, to guide the plan of clinical procedures, which has not been reported before.

Supplement 2: Preoperative DECT did not delay radioiodine ablation in patients with PTC.

NCCN guidelines (version 2018 and version 2020 V1) (4, 5) both clearly state that iodinated contrast is required for optimal cervical imaging using CT and potential delay in radioactive iodine (RAI) treatment will not cause harm.

Michael W. Yeh's working group researched the content "Use of Iodinated Contrast and Impact on Subsequent Treatment" (6). The results showed that CT imaging of the neck was optimized by iodinated intravenous contrast. This advantage must be balanced against the impact the iodine load would have in causing what was usually a minor delay in subsequent postoperative RAI ablation. After the administration of iodinated contrast, an awaiting period of at least one month was recommended to allow urinary iodine levels to return to baseline levels before moving forward with RAI ablation (7). CSCO expert consensus on the evaluation of ^{131}I before the treatment of differentiated thyroid cancer gave similar guidance. At present, there was no evidence to suggest that delays of this scale adversely affect thyroid cancer outcomes.

As we all know, more than 90% of the administered iodine was excreted via urine, and the thyroid being the major reservoir of iodine in the body, iodine content should fall rapidly after total thyroidectomy even in patients having preoperative DECT (8). Furthermore, the recommendations against performing contrast-enhanced CT seem to be based on studies conducted in the past when lipophilic contrast agents were in use, which tend to get stored in adipose tissues for a long time. Whereas currently, the

majority of centers used water-soluble ionic contrast agents (such as iohexol, which was used in our study), which were unlikely to be retained in extracellular fluids (8). Therefore, unless there was further iodine contamination, the urinary iodine concentration (UIC) should soon revert to the previous equilibrium after DECT examination. Many studies showed that the time for UIC to normalize was 30 to 43 days (7-10). In addition, in routine practice, if the patients with PTC who came to our hospital for the surgery needed postoperative RAI therapy, the whole process "preoperative examination → thyroidectomy → postoperative rehabilitation and discharge → appointment and preparation before RAI therapy → admission for RAI therapy" needed to be completed. The whole process took at least six weeks without any delay, which was longer than required in the ATA guidelines. In 2015 ATA guidelines, postoperative RAI therapy should be routinely administered only in high-risk differentiated thyroid cancer (DTC); it was not recommended in low-risk DTC and should only be considered in ATA intermediate-risk group (11). And the majority of studies showed that the timing of post-thyroidectomy initial RAI therapy did not affect the overall survival or long-term outcomes (12-16). Therefore, RAI administration may be safely planned according to the logistics of the local health and the patient itself (12).

In the current study, all patients who underwent DECT examination before surgery should be guaranteed at least one month apart before undergoing ^{131}I treatment after surgery, and the delay did not cause any harm according to our follow-up results.

Supplement 3: Specific US and CT diagnostic criteria of cervical lymph node metastasis from PTC

Sonographic features suggestive of abnormal metastatic lymph nodes according to 2015 American Thyroid Association (ATA) Management Guidelines for Adult Patients with Thyroid Nodules and Differentiated Thyroid Cancer (11), include enlargement, loss of the fatty hilum, a rounded rather than oval shape, hyperechogenicity, cystic change, calcifications, and peripheral vascularity. The location of the lymph nodes may also be useful for decision-making. Malignant lymph nodes are much more likely to occur in levels III, IV, and VI than in level II. No single sonographic feature is adequately sensitive for the detection of lymph nodes with metastatic thyroid cancer (17).

Metastatic lymph nodes were deemed to be present in CT images when at least one of the following criteria was fulfilled: size larger than or equal to 10 mm, strong enhancement, heterogeneous enhancement, calcification, cystic and/or necrotic change, and extrathyroidal extension (ETE) (18, 19). Lymph node size was determined by using the maximal short-axis diameter. Strong enhancement was considered to be similar to that of the pharyngeal mucosa. Fuzzy boundaries and/or invasion into adjacent tissues were considered to indicate ETE (20).

Supplement 4: DECT Examination

Patients held their breath during eupnea before the horizontal scan in a transverse position. All patients were scanned craniocaudally in the supine position with the bilateral upper limbs placed on both sides, shoulders drooping as much as possible, head slightly tilted. And the longitudinal alignment of the positioning cursor was aligned on the central sagittal plane of the cervicothoracic region. The orthotopic scanning was performed firstly, and then the scanning baseline and range were confirmed according to the scout view. The whole neck was scanned from the upper edge of the aortic arch to the lower edge of the submandibular gland, which covered the thyroid and cervical lymph nodes area.

Keep the patient's heart rate at a normal level throughout the scan. After CT scanning, arterial phase and venous phase contrast-enhanced scanning were performed. The images were acquired in the dual-energy mode by using the following parameters: tube current 600 mA, helical thickness 6 mm, helical pitch 0.9, rotation speed 0.28 s, detector width 40 mm, collimation 64×0.6 mm. The scan parameters were set according to the concept of as low as reasonably achievable for radiation protection. A fast rotation speed and a moderate helical pitch were chosen to obtain fast scanning speed and to reduce motion artifacts of neck and radiation dose. For contrast-enhanced scanning, an iodinated nonionic contrast agent (iohexol; 350 mg/dl iodine, Somatom Defination Flash, Siemens Healthcare, Forchheim, Germany) was administered through the right elbow median vein by a dual-head injector. The dosage was 1 ml/kg with a flow rate of 3 ml/s, the total injection dose was 60 - 70 ml,

followed by a bolus injection of 40 ml saline given at the same flow rate. The timing of arterial phase scanning was determined by automatic trigger technique, and the scanning delay was 25 s at the beginning of arterial phase scanning. The delay time of the venous scan was 20 s after the end of the arterial scan.

All the original CT data were reconstructed into contiguous axial images with a section thickness of 1 mm, a field of view (FOV) of 200 mm and a matrix of 512 × 512. The DECT data of arterial and venous phases were transferred to SIEMENS Syngovia workstation (Syngo DE, Siemens Healthcare, Forchheim, Germany) for analysis, the Liver VNC function keys for computer automatic processing, then the iodine maps were obtained.

Table S1: The reference range of each thyroid functional index

thyroid functional indicators	reference ranges
TSH	0.27 - 4.2m IU/l
Tg	1.15 - 130.70 ng/ml
Anti-Tg	0 - 115 IU/ml
Anti-TPO	0.00 - 34.00 IU/ml

TSH = thyroid stimulating hormone, Tg = thyroglobulin, Anti-Tg = anti-thyroid stimulating hormone, Anti-TPO = anti-thyroid peroxidase

Table S2: The status of lymph node metastasis in the current study

	LLNM (-) (n = 278)	LLNM (+) (n = 128)
CLNM (-)	206 (74.1%)	16 (12.5%) *
CLNM (+)	72 (25.9%)	112 (87.5%)

* skip metastases, meaning LLNM without CLNM.

LLNM = lateral cervical lymph nodes metastasis, CLNM = central cervical lymph nodes metastasis

Table S3: The consistency analysis of the measurement indexes of the two readers

Parameters	ICC (95%CI)	*P* Value
IC in the arterial phase		
Doctor A	0.974(0.970-0.978)	0.000
Doctor B	0.964(0.958-0.969)	0.000
Doctor A and doctor B	0.916(0.902-0.928)	0.000
IC in the venous phase		
Doctor A	0.963(0.957-0.969)	0.000
Doctor B	0.923(0.910-0.934)	0.000
Doctor A and doctor B	0.913(0.899-0.926)	0.000

IC = iodine concentration, ICC = intraclass correlation coefficient, CI = confidence interval

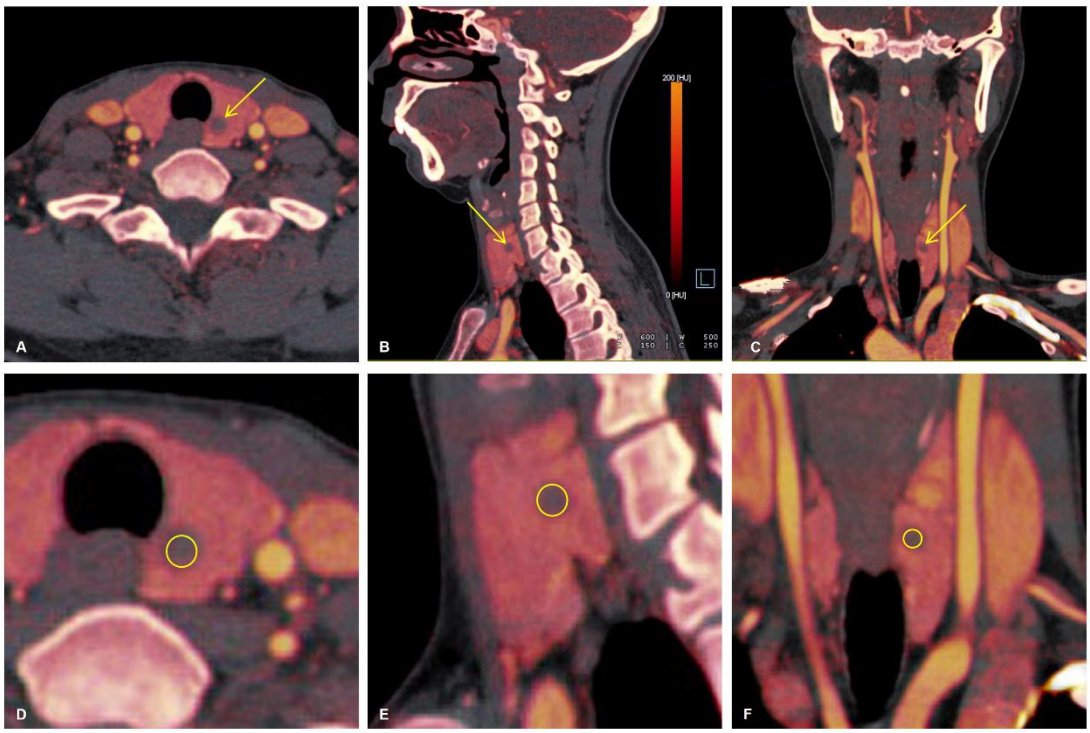

Figure S1: A-C, The yellow arrow indicated a lesion located on the dorsal inferior pole of the left lobe of thyroid in axial, sagittal, and coronal iodine maps. D-F, A ovoid region of interest (yellow; area, 78 mm^2) was placed in the solid part, including the entire lesion as large as possible, to avoid peripheral fat, cystic, necrosis and calcification.

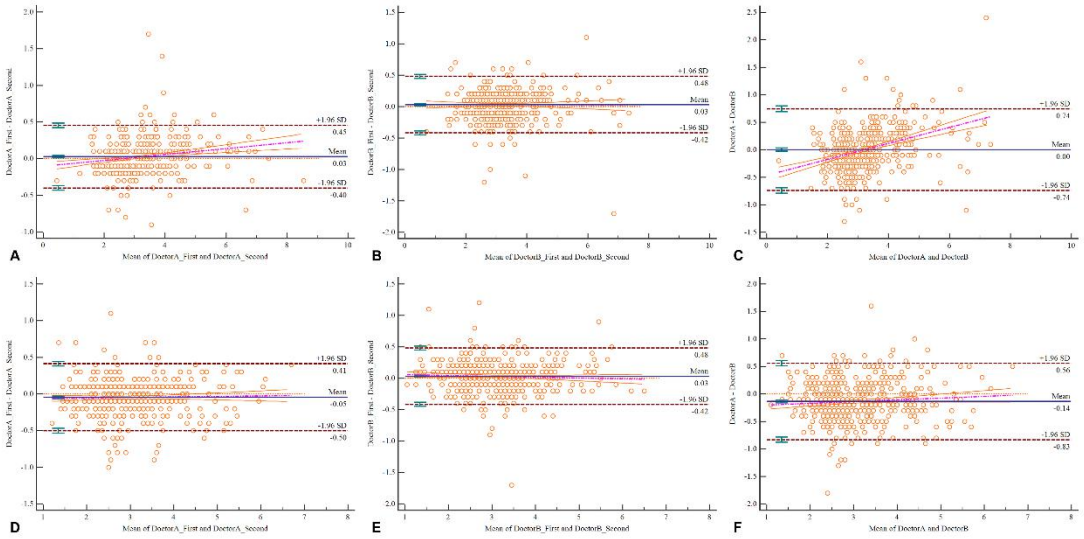

Figure S2: Bland-Altman plots of iodine concentration measurements in arterial and venous phases by two doctors. A, Doctor A intra-observer in iodine concentration in the arterial phase. B, Doctor B intra-observer in iodine concentration in the arterial phase. C, Doctor A and B inter-observer in iodine concentration in the arterial phase. D, Doctor A intra-observer in iodine concentration in the venous phase. E, Doctor B intra-observer in iodine concentration in the venous phase. F, Doctor A and B inter-observer in iodine concentration in the venous phase.

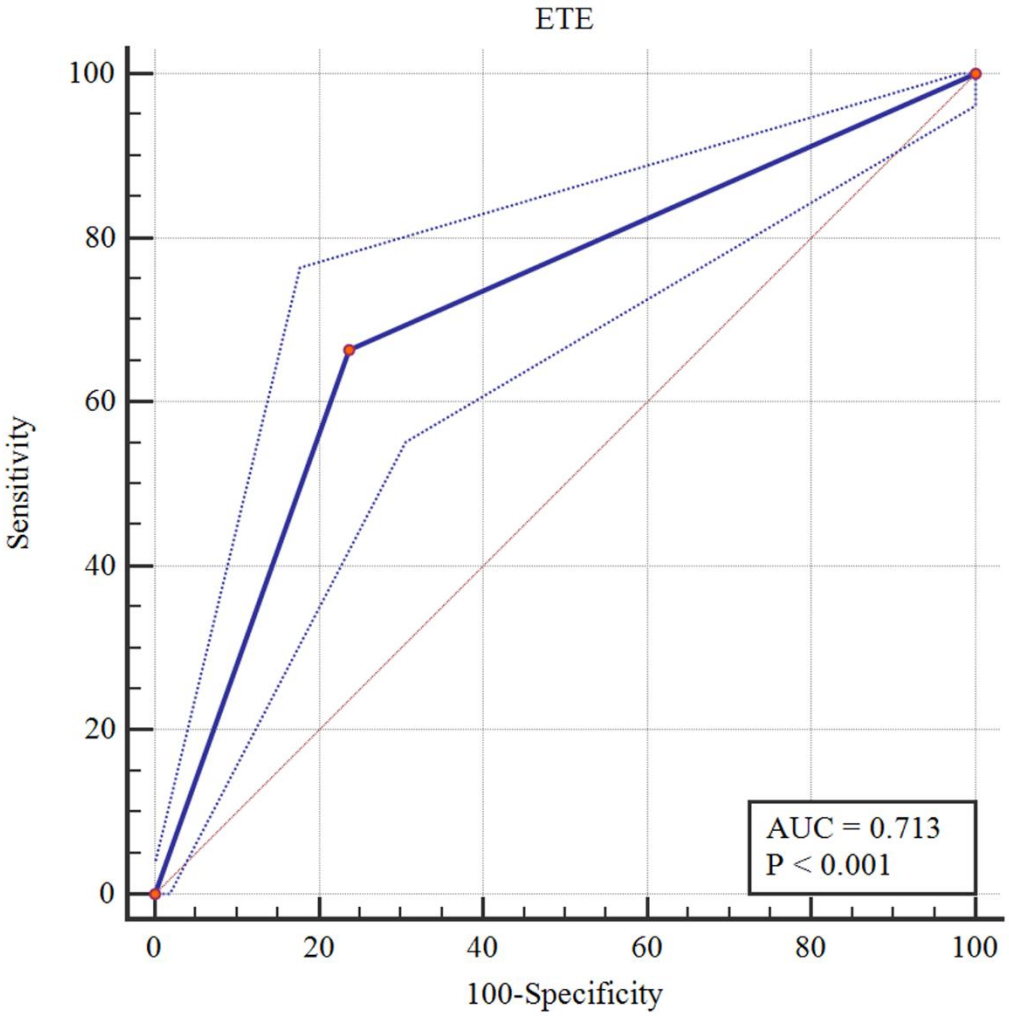

Figure S3：ROC curves of ETE in patients with PTC. AUC was 0.713.

ROC = receiver operating characteristic, PTC = papillary thyroid carcinoma, AUC = area under the curve, ETE = extrathyroidal extension

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