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FULL PAPER

Can we differentiate histologic subtypes of neuroendocrine tumour liver metastases at a single phase contrast-enhanced CT—correlation with Ga-68 DOTATATE PET/CT findings

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Objective: To assess the usefulness of a single-phase contrast-enhanced CT to differentiate subtypes of neuroendocrine tumour (NET) liver metastases and to evaluate the correlation between CT features and Ga-68 DOTATATE positron emission tomography/CT (PET/CT) findings.

Methods: Between December 2017 and April 2019 patients with liver metastases of neuroendocrine tumours who underwent CT and Ga-68 DOTATATE PET/CT were enrolled in the study. All patients involved in the study had undergone a standardised single-phase contrast-enhanced CT. Whole body PET/CT images were obtained with a combined PET/CT scanner. All CT images were retrospectively analysed by two radiologists. Enhancement patterns of lesions were assessed. For quantitative examination; CT attenuation values of metastatic lesions, liver parenchyma and aorta were measured using a free-hand ROI and tumour-to-liver ratio [T-L = (Tumour-Liver) / Liver] and tumour-to-aorta ratio [T-A = (Tumour-Aorta) / Aorta] were calculated. The lesion with the highest Ga-68 DOTATATE uptake in the liver was used for calculations. The metabolic tumour volume (MTV), maximum standardised uptake value (SUV_{max}) and SUV_{mean} were calculated for the target liver lesion.

Results: A total of 137 NET liver metastases divided into three groups: 49 (35.7%) pancreatic, 60 (44.5%) gastroenteric and 26 (18.9%) lung NET liver metastases were analysed. Gastroenteric NET metastases often showed heterogeneous enhancement which was significantly

higher than in the pancreas and lung NET liver metastases ($p < 0.001$). 96.72% ($n = 59$) of the gastroenteric NET liver metastases were hypoattenuating whereas the most frequent presentation for the pancreatic group was hyperattenuation (63.26%, $n = 31$). The difference in enhancement patterns of the liver metastases was statistically significant ($p < 0.001$) with respect to the location of the primary tumour. For quantitative analysis; tumour CT values were significantly different between the groups ($p < 0.001$). The T-L ratio was statistically different between gastroenteric and pancreatic NET liver metastases and pancreatic and lung NET groups ($p < 0.001$). The T-A ratio was significantly higher in the pancreatic NET metastases ($p < 0.001$). SUV_{max}, SUV_{mean} and MTV values, however, were not significantly different between the subgroups. There was a weak positive correlation between T-L ratio and SUV_{mean} values.

Conclusion: We noticed statistically significant differences in both qualitative and quantitative CT features between histologic subgroups of neuroendocrine tumour liver metastases at a single phase contrast-enhanced CT.

Advances in knowledge: Our study will be the first in the literature which extensively focus on assessing the CT features of liver metastases of NETs at a single phase CT and Ga-68DOTATATE PET/CT. As the different histological subtypes of NET liver metastases exhibit different clinical outcomes, these features might help to identify the primary tumour to provide optimal treatment.

INTRODUCTION

The prevalence and incidence of neuroendocrine tumours (NETs) have notably increased over the past two decades.^{1,2} NETs can arise in various areas of the body, but the

gastrointestinal system, the pancreas and the bronchopulmonary system are the most common sites.³ NETs can be functioning, with peptide hormone secretion, or can be non-functioning, which are often associated with

liver metastases at the time of diagnosis. Due to their comparatively slow course, NETs are very often detected in an advanced stage, with the presence of liver metastases (LM) being the most common clinical occurrence.^{4,5} The existence and extent of LM is the decisive prognostic factor in NETs.³ Neuroendocrine LM with an unknown primary origin make up about 5–10% of total cases in clinical practice.⁶

A detailed evaluation of the primary mass and the extent of the metastatic disease can sometimes be challenging. A multi-modality perspective, including radiology, nuclear medicine, endoscopy and sometimes exploratory surgery, is necessary in the assessment of LM of NETs of unknown origin.^{5,6} Although the introduction of Gallium-68 (Ga-68) labeled somatostatin analogues (Ga68 DOTA-TOC, Ga-68 DOTA-NOC and Ga-68 DOTA-TATE) for positron emission tomography/CT (PET/CT) has emerged as a promising alternative for diagnosis, staging and follow up of NETs, because its sensitivity highly correlated with somatostatin receptor expression of tumour, CT scan remains the most decisive factor in a patient's staging.^{7–12} Many studies have analysed the role of CT in NETs, but only a few of these studies have investigated the CT features of the NET LM, and most of these studies have examined the enhancement patterns at multiphase CT.^{13–16} To the best of our knowledge, our study will be the first to extensively focus on assessing the CT features of LM of NETs at a single-phase contrast-enhanced CT.

Describing CT characteristics of different histological subtypes of NET LM would help determine the optimal management strategy because the different histological subtypes of NET exhibit different clinical outcomes and require different therapy planning.

The primary aim of our study is to assess the usefulness of single-phase contrast-enhanced CT to differentiate subtypes of NET LM and to examine the possibility of estimating the origin of the primary tumour.

METHODS AND MATERIALS

Study design

This was a single centre retrospective study. Our study protocol was approved by The Institutional Ethics Committee, and the requirement for written informed consent was waived. The study was conducted in accordance with the principles of the Declaration of Helsinki.

Patient population

Between December 2017 and April 2019 patients with NETs were verified in Ankara University School of Medicine hospital's database using the Radiology Information System/Picture Archiving and Communication System (RIS/PACS, Centricity 5.0 RIS GE Healthcare, Milwaukee, WI, USA) by a search for "NET". Our inclusion criteria were as follows: (1) histopathological proof of primary tumour as "NET"; (2) histopathological proof of at least one liver metastasis; and (3) available multidetector CT and Ga-68 DOTATATE PET/CT.

We excluded patients with primary origins from other than the lung, pancreatic or gastroenteric NET and those who underwent treatment (including regional and systemic therapy) before the first available CT or Ga-68 DOTATATE PET/CT. Patients who had incomplete or insufficient CT or PET images, co-existing malignancies or patients with marked steatosis were also excluded.

CT technique

CT images were obtained using a 64-multidetector CT scanner (Toshiba Aquillion 64; Toshiba Medical Systems; Tokyo, Japan). All patients involved in the study had undergone a single-phase contrast-enhanced CT of the abdomen on the same scanner. CT images were acquired with a standardised protocol of a slice thickness of 5 mm, a reconstruction interval of 1 mm, 120 kV, automatic tube current modulation and a tube rotation time of 0.5 s. The scanning area was from the dome of the diaphragm to the lesser trochanters, and the scanning direction was cranio-caudal. Patients were given 2 mL/kg of non-ionic iodinated contrast medium at 350 mg mL⁻¹ iodine intravenously through a 22-gauge catheter into the antecubital vein at a rate of 3.5 mL s⁻¹ by automatic power injector. The timing of the acquisition was in the portal venous phase established in all cases timed to be approximately 70 s after contrast agent administration.

Ga-68 DOTATATE PET/CT protocol

Whole body PET/CT images from vertex to upper thigh were obtained with a combined PET/CT scanner (Discovery 710, General Electric Company) 45–60 min after intravenous injection of approximately 100–200 MBq Ga-68 DOTATATE in a supine position. PET images were acquired for 3 min per bed position. PET images were reconstructed with non-contrast CT images. CT images were acquired with a standardised protocol of 70 mA, 140 kV, tube rotation time of 0.5 s per rotation, a slice thickness of 5 mm and a pitch of 6. Attenuation-corrected PET/CT fusion images were reviewed in coronal, sagittal and transaxial planes on Advance Workstation Volumeshare 5 (GE Medical Systems).

Image analysis

All CT images were retrospectively analysed by two radiologists with 8 and 10 years of experience in abdominal radiology. The readers knew that all of the liver lesions were metastatic lesions of NETs but they were blinded to the histologic subtype. At first, readers were asked to assess the size, location and number of each lesion. Then, they analysed the tumour attenuation of the lesion which was identified as "hypoattenuating", "isoattenuating" or "hyperattenuating" compared to the surrounding liver parenchyma. Readers also evaluated the tumour enhancement as "heterogeneous enhancement", "peripheral enhancement" or "homogeneous enhancement".

For quantitative examination; CT attenuation values of metastatic lesions, liver parenchyma and aorta were measured using a freehand region of interest (ROI) for reflecting the blood supply of the metastatic lesion and the following parameters were computed: tumour-to-liver ratio [T-L = (Tumour - Liver) / Liver] and tumour-to-aorta ratio [T-A = (Tumour - Aorta) / Aorta].

Figure 1. Axial fusion Ga-68 Dotatate images; multifocal pathological uptake throughout the liver, with the most intense uptake on the left lobe.

The measurements of the two radiologists were used to calculate inter-reader reproducibility.

Data interpretation and measurement on Ga-68 DOTATATE PET/CT

All Ga-68 DOTATATE PET/CT images were analysed retrospectively by a nuclear medicine specialist with 10 years of experience. Volumetric and semiquantitative data were acquired by using the PET VCAR software (GE Healthcare). The lesion with the highest Ga-68 DOTATATE uptake in the liver was used for calculations. Automatic volumes of interest (VOI) were drawn around the lesions using the isocontouring method. The threshold used was the liver activity as determined by a reference VOI drawn automatically. The metabolic tumour volume (MTV), SUV_{max} and SUV_{mean} were then calculated for the target liver lesion (Figure 1).

Statistical analysis

Descriptive statistics were given as counts and percentages for categorical variables; standard and mean deviations were given for continuous variables. χ^2 test was performed for clustered data and non-parametric analysis of clustered receiver operating characteristics (ROCs),¹⁷ which were performed in order to account for intracluster correlation among multiple measurements from the same patient. A ROC curve was used to decide the diagnostic value of significant parameters to distinguish histological subgroups. The areas under the ROC curves and 95% confidence intervals for all variables were quantified. Cut-off values were chosen using Youden's Index. Measurements were dichotomised according to cut-off values, and specificity, sensitivity and negative and positive predictive values were calculated. A *p*-value of < 0.05 was considered statistically significant. We used R v. 3.4.2 for statistical analysis and clustered ROC function. Spearman's rank correlation coefficient was performed to evaluate the correlation between quantitative CT features and Ga-68 DOTATATE PET/CT values.

RESULTS

Clinical characteristics

Patients with proven NET LM who had undergone CT and Ga-68 DOTATATE PET/CT examination were enrolled in this study. A total of 137 NET LM were analysed in 49 patients; [28 females (57%) and 21 males (43%) with a mean age of 50.7 ± 14.5] divided into 3 groups: 49 (35.7%) pancreatic, 60 (44.5%) gastroenteric and 26 (18.9%) lung NET LM.

Difference of qualitative CT features between histologic subtypes—tumour characteristics and enhancement patterns

NET LM of gastroenteric origin were significantly larger (42.5 ± 27.6 mm, $p < 0.001$) than pancreatic NET metastases (26.9 ± 17.7 mm) and lung NET metastases (25.3 ± 14.5 mm); the difference in the size of the subgroups was statistically significant ($p < 0.001$).

Contrast enhancement of LM was homogeneous in 50.7% of patients ($n = 69$), which was significantly more frequent in patients with pancreatic NET than in those with gastroenteric NET LM ($n = 41$, 83.% vs $n = 11$, 18.7%; $p < 0.001$). Gastroenteric NET metastases often showed heterogeneous enhancement and this was significantly higher than in the pancreas and lung groups (82 vs 16.3 and 34.6%; $p < 0.001$).

Most of the NET LM ($n = 83$, 61.9%) were hypoattenuating on single phase CT, and tumour hypoattenuation was significantly more frequent in the gastroenteric group. To be precise, 96.72% ($n = 59$) of the gastroenteric NET LM showed hypoattenuation relative to the surrounding liver parenchyma (Figure 2A). Whereas, for the lung NET group, 88.27% ($n = 24$) of the lesions were hypoattenuating and 3.27% ($n = 2$) were isoattenuating (Figure 2B). For the pancreatic group, only 20.40% ($n = 10$) of NET LM were hypoattenuating. The most frequent presentation for the pancreatic group was hyperattenuation (63.26%, $n = 31$) (Figure 2C). The difference in enhancement patterns of the LM was statistically significant ($p < 0.001$) between pancreas and lung NET LM and between pancreas and gastroenteric NET liver metastasis.

CT parameters of NET liver metastases—quantitative analysis

The ROC analysis of the clustered data showed statistically significant differences between the histologic subtypes in terms of tumour CT value, tumour-to-liver (T-L) ratio and tumour-to-aorta (T-A) ratio ($p < 0.001$).

LM of pancreatic NETs were more enhanced than lung NETs and gastroenteric NETs. Tumour CT values were significantly different between pancreas and gastroenteric and between pancreas and lung groups ($p < 0.001$). Tumour CT values might help to discriminate gastroenteric and pancreatic NET metastases and lung and pancreatic NET metastases. The cut-off for CT value was 90.5 to differentiate pancreatic and gastroenteric NET metastases with a sensitivity of 92% and a specificity of 98%, and it was 103 to differentiate the pancreatic from the lung group with a sensitivity of 89.8% and a specificity of 92.3%.

Figure 2. (a) Neuroendocrine tumour liver metastasis in a 70-year-old male patient with gastroenteric primary origin. Metastatic lesion was significantly large in size with marked heterogenous enhancement. (b) Liver metastases in a 60-year-old male patient with primary origin lung neuroendocrine tumour. Lesions were hypoattenuating on single phase contrast-enhanced CT. (c) Whereas 54-year-old female with pancreatic neuroendocrine tumour, metastatic lesions were hyperattenuating compared to the surrounding liver parenchyma (arrows).

The tumour-to-liver ratio was statistically different between gastroenteric and pancreatic NET LM and pancreatic and lung NET groups ($p < 0.001$). The cut-off value for the tumour-to-liver ratio was -0.085 to differentiate gastroenteric and pancreatic NET metastases, with a sensitivity of 89% and a specificity of 100%. The T-L ratio might also help to differentiate lung and pancreatic NET metastases; the best cut-off value for the T-L ratio was -0.18 , with a sensitivity of 95.9% and a specificity of 96.2%. The difference in T-L ratio between the gastroenteric and lung NET metastases, however, was not significantly different ($p > 0.05$).

The tumour-to-aorta ratio was significantly higher ($-0.17 + -0.10$) in the pancreatic NET metastases ($p < 0.001$). The tumour-to-aorta ratio might help to differentiate pancreatic and gastroenteric NET groups. The ROC curve demonstrated the best cut-off value of tumour-to-aorta ratio to differentiate gastroenteric and pancreatic NET subgroups: -0.345 with a sensitivity of 98% and a specificity of 96.7%. The tumour-to-aorta ratio was also different for the lung and the pancreas NET metastases, and it was statistically significant ($p < 0.001$). There was not any statistically significant difference between gastroenteric and lung NET metastases in terms of tumour-to-aorta ratio ($p > 0.05$).

The quantitative CT parameters of NET LM are shown in Table 1 and ROC curved analysis of quantitative CT parameters are shown in Figure 3. For the diagnostic performance of the tests area under curves (AUCs) are compared with Hanley and Mc Neil method and the results are demonstrated in Table 2.

The interobserver agreement of quantitative image analyses between the two readers was perfect for all quantitative CT features. intraclass correlation coefficient: 0.999 (95% CI: 0.994–1) for tumour density; ICC: 0.998 (95% CI: 0.990–0.999) for aorta density; ICC: 0.997 (95% CI: 0.988–0.999) for liver density; ICC: 0.998 (95% CI 0.991–1) for T-A ratio and ICC: 0.999 (95% CI 0.995–1) for T-L ratio.

Ga-68 DOTATATE PET/CT parameters of NET liver metastases

The mean SUV_{max} level was 32.9 for the whole cohort, while it was 34.9 for pancreatic; 34.6 for gastroenteric and 24.8 for lung NET LM. There was no significant difference between the subgroups in terms of the SUV_{max} values ($p = 0.847$). We did not observe any significant differences between pancreas, lung and gastroenteric NET LM in terms of SUV_{mean} and MTV as well ($p >$

Table 1. The quantitative CT parameters of NET liver metastases are shown in Table 1.

	Cut-off	Sensitivity 95% CI	Specificity 95% CI	PPV 95% CI	NPV 95% CI
Pancreas vs GIS T-A ratio	-0.345	0.98 (0.89–0.99)	0.96 (0.88–0.99)	0.96 (0.86–0.98)	0.98 (0.91–0.99)
Pancreas vs GIS T-L ratio	-0.085	0.89 (0.78–0.95)	1 (0.94–1)	1 (0.91–1)	0.92 (0.83–0.96)
Pancreas vs GIS HU	90	0.91 (0.80–0.96)	0.98 (0.91–0.99)	0.97 (0.88–0.99)	0.93 (0.85–0.97)
Pancreas vs Lung T-A ratio	-0.085	0.89 (0.82–0.96)	1 (0.87–1)	1 (0.91–1)	0.83 (0.67–0.92)
Pancreas vs Lung T-L ratio	-0.18	0.95 (0.86–0.98)	0.96 (0.81–0.99)	0.97 (0.89–0.99)	0.92 (0.76–0.97)
Pancreas vs Lung HU	103	0.89 (0.78–0.95)	0.92 (0.75–0.97)	0.95 (0.85–0.97)	0.82 (0.65–0.92)

CI, confidence interval; NET, neuroendocrine tumour.

Figure 3. ROC curved analysis of quantitative CT parameters are shown in Figure 3. ROC,receiver operating characteristic.

Diagonal segments are produced by ties.

0.05). Detailed Ga-68 DOTATATE PET/CT measurements were given in Table 3.

Spearman's rank correlation coefficient was used to evaluate the correlation between quantitative CT features (tumour CT value, tumour-to-aorta ratio and tumour-to-liver ratio) and Ga-68 DOTATATE PET/CT values (SUV_{max} , SUV_{mean} and MTV). Spearman's rank correlation coefficient showed a *weak* positive correlation between tumour-to-liver ratio and SUV_{mean} values ($p = 0.036$, $r = 0.301$). No correlation exists between other variables.

DISCUSSION

In many cases, NETs are identified in an advanced stage with the presentation of LM.^{4,5,18} The anatomical site of the primary tumour, staging and the presence of LM can have an intense impact on management choices for patients, and it must therefore be properly identified in patients with NET. The most important factor that affects a patient's survey is the existence of LM, which

is associated with the origin of the primary tumour.^{19–21} Localisation of the primary tumour is often challenging. Differentiation between the different histologic subtypes is one of the most important diagnostic steps that can be taken; it indicates significant differences in survival and treatment strategy between the subgroups.

Imaging plays a crucial role in both the detection and therapy planning of LM of NETs. Although functional imaging helps quantify somatostatin receptor status and adds valuable additive information to conventional cross-sectional imaging, CT remains crucial for staging. It is well-known that CT detects NET LM; many studies have concentrated on the diagnostic value of multiphase contrast-enhanced CT but few have studied the differentiation between the histologic subtypes of LM.^{13–16} Our study has evaluated the usefulness of single-phase contrast-enhanced CT in differentiating between histological subtypes of NET LM. NET LM from pancreatic and gastroenteric tumours

Table 2. For the diagnostic performance of the tests AUCs are compared with Hanley and McNeil method and the results are shown in Table 2.

	Pancreas vs GIS AUC (p)	Pancreas vs Lung AUC (p)	GIS vs Lung AUC (p)
CT value	0.9848 (0.0147)	0.9647 (0.0285)	0.4464 (0.1282)
T-A ratio	0.9968 (0.0034)	0.9776 (0.0192)	0.5441 (0.1218)
T-L ratio	0.9804 (0.0153)	0.9878 (0.0129)	0.6037 (0.1224)

AUC, area under curves.

Table 3. Ga-68 DOTATATE PET/CT measurements were demonstrated in Table 3.

	Total	Pancreas	Gastroenteric	Lung
SUV _{max}	32.9 ± 21.6	34.9 ± 24.5	34.6 ± 20.6	24.8 ± 19.8
SUV _{mean}	19.3 ± 13.6	21.7 ± 16.9	19.6 ± 11.6	13.9 ± 11.0
MTV	54.7 ± 80.4	51.5 ± 88.5	57.7 ± 76.7	53.4 ± 83.4

MTV, metabolic tumour volume; SUV, standardised uptake value.

are commonly thought to have much the same appearance, but our results do not support this opinion. We found statistically significant differences in terms of qualitative CT features. For example, gastroenteric NET metastases often showed heterogeneous enhancement which was significantly higher than pancreas and lung NET LM. Most gastroenteric NET LM showed hypoattenuation (96.72%), while only 20.40% of the pancreatic group were hypoattenuating. These results were parallel with previous studies, which clarifies that the portal venous phase is the best phase for optimal visualisation of most gastroenteric NET LM.^{14,22–25} The most frequent presentation for the pancreatic NET LM was hyperattenuation (63.26%, $n = 31$).

We also found significant differences in quantitative CT parameters that might help to discriminate histologic subtypes of NET LM. LM of the pancreatic group were more enhanced than LM of gastroenteric NETs and lung NETs. Tumour CT values can help to differentiate gastroenteric and pancreatic NET metastases and also lung vs pancreatic NET metastases. There was also a notable difference in terms of tumour-to-liver and tumour-to-aorta ratio between gastroenteric and pancreatic NET LM and between lung and pancreatic NET metastases.

Ga 68-DOTATATE PET/CT is a promising diagnostic tool in deciding the primary origin of LM of NETs; whole body imaging procedure provides overall evaluation of all possible sites of metastasis and single step determination of the extent of the disease. It has a notable impact on the management of well-differentiated tumours.^{26,27 28,29} Although it has been reported to have a high diagnostic power for localising primary tumour in known metastatic cases, to our knowledge, no published studies have focused on differentiating the Ga-68 DOTATATE PET/CT characteristics of different subtypes of NET LM in detail.³⁰ In a study by Kunikowska *et al*, the aim was to analyse the frequencies of metastatic sites differences in SUVmax values depending on the primary tumours' location. The study revealed that there was a significant difference between SUVmax in metastatic lymph nodes from intestinal and pancreatic NET in comparison to lung NET, in SUVmax of bone metastases from the intestines compared with that from the lungs and pancreas, but there was no statistical difference between the SUVmax of LM according to the primary tumour site. No metabolic parameters were of concern.³¹ In a relatively recent study, investigators studied the contributive role of volumetric data derived from combined evaluation of Ga-68 DOTATATE PET/CT and ¹⁸F-FDG PET/CT. The somatostatin receptor density and total lesion somatostatin receptor expression calculated from Ga-68 DOTATATE PET/CT images were correlated with Ki-67 levels. These parameters were found to be inversely correlated with

grade and was thus indicative of prognosis. However, there were no comments on predictive role of quantitative receptor imaging findings regarding to the origin of the primary tumour.³² Our results showed that SUV_{max}, SUV_{mean} and MTV values were not significantly different between the gastroenteric, pancreas and lung NET LM. Despite the promising results of Ga-68 labelled peptide PET/CT in well-differentiated tumours, the use of Ga-68 DOTATATE PET/CT in the poorly differentiated group is still questionable. Therefore, we believe that conventional CT features could help to determine the origin of the primary tumour especially in poorly differentiated Grade III NET LM with unknown primary origin.

The prognosis of NET differs based on the primary origin of the tumour, the presence of metastatic disease and tumour grade.^{19–21} LM of NET from different histological subtypes have different clinical results, and there are multidisciplinary treatment options for different subtypes.^{3,4,20,21} If the liver involvement is diffuse, surgery and regional therapies are not suggested; transarterial treatment is required. The primary origin of the tumour is one of the predictive factors of tumour response following intra-arterial therapies.^{33,34} Also, for the progressive metastatic disease, the invention of target-directed therapies as well as next-generation multireceptor targeted and radiolabelled somatostatin analogues might be an alternative. Verification of the origin of the primary tumour becomes crucial here because the target-directed therapies are only indicated in some specific histologic subtypes.^{35,36} For that reason, it is critical to specify the origin of the primary tumour to supply an optimal therapy strategy.

Our study had some limitations. First of all, it was a retrospective, single centre study. However, we did choose patients with NET LM who underwent single phase CT and Ga-68 DOTATATE PET/CT which could limit the possibility of a sampling bias. Additionally, all patients involved in this study underwent the same CT and Ga-68 DOTATATE PET/CT protocol. Although all patients had histological proof of NET liver metastases, some cases had diffuse liver involvement, and because of the diffuse involvement, not all metastatic lesions were proved with pathology. Finally, because of our rigid inclusion criteria (such as specific primary tumour sites and lack of treatment before the first CT or PET/CT), our study sample was limited. But we considered this necessary, as these factors may change the CT features of the lesions. As this a single centre study with a modest number of patients, the quantitative CT variables and suggested cut-off values would need validation in larger studies.

In conclusion, we noticed statistically significant differences in both qualitative and quantitative CT features (T–A ratio, T–L

ratio, enhancement patterns) between histologic subgroups of NET LM at a single phase contrast-enhanced CT. These CT features might be useful when determining the primary

tumour site of NET liver metastases with unknown primary origin to verify accurate tumour staging and to supply optimal management.

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