Assessment of Added Value of Noncontrast to Contrast-Enhanced Abdominal Computed Tomography Scan for Characterization of Hypervascular Liver Metastases

Gelareh Sadigh, Emory University
Sadhna B. Nandwana, Emory University
Courtney Moreno, Emory University
Kelly Lynn Cox, Emory University
Deborah A Baumgarten, Emory University
Jeffrey M. Switchenko, Emory University
Tiffany Easter, Emory University
Kimberly E Applegate, Emory University

Journal Title: Current Problems in Diagnostic Radiology
Volume: Volume 45, Number 6
Publisher: Elsevier: 12 months | 2016-11-01, Pages 373-379
Type of Work: Article | Post-print: After Peer Review
Publisher DOI: 10.1067/j.cpradiol.2016.05.003
Permanent URL: https://pid.emory.edu/ark:/25593/s67wh

Final published version: http://dx.doi.org/10.1067/j.cpradiol.2016.05.003

Copyright information:
© 2016 Elsevier Inc.

Accessed January 1, 2020 11:36 PM EST
Assessment of Added Value of Noncontrast to Contrast-Enhanced Abdominal Computed Tomography Scan for Characterization of Hypervascular Liver Metastases

Gelareh Sadigh, MD1,*, Sadhna B. Nandwana, MD1, Courtney Moreno, MD1, Kelly L. Cox, DO1, Deborah A. Baumgarten, MD, MPH, FACR1, Jeffrey Switchenko, PhD1,2, Tiffany Easter, BA1,3, and Kimberly E. Applegate, MD, MS, FACR1,2,3

1Department of Radiology and Imaging Sciences, Emory University School of Medicine, Atlanta, GA
2Department of Biostatistics & Bioinformatics, Rollins School of Public Health, Atlanta, GA
3Department of Radiology, Children’ s Hospital of Atlanta, Atlanta, GA

Abstract

Assess the added value of nonenhanced computed tomography (NECT) to contrast-enhanced CT (CECT) of the abdomen for characterization of hypervascular liver metastases and incidental findings. Institutional review board approved, Health Insurance Probability and Accountability Act compliant, retrospective study of patients with melanoma, neuroendocrine tumor, or thyroid cancer. First available triphasic abdomen CT after initial diagnosis was reviewed by 3 radiologists. The 3 most suspicious lesions were characterized on the CECT as benign or malignant and then recharacterized after reviewing the NECT with CECT. Incidental renal and adrenal lesions were characterized similarly. Diagnostic performance of CECT vs its combination with NECT was assessed. Statistical significance level was set at P < 0.05. A total of 81 patients were included (mean age = 55 years; 52% male; 64% with liver lesions; 27% and 11% with incidental renal and adrenal lesions, respectively). Percentage area under the curve and 95% CI of CECT vs combination with NECT for characterization of liver metastases was 98(94–100) vs 99(96–100) for reviewer 1 (P = 0.35), 93(86–100) vs 94(87–100) for reviewer 2 (P = 0.23), and 96(90–100) vs 99(97–100) for reviewer 3 (P = 0.32). Mean difference in area under the curve and 95% CI between 2 protocols for characterization of liver, renal, and adrenal lesions were −0.007(−0.05 to 0.04) (P = 0.63), −0.09(−0.25 to 0.07) (P = 0.22), and −0.01(−0.05 to 0.02) (P = 0.27), respectively. After addition of NECT, confidence level for lesion characterization increased 4%–15% for liver metastases, 18%–59% and 33%–67% for renal and adrenal lesions, respectively. In conclusion, while addition of NECT to CECT improved radiologist’ confidence, there was no statistically significant change in characterization of hypervascular liver metastases or incidental renal and adrenal lesions.

*Research reported in this publication was supported in part by the Biostatistics and Bioinformatics Shared Resource of Winship Cancer Institute of Emory University and NIH, United States/NCI, United States under Award no. P30CA138292. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

Reprint request: Gelareh Sadigh, MD, Department of Radiology and Imaging Sciences, Emory University School of Medicine, 1364 Clifton Rd NE, Room 125D, Atlanta, GA 30322. gsadigh@emory.edu (G. Sadigh).
**Introduction**

Dual blood supply of liver by both the hepatic artery (25%–30%) and portal vein (70%–75%) influences the vascularity of hepatic metastases, with those supplied by the hepatic arterial system often times being hypervascular vs those supplied by the portal venous system [1]. Typically, hypovascular hepatic metastases are best evaluated during the portal venous phase approximately 60–70 seconds after injection of the bolus [1,2]. However, prior studies have shown that hypervascular hepatic metastatic lesions, such as melanoma, neuroendocrine tumors (NET), thyroid cancer, renal cell carcinoma (RCC), sarcomas and some breast cancers may be optimally detected during the arterial phase (25–30 seconds after injection of contrast media) rather than the portal venous phase (Fig 1) [1,2].

Value of triphasic computed tomography (CT) that includes a nonenhanced CT (NECT) with an arterial and portal phase contrast-enhanced CT (CECT) for characterization of hypervascular liver metastases has been previously investigated with controversial results [3–6]. As such, protocols for evaluation of hypervascular liver metastases vary among different institutions. For example, at some institutions, triphasic CT is used for imaging of hypervascular liver metastases such as RCC patients whereas other institutions use only arterial and portal phases without NECT for melanoma, NET, and thyroid cancer patients [7].

In the 2014 American College of Radiology (ACR) appropriateness criteria, CECT of abdomen was given the same rating as its combination with NECT for initial characterization of indeterminate liver lesions, in patients with a known history of an extra hepatic malignancy, when magnetic resonance imaging with contrast is not available [8]. In addition, for suspected hypervascular liver metastases, the ACR appropriateness criteria specifically suggest NECT is helpful for lesions with hemorrhage or calcifications [1]. Another factor in consideration of using NECT as part of a metastatic workup is the potential added value in management of incidental renal and adrenal lesions in these patients [9–11].

Previously reported sensitivities and specificities for CECT characterization of hypervascular liver metastases, range from 72%–83% and 37%–92% [12,13]. The added value of NECT images to arterial and portal phase CECT for characterization of hypervascular liver metastases is debated with the most of the studies published for more than 10 years ago [3–6]. Therefore, the purpose of this study is to reevaluate the benefit (if any) of the addition of NECT in the characterization of hypervascular liver metastases and incidental renal and adrenal lesions on current multidetector CT scanners [7].

**Methods**

Institutional review board approval and a waiver of informed consent were obtained for this retrospective review. The study was Health Insurance Probability and Accountability Act compliant.
Study Population

The radiology information system database was searched for consecutive patients 18 years or older using International Classification of Diseases 9 codes associated with known melanoma, NET, or thyroid cancer and who were seen at our institution between 2010 and 2012. The first available triphasic CT of the abdomen (which includes a NECT, arterial and portal phase CECT) after the documented date of diagnosis were included in the study. Patients without a triphasic CT, indeterminate pathology, or those later found to have metastases from cancers other than melanoma, neuroendocrine, or thyroid cancer that were identified by a chart review were excluded.

Imaging Technique

All CT scans were performed using either a GE Light Speed VCT 64-slice or a Siemens Somatom 64-slice or a GE Bright Speed 16-slice scanner. Patients underwent volumetric acquisition NECT (0.625 mm for 64-slice scanners and 1.25 mm for 16-slice scanner) with a reconstructed slice thickness of 5 mm to include the entire liver. A weight-based dose of nonionic contrast (maximum 150 mL) was administered at the rate of 3.5 mL/s. Using SmartPrep technique on the aorta at the level of the liver, which was triggered at 150 HU, volumetric arterial phase images were obtained at around 25–30 seconds after contrast injection with a reconstructed 2.5 mm slice thickness and volumetric portal venous images were obtained 30 seconds later with a reconstructed 2.5 mm slice thickness.

Image Review

A total of 3 board certified abdominal radiologists with 2, 2, and 6 years postsub-specialty training, respectively, were blinded to patient's final diagnosis of liver pathology and independently reviewed the CECT followed by the NECT plus the CECT images. The 3 most suspicious lesions as determined by imaging characteristics for each patient were identified on each study and their size was measured and documented. To assess interobserver agreement and ensure all reviewers assessed the same 3 lesions, each reviewer was responsible for identifying and documenting the image number and size for (up to) 3 lesions in one-third of the patients. Subsequently, each reviewer independently characterized each identified lesion on CECT imaging alone (protocol 1) and then recharacterized each lesion after the addition of NECT with the CECT images (protocol 2) using a 4-point scale (1 = definitely benign, 2 = probably benign, 3 = probably malignant, and 4 = definitely malignant). Lesions with enhancement on arterial phase and washout on portal phase were considered malignant. Reviewers were blinded to each other's characterization of lesions on both protocols. Similarly, the reviewers identified and characterized incidental renal and adrenal lesions measuring greater than 1 cm using the same 4-point scale on both protocols (CECT alone followed by NECT plus CECT imaging review).

Reference Standard

The electronic medical record was reviewed in September 2013 (1–3 years after diagnosis depending on the time of diagnosis) for liver lesions and in July 2015 (2.5–4.5 years after diagnosis) for incidental renal and adrenal lesions by an additional board certified abdominal radiologist with 19 years of practice. Reference standard of benign or malignant lesions
were established by reviewing histopathology records following surgical excision or biopsy results. When histopathological examination or biopsy results were not available, remote and follow-up imaging studies in comparison to the index scan were reviewed. Progression of disease or response to therapy (excluding ablations), as documented through imaging, were used to determine benign vs malignant lesions.

Statistical Analysis

Sensitivity, specificity and 95% CI of CECT alone vs its combination with NECT for characterization of liver lesions on a per patient and a per lesion basis were calculated for each reviewer and the 2 protocols’ diagnostic performance were compared using McNemar test. Receiver operator characteristic (ROC) curves were constructed to determine the area under the curve (AUC) for each reviewer using STATA 10 (Stata Corp, College Station, TX). Further, we implemented a multireader multicase (MRMC) analysis to handle comparison AUC between the 2 protocols whereas accounting for more than 1 reviewer in the analysis, using the software package OR-DBM MRMC 2.4 (Obuchowski-Rockette method extension) [14]. A jackknife procedure was used to estimate the covariance matrix [15] and the trapezoidal or Wilcoxon nonparametric was used to estimate the ROC curve for each reader and group. Mean difference in AUC between groups, CI of the differences and P values were reported at patient level. A subgroup analysis of liver lesions 1 cm or larger was further performed and the AUC on a per lesion basis was compared for the 2 protocols. Statistical significance was set at P < 0.05.

Additionally, sensitivity, specificity, and 95% CI of CECT vs its combination with NECT for characterization of incidental renal and adrenal lesions on a per patient basis were calculated and compared using McNemar test. A MRMC analysis was performed to compare the AUCs as described later.

Kappa analyses were performed to assess agreement among the 3 reviewers using both the 4-point scale for analysis of change in confidence levels as well as a 2-point scale (benign vs malignant) for analysis of characterization of lesions. K values of 0.00–0.20 indicated slight agreement; 0.21–0.40, fair agreement; 0.41–0.60, moderate agreement; 0.61–0.80, substantial agreement; and 0.81–1.00, almost perfect agreement [16].

Results

Study Population

Overall, 81 patients were included in this study (Fig 2). Baseline characteristics of patients are shown in Table 1. In all, 52% (42/81) were male. Patients' age ranged from 24–82 years (mean = 55 years). Overall, 51% (41/81) had melanoma, 44% (36/81) had NET, and 5% (4/81) had thyroid cancer.

Reference standard was documented histopathology in 16% (13/81) of patients and findings of progression of disease or response to therapy on additional imaging studies in 84% (68/81) of patients.
A total of 128 liver lesions were identified in 52 of 81 patients (64%). Of the 128 liver lesions reviewed, one with indeterminate pathology and no additional imaging available to determine reference standard and one with postablative changes were excluded. Both of these excluded lesions were in patients with more than 1 liver lesion for which a reference standard existed. Of the remaining 126 lesions, 48% (60/126) were malignant in 22 patients and 52% (66/126) were benign in 30 patients, based on the reference standard. Mean size of the liver lesions was 2.1 ± 2.4 cm (median = 1.2 cm), ranging from 0.3–11.8 cm. Overall, 51 lesions (40%) were less than 1 cm.

**Added Value of NECT to CECT for Characterization of Liver Lesions**

**Per Patient Analysis**—The sensitivity, specificity, 95% CI and area under ROC of CECT and its combination with NECT for detection and characterization of patients with malignant vs benign liver lesions is shown in Table 2. ROC curves are demonstrated in Figure 3. Using MRMC analysis, the mean difference in AUC between the 2 protocols was −0.007 (95% CI: −0.05 to −0.04; \( P = 0.60 \)). Interobserver agreement for characterization of malignancy on CECT imaging alone among the 3 reviewers was 0.69 and on combination of CECT with NECT imaging review was 0.69 consistent with substantial agreement when using a 2-point scale (benign vs malignant lesions).

The addition of NECT improved reviewer 1’s confidence level for characterization in 15% (8/52) of patients with liver lesions and decreased confidence level for characterization in 2% (1/52) of patients. For reviewer 2, the confidence level improved in 4% (2/52) of patients. There was no change in benign vs malignant characterization of patients for reviewers 1 and 2. For reviewer 3, the confidence level improved in 4% (2/52) of patients resulting in a correct change in characterization. Additionally, the confidence level decreased in 4% (2/52) of patients, resulting in an incorrect change in characterization (Figs 4 and 5).

**Per Lesion Analyses**—The diagnostic performance of CECT and its combination with NECT for detection and characterization of 126 liver lesions is shown in Table 2. Interobserver agreement for characterization of malignancy on CECT imaging alone among the 3 reviewers was 0.77 and with combination of CECT and NECT imaging was 0.74, consistent with substantial agreement when using a 2-point scale (benign vs malignant lesions).

The AUC for characterization of liver lesions 1 cm or larger was 96% (95% CI: 91%–100%) for reviewer 1, 93% (95% CI: 87%–100%) for reviewer 2, and 96% (95% CI, 91%–100%) for reviewer 3 with CECT and did not change after addition of NECT, with AUC of 97% (95% CI: 92%–100%) (\( P = 0.23 \)) for reviewer 1, 94% (95% CI: 88%–100%) (\( P = 0.28 \)) for reviewer 2 and 96% (95% CI: 91%–100%) (\( P = 0.38 \)) for reviewer 3.

The AUC for characterization of liver lesions smaller than 1 cm was 85% (95% CI: 65%–100%) for reviewer 1, 79% (95% CI: 63%–94%) for reviewer 2, and 80% (95% CI: 59%–100%) for reviewer 3 with CECT, and similarly did not change after addition of NECT, with AUC of 87% (95% CI: 68%–100%) (\( P = 0.40 \)) for reviewer 1, 80% (95% CI: 65%–95%) (\( P = 0.19 \)) for reviewer 2, and 87% (95% CI: 68%–100%) (\( P = 0.23 \)) for reviewer 3.
Comparison of the AUC for characterization of liver lesions 1 cm or larger vs those smaller than 1 cm using CECT showed no significant difference for any of the reviewers ($P = 0.35$ for reviewer 1, $P = 0.09$ for reviewer 2, and $P = 0.14$ for reviewer 3).

**Added Value of NECT to CECT for Characterization of Renal and Adrenal Findings**

**Renal Lesions**—Overall, 27% (22/81) of patients had 1 renal lesion at least 1 cm in size. Reference standard for all these lesions was prior or follow-up imaging, except for one with histopathology. In all, 3 of 28 lesions were malignant and 25 of 28 were benign. The diagnostic performance of CECT and its combination with NECT for characterization of patients with renal lesions is shown in Table 3. Using MRMC analysis, the mean difference in AUC between the 2 protocols was $-0.09$ (95% CI: $-0.25$ to $0.07$; $P = 0.225$). Interobserver agreement for characterization of renal malignancy on CECT imaging alone among the 3 reviewers was 0.82 and on combination of CECT and NECT imaging review was 0.82, consistent with almost perfect agreement using a 2-point scale (benign vs malignant).

The addition of NECT improved reviewer 1’s confidence level for characterization in 45% (10/22) of patients with incidental renal lesions resulting in a correct change in characterization of 4% (1/22) of patients. For reviewer 2, confidence level improved in 18% (4/22) of patients without a change in benign vs. malignant characterization. For reviewer 3, confidence level improved in 59% (13/22) of patients with an incorrect change in benign vs malignant characterization in 4% (1/22) of patients.

**Adrenal Lesions**—Overall, 11% (9/81) of patients had 1 adrenal lesion at least 1 cm in size. Reference standard for all these lesions was prior or follow-up imaging. A total of 3 of 9 lesions were malignant and 6 of 9 lesions were benign based on the reference standard. The diagnostic performance of CECT and its combination with NECT for characterization of patients with adrenal lesions is shown in Table 3. Using MRMC analyses, the mean difference in AUC between the 2 protocols was 0.01 (95% CI: $-0.05$ to $0.02$; $P = 0.27$). Interobserver agreement for characterization of adrenal malignancy on CECT imaging alone among 3 reviewers was 0.59 and on combination of CECT and NECT imaging review was 0.68, consistent with moderate to substantial agreement.

The addition of NECT improved reviewer 1’s confidence level for characterization in 67% (6/9) of patients with an incidental adrenal lesion resulting in a correct change in characterization for 22% (2/9) patients. For reviewer 2, confidence level improved in 33% (3/9) of patients without a change in benign vs malignant characterization. For reviewer 3, confidence level improved in 44% (4/9) of patients with a correct change in benign vs malignant characterization of 11% (1/9) of patients.

**Discussion**

In this study of 52 patients with 126 liver lesions and known history of melanoma, NET, or thyroid cancer, there was no statistically significant added value of NECT to arterial and portal phase CECT imaging for accuracy of characterization of liver lesions, incidental renal and adrenal lesions.
The addition of NECT resulted in improvement in radiologist's confidence level for characterization of liver lesions in only 4%–15% of patients with a correct change in benign vs malignant characterization in 0%–4% of patients for the 3 reviewers. In addition, it decreased radiologists' confidence level for 0%–4% of cases with a 0%–4% incorrect change in benign vs malignant characterization. Therefore, although there was no statistically significant added value in accurate characterization of lesions with NECT, the overall confidence level of radiologists' characterization did minimally improve with NECT. For characterization of renal lesions, there was an 18%–59% increase in confidence level with 0%–4% correct change and 0%–4% incorrect change in characterization for the 3 reviewers. For characterization of adrenal lesions, there was a 33%–67% increase in radiologists' confidence level with 0%–22% correct change in characterization for the 3 reviewers.

Although it is considered standard of practice to evaluate renal and adrenal lesions based on the presence or absence of enhancement on CT or magnetic resonance imaging using both noncontrast and contrast-enhanced imaging based on ACR Appropriateness Criteria [17,18], this was not the purpose of our study and we only evaluated incidental findings identified on staging or surveillance imaging of patients with suspected liver metastasis.

Currently, there is a lack of consensus for a standard CT protocol in the evaluation of hypervascular liver metastases, with some institutions using triphasic imaging (NECT, arterial and portal phases) and other institutions using only arterial and portal phases (biphasic imaging). The biphasic imaging protocol results in a substantial decrease (by approximately one-third) in the amount of radiation exposure to the patient when compared with the triphasic protocol. In addition, the time for image acquisition and interpretation by the radiologist is also decreased, which would increase patient throughput [7]. The results of this study support the use of a biphasic abdominal CT protocol in patients with hypervascular liver metastasis without compromising lesion characterization.

Prior studies have demonstrated varying results when evaluating the benefit of a NECT to the CT protocol for evaluation of hypervascular liver metastases. The addition of NECT to CECT has been reported to make no change to very small differences in sensitivity for liver lesion detection and characterization in studies published in 1993 and 1998 [3,4,19]. However, a single study published in 1997, reported a 16% improvement in sensitivity with the addition of NECT to portal and arterial phase CECT [20]. Given the rapid changes in CT technology over time, including thinner slice thickness, and volumetric images from multidetector CT, these studies' results might not be generalizable to CT scanners that are currently available [7].

The added value of NECT to CECT in increasing radiologists' confidence level in this study was 4%–15% for characterization of patients with liver lesions, however, this may not be sufficient to justify the increase in radiation exposure associated with addition of NECT to the biphasic protocol. Although the radiologist's level of confidence significantly increased in characterization of patients with incidental renal lesions (18%–59%) and adrenal lesions (33%–67%); the addition of NECT did not impact the accuracy of characterization of these lesions. Given the marked increase in confidence for incidental lesions, institutions may consider omitting the NECT on initial staging studies, and recommend a triphasic study only on follow-up surveillance imaging in the small number of patients with an incidental renal or...
adrenal lesion identified on the initial study. This would effectively maintain a lower radiation dose in most of the patients that undergo imaging.

By removing the NECT portion of these studies, institutions would also be able to effect both the registered CT dose indices in ACR does index registry [21] and the required reporting of imaging efficiency quality metrics (eg, the percentage of abdomen CT studies that are performed with and without contrast) used by Center for Medicare & Medicaid Services (CMS) for use of medical imaging [22]. As such, efforts have been made at our institution to optimize abdominal CT protocols in regards to evaluation of hypervascular liver metastases and reduce the number of triphasic imaging by omitting the NECT portion. This was primarily achieved by communication with referring clinicians and tailoring the protocol. Additionally, we have enrolled in the ACR dose index registry and implemented use of adaptive statistical iterative reconstruction for further radiation dose reduction in keeping with the Image Wisely initiative.

This study has several limitations, including its retrospective nature and small sample size, which does not allow for a subgroup analysis based on malignancy type and stage. In addition, recent studies have also suggested a limited benefit (if any) of NECT in the evaluation of primary malignant liver lesions such as hepatocellular carcinoma [23–28] and while this was beyond the scope of this paper, future studies could include this patient population. Furthermore, this study evaluates only the accuracy of characterization of liver lesions between the 2 protocols and we did not specifically evaluate differences in lesion detection or potential dose reduction if NECT was excluded. For accurate characterization, not all lesions had histopathological records or biopsy results available (the gold standard) and reference standard was determined by prior and follow-up imaging showing progression of disease or response to therapy. The follow-up imaging period was within 1–3 years after diagnosis for liver lesions and 2.5–4.5 years for incidental renal and adrenal lesions. However, some lesions may have very slow interval growth and our follow-up time (2.5–4.5 years) may not have been sufficient in these slow growing malignancies, such as incidental RCCs [29]. Finally, the reviewers characterized lesions on CECT alone, followed by CECT plus NECT images in a single session. Although they were not allowed to change their characterization between the 2 protocol imaging reviews, there may have been some inherent biases that may have been avoided if the 2 reviews were separated in time.

In summary, the results of the current study demonstrate no statistically significant change in lesion characterization between CECT imaging alone vs addition of NECT in the evaluation of hypervascular liver metastases with minimal improvement in radiologists’ confidence level in lesion characterization. Additionally, despite greater improved confidence level in characterization of adrenal or renal incidental lesions, there was no statistically significant added value in accurate characterization of these lesions. Our findings support using only arterial and portal phase CECT with elimination of NECT as a more efficient approach with a lower radiation dose for protocol optimization in this patient population.
References


Fig. 1.
Patient with neuroendocrine tumor and liver metastasis. The liver lesion is hypodense in the noncontrast images and hyperenhancing during arterial phase and the lesion enhancement begins to diminish during portal venous phase. The noncontrast images did not change the reviewers' confidence level. (Color version of figure is available online.)
120 Patients selected for review

39 Patients excluded:
- Not triple phase CT (n = 22)
- CT images not found in PACS or error loading images (n = 7)
- Pathologies other than melanoma, neuroendocrine, or thyroid cancer (n = 4)
- Indeterminate pathology (n = 4)

81 Patients included

**FIG 2.**
Flowchart of patient inclusion.
Fig. 3.
Graphs show receiver operating characteristics (ROC) curves with the area under the curve for each of the 3 reviewers (A–C). The dashed line shows the ROC curve for contrast-enhanced CT (CECT), whereas the solid line shows the ROC curve for the combination of CECT and NECT. (Color version of figure is available online.)
Fig. 4.
Added value of NECT to CECT in reviewers’ characterization of patients with liver lesions. There were 4 ratings that were corrected by the review of the NECT images and 4 ratings that were incorrectly changed either from benign to malignant or vice versa. BOLD text shows the change in liver lesion characterization as a result of adding NECT. For example, at the bottom of figure, left, reviewer one correctly revised 1 patient with malignant liver mass rating from “Probably benign” to “Definitely malignant”. Def, definitely; Prob, probably; B, benign; M, malignant.
Fig. 5.
Patient with malignant melanoma and liver metastasis. The liver lesion was interpreted as a probably benign lesion by one of the reviewer after reviewing arterial and portal CECT. However, after reviewing the NECT, the reviewer's interpretation changed to definitely malignant. (Color version of figure is available online.)
Table 1

Baseline characteristics of 81 included patients

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age, y (SD)</td>
<td>55 (12)</td>
</tr>
<tr>
<td>Gender, N(%)</td>
<td></td>
</tr>
<tr>
<td>Males</td>
<td>42 (52)</td>
</tr>
<tr>
<td>Females</td>
<td>39 (48)</td>
</tr>
<tr>
<td>Diagnosis, N(%)</td>
<td></td>
</tr>
<tr>
<td>Melanoma</td>
<td>41 (51)</td>
</tr>
<tr>
<td>Neuroendocrine tumor</td>
<td>36 (44)</td>
</tr>
<tr>
<td>Thyroid cancer</td>
<td>4 (5)</td>
</tr>
</tbody>
</table>

SD, standard deviation; N, number.
Table 2
Diagnostic performance of CECT vs its combination with NECT for characterization of liver lesions

<table>
<thead>
<tr>
<th></th>
<th>Reviewer 1 CECT</th>
<th>CECT + NECT</th>
<th>P value</th>
<th>Reviewer 2 CECT</th>
<th>CECT + NECT</th>
<th>P value</th>
<th>Reviewer 3 CECT</th>
<th>CECT + NECT</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Per patient analyses</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sensitivity, % (95% CI)</td>
<td>95 (76–100)</td>
<td>95 (76–100)</td>
<td>&gt;0.99</td>
<td>90 (70–99)</td>
<td>90 (70–99)</td>
<td>&gt;0.99</td>
<td>95 (76–100)</td>
<td>100 (84–100)</td>
<td>&gt;0.99</td>
</tr>
<tr>
<td>Specificity (%) (95% CI)</td>
<td>94 (79–99)</td>
<td>90 (74–98)</td>
<td>&gt;0.99</td>
<td>84 (66–95)</td>
<td>84 (66–95)</td>
<td>&gt;0.99</td>
<td>71 (52–86)</td>
<td>68 (49–83)</td>
<td>&gt;0.99</td>
</tr>
<tr>
<td>AUC (%) (95% CI)</td>
<td>98 (94–100)</td>
<td>99 (96–100)</td>
<td>0.35</td>
<td>93 (86–100)</td>
<td>94 (87–100)</td>
<td>0.23</td>
<td>96 (90–100)</td>
<td>99 (97–100)</td>
<td>0.32</td>
</tr>
<tr>
<td>Per lesion analyses</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sensitivity (%) (95% CI)</td>
<td>92 (82–97)</td>
<td>93 (84–98)</td>
<td>&gt;0.99</td>
<td>90 (79–96)</td>
<td>90 (79–96)</td>
<td>&gt;0.99</td>
<td>93 (84–98)</td>
<td>95 (86–99)</td>
<td>&gt;0.99</td>
</tr>
<tr>
<td>Specificity (%) (95% CI)</td>
<td>94 (85–98)</td>
<td>92 (83–97)</td>
<td>&gt;0.99</td>
<td>85 (74–92)</td>
<td>86 (76–94)</td>
<td>&gt;0.99</td>
<td>74 (62–84)</td>
<td>73 (60–83)</td>
<td>0.62</td>
</tr>
<tr>
<td>AUC (%) (95% CI)</td>
<td>94 (89–99)</td>
<td>95 (90–100)</td>
<td>0.14</td>
<td>92 (88–97)</td>
<td>93 (88–98)</td>
<td>0.11</td>
<td>93 (88–99)</td>
<td>94 (89–99)</td>
<td>0.27</td>
</tr>
</tbody>
</table>
### Table 3
Diagnostic performance of CECT vs its combination with NECT for characterization of renal and adrenal lesions

<table>
<thead>
<tr>
<th></th>
<th>Reviewer 1 CECT</th>
<th>CECT + NECT</th>
<th>P value</th>
<th>Reviewer 2 CECT</th>
<th>CECT + NECT</th>
<th>P value</th>
<th>Reviewer 3 CECT</th>
<th>CECT + NECT</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Renal lesions</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sensitivity (%) (95% CI)</td>
<td>100 (29–100)</td>
<td>100 (29–100)</td>
<td>&gt;0.99</td>
<td>67 (9–99)</td>
<td>67 (9–99)</td>
<td>&gt;0.99</td>
<td>100 (29–100)</td>
<td>100 (29–100)</td>
<td>&gt;0.99</td>
</tr>
<tr>
<td>Specificity (%) (95% CI)</td>
<td>95 (74–100)</td>
<td>100 (82–100)</td>
<td>&gt;0.99</td>
<td>100 (82–100)</td>
<td>100 (82–100)</td>
<td>&gt;0.99</td>
<td>95 (74–100)</td>
<td>&gt;0.99</td>
<td></td>
</tr>
<tr>
<td>AUC (%) (95% CI)</td>
<td>97 (92–100)</td>
<td>100 (100–100)</td>
<td>0.32</td>
<td>70 (12–100)</td>
<td>71 (14–100)</td>
<td>0.47</td>
<td>100 (100–100)</td>
<td>100 (100–100)</td>
<td>&gt;0.99</td>
</tr>
<tr>
<td>Adrenal lesions</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sensitivity (%) (95% CI)</td>
<td>67 (9–99)</td>
<td>67 (9–99)</td>
<td>&gt;0.99</td>
<td>67 (9–99)</td>
<td>67 (9–99)</td>
<td>&gt;0.99</td>
<td>100 (29–100)</td>
<td>100 (29–100)</td>
<td>&gt;0.99</td>
</tr>
<tr>
<td>Specificity (%) (95% CI)</td>
<td>67 (22–96)</td>
<td>100 (54–100)</td>
<td>0.50</td>
<td>83 (36–100)</td>
<td>83 (36–99)</td>
<td>&gt;0.99</td>
<td>50 (12–88)</td>
<td>67 (22–96)</td>
<td>0.62</td>
</tr>
<tr>
<td>AUC (%) (95% CI)</td>
<td>53 (3–100)</td>
<td>69 (9–100)</td>
<td>0.24</td>
<td>64 (8–100)</td>
<td>64 (8–100)</td>
<td>&gt;0.99</td>
<td>58 (19–98)</td>
<td>75 (41–100)</td>
<td>0.32</td>
</tr>
</tbody>
</table>