

# Reproducibility and variability of very low dose hepatic perfusion CT in metastatic liver disease

Osman Melih Topcuoğlu  
Muşturay Karçaaltıncaba  
Deniz Akata  
Mustafa Nasuh Özmen

## PURPOSE

We aimed to determine the intra- and interobserver agreement on the software analysis of very low dose hepatic perfusion CT (pCT).

## METHODS

A total of 53 pCT examinations were obtained from 21 patients (16 men, 5 women; mean age, 60.4 years) with proven liver metastasis from various primary cancers. The pCT examinations were analyzed by two readers independently and perfusion parameters were noted for whole liver, whole metastasis, metastasis wall, and normal-looking liver (liver tissue without metastasis) in regions of interest (ROIs). Readers repeated the analysis after an interval of one month. Intra- and interobserver agreements were assessed with intraclass correlation coefficients (ICC) and Bland-Altman statistics.

## RESULTS

The mean ICCs of all ROIs between readers were 0.91, 0.93, 0.86, 0.45, 0.53, and 0.66 for blood flow (BF), blood volume (BV), permeability, arterial liver perfusion (ALP), portal venous perfusion (PVP) and hepatic perfusion index (HPI), respectively. The mean ICCs of all ROIs between readings were 0.86, 0.91, 0.81, 0.53, 0.56, and 0.71 for BF, BV, permeability, ALP, PVP, and HPI, respectively. There was greater agreement on the parameters measured for the whole metastasis than on the parameters measured for the metastasis wall. The effective dose of all perfusion CT studies was 2.9 mSv.

## CONCLUSION

There is greater intra- and interobserver agreement for BF and BV than for permeability, ALP, PVP, and HPI at very low dose hepatic pCT. Permeability, ALP, PVP, and HPI parameters cannot be used in clinical practice for hepatic pCT with an effective dose of 2.9 mSv.

Despite all improvements and efforts in the last ten years, hepatic perfusion computed tomography (pCT) is still a developing modality for assessing tissue blood perfusion quantitatively (1, 2). Although hepatic pCT is also used for nononcologic applications, it is mainly utilized for oncologic imaging and many studies showed that it could demonstrate perfusion changes of the tissue of interest or tumor before and after the therapy (3–5). Thus pCT has the potential for monitoring therapy response earlier than the conventional methods such as regular CT follow-ups using mRECIST criteria (6, 7). Although it has the advantage of detecting perfusion changes, lack of standard for CT protocol and relatively limited experience in the literature with many studies of small sample size and various methods are the main limitations, which hamper its clinical application. Besides these limitations, considering that an oncology patient needs recurrent multiple perfusion studies in order to determine the therapy response accurately, the leading handicap of pCT is the high radiation dose (4). At high radiation doses ranging from 7 to 30.7 mSv, pCT has limited potential for routine clinical utilization (4, 8–13). Although there are several methods to lessen the radiation dose of pCT, it must be emphasized that the signal used for perfusion calculations will decrease along with the radiation. Before any clinical low dose study, it is important to determine which of the perfusion parameters remain reproducible at low dose and low signal, because quantitative evaluation of perfusion parameters are quite variable between readings and between readers (14). In addition, perfusion measurements change between different vendors and commercial software programs (15, 16).

From the Department of Radiology (O.M.T. ✉ [omtopcuoglu@gmail.com](mailto:omtopcuoglu@gmail.com)), Yeditepe University School of Medicine, Istanbul, Turkey; the Department of Radiology (M.K., D.A., M.N.Ö.), Hacettepe University School of Medicine, Ankara, Turkey.

Received 24 December 2015; revision requested 28 January 2016; last revision received 7 April 2016; accepted 20 April 2016.

Published online 19 October 2016.  
DOI 10.5152/dir.2016.16612

The purpose of this prospective study was to determine the intra- and interobserver agreement on the software analysis of very low dose hepatic pCT and to determine the parameters that are reproducible to guide further studies.

## Methods

### Patient selection

This prospective study was performed with institutional review board approval and all patients gave written informed consent. Patients with proven liver metastasis from various primary cancers were included in the study. Patients with a history of hepatic surgery, previous chemotherapy, diameter of the metastasis <1 cm, serum bilirubin levels >3 mg/dL, serum creatinine levels >1.5 mg/dL, portal vein thrombosis, patients without pathologic diagnosis, and patients with metallic stents, surgical implants, or prostheses were excluded. Exclusion criteria were established based on conditions that can alter hepatic perfusion. In addition, patients with elevated serum creatinine levels were excluded as extra contrast material can negatively affect the renal functions, and metallic stents were excluded as they can cause artifacts leading to miscalculations.

We planned to obtain four hepatic pCT scans for each patient: before the first chemotherapy and at one week, two weeks, and one month after the first chemotherapy. As some patients were lost to follow-up or died before the end of the study, a total of 53 pCT scans were performed.

### pCT technique

All perfusion CT scans were obtained with a dual-source, 64-row multidetector

CT scanner (Definition, Siemens Healthcare) using an adaptive 4D spiral mode. First, an unenhanced no breath-hold CT of the liver was obtained for the localization of the metastasis. All steps in pCT protocol were designed to lessen the radiation dose as low as possible without affecting the calculations, and CT parameters were chosen to decrease the dose. Thus, tube voltage, tube current, scan length, total scan time, and cycle times were all decreased. After localization of the metastasis, a 2 cm scan length was selected covering the largest metastasis. Following contrast material administration (50 mL of nonionic iodinated contrast medium; 300 mg iodine per mL) a dynamic study of the selected area was performed without a breath-hold. All images were obtained without breath-hold because in the contrast-enhanced series it was difficult to obtain a CT slice that corresponds to the same slice in the precontrast series. Contrast medium was injected at a rate of 5–6 mL/s, through an 18-gauge intravenous cannula and after a delay of 7 seconds (s) cine images were acquired. CT parameters of the dynamic study were: 0.33 s gantry rotation time, 80 kVp, 80 mA, 3 mm reconstructed section thickness, 24×1.2 detector configuration and 512×512 matrix size. All perfusion images were acquired for a total duration of 48 s and a cycle time of 1 s for the first 20 s, decreased to a cycle time of 2 s for the next 16 s, and finally further decreased to a cycle time of 3 s for the last 12 s. After completing the perfusion CT, routine chest and abdominal CTs were obtained with an additional 50 mL of contrast medium. If there was a diffuse disease on the unenhanced CT, the largest metastasis was chosen for pCT and if there was no visible lesion, hepatic pCT was not obtained.

### Image analysis

Two readers independently analyzed the acquired data twice with at least one month interval between the readings. Readers 1 and 2 had 25 and five years of experience in abdominal radiology, respectively, and both readers had three years of experience in hepatic pCT. Data were processed at a workstation (CT workplace; Siemens) using a commercially available perfusion software (Syngo, body VPCT; Siemens Medical Solutions). The software requires placing the region of interests (ROIs) in the aorta, portal vein, and spleen. Perfusion parameters comprised blood flow (BF), blood volume (BV), permeability, arterial liver perfu-

sion (ALP), portal venous perfusion (PVP), and hepatic perfusion index (HPI); all perfusion parameters were displayed as colored maps by the software. The model used by the software is called double compartmental method, and it performs the perfusion analysis by using interstitial and intravascular compartments. On color maps, four ROIs were hand drawn for whole liver (along the borders of the liver), normal-looking liver (liver tissue without metastasis), whole metastasis including the enhancing wall, and only metastasis wall (without extension beyond the metastasis wall) in order to determine whether agreement on calculations would change at different ROI localizations between readings and between readers. In other words, with different ROIs we aimed to show the discrepancy between agreements at the metastasis wall and at the whole metastasis because a metastasis with a necrotic center may have already decreased perfusion values due to dead tumor cells in the center, and this may lead to miscalculations and incorrectly decreased perfusion values for the whole metastasis. The ROIs were same size for the whole liver, but the ROIs for normally looking liver, whole metastasis, and metastasis wall were not equivalent in size because the analysis was performed independently by the readers. If there was more than one metastasis, ROI was drawn for the largest lesion. ROIs for normal-looking liver were drawn distant from the metastases. Neighboring portal vein, hepatic artery, partial volume effects, and vascular structures were not involved in the ROIs.

### Statistical analysis

Intra- and interobserver agreement for all perfusion parameters were determined by Bland-Altman analysis; intraclass correlation coefficients (ICCs; 95% confidence intervals) were also calculated. ICCs greater than 0.85 were accepted as good agreement, ICCs between 0.75–0.85 were accepted as substantial agreement and ICCs less than 0.75 were accepted as poor or weak agreement. SPSS version 21.0 (IBM Corp.) was used for all statistical analyses.

## Results

A total of 53 pCT examinations were performed in 21 adult patients (16 men, five women; mean age, 60.4±12.3 years). No breathhold problems were detected during pCT acquisitions. Primary cancers consisted

### Main points

- Although hepatic perfusion CT (pCT) has the advantage of detecting perfusion changes, lack of standard values of CT protocol, relatively minimal experience in the literature with many studies each with small samples and various methods, and high radiation dose (7–30 mSv) are the main limitations that hamper its clinical application.
- Hepatic pCT can be performed at an effective dose of 2.9 mSv.
- Intra- and interobserver agreement for BF and BV were greater than for permeability, ALP, PVP, and HPI at very low dose hepatic pCT.

**Table 1.** List of primary cancers

Primary cancer	Number of patients
Colorectal adenocarcinoma	16
Pancreatic adenocarcinoma	2
Pancreatic neuroendocrine tumor	1
Malignant melanoma	1
Pheochromocytoma	1

**Table 2.** Intra- and interobserver ICCs (95% CI) for measurements of perfusion CT parameters

Parameter/ROI	Intraobserver agreement		Interobserver agreement	
	First analysis	Second analysis	Reader-1	Reader-2
<b>BF/</b>				
WL	0.98 (0.96, 0.99)	0.96 (0.93, 0.98)	0.95 (0.92, 0.97)	0.98 (0.98, 0.99)
Mx	0.97 (0.95, 0.99)	0.87 (0.77, 0.92)	0.88 (0.79, 0.93)	0.95 (0.97, 0.91)
NL	0.89 (0.80, 0.93)	0.76 (0.59, 0.86)	0.57 (0.23, 0.74)	0.84 (0.72, 0.91)
MxW	0.94 (0.90, 0.97)	0.84 (0.73, 0.91)	0.85 (0.73, 0.91)	0.87 (0.77, 0.92)
<b>BV/</b>				
WL	0.99 (0.98, 0.99)	0.98 (0.96, 0.99)	0.98 (0.97, 0.99)	0.99 (0.98, 0.99)
Mx	0.98 (0.96, 0.99)	0.92 (0.86, 0.95)	0.92 (0.87, 0.96)	0.96 (0.93, 0.98)
NL	0.92 (0.85, 0.95)	0.85 (0.74, 0.91)	0.82 (0.69, 0.90)	0.88 (0.80, 0.93)
MxW	0.91 (0.84, 0.95)	0.89 (0.81, 0.94)	0.81 (0.67, 0.89)	0.92 (0.87, 0.92)
<b>Permeability/</b>				
WL	0.95 (0.91, 0.97)	0.90 (0.83, 0.94)	0.87 (0.78, 0.93)	0.95 (0.92, 0.97)
Mx	0.91 (0.85, 0.95)	0.87 (0.77, 0.92)	0.84 (0.72, 0.91)	0.93 (0.88, 0.96)
NL	0.89 (0.80, 0.93)	0.79 (0.63, 0.88)	0.55 (0.22, 0.74)	0.84 (0.73, 0.91)
MxW	0.82 (0.69, 0.90)	0.68 (0.44, 0.82)	0.66 (0.41, 0.81)	0.89 (0.80, 0.93)
<b>ALP/</b>				
WL	0.30 (0.15, 0.42)	0.41 (0.20, 0.62)	0.45 (0.22, 0.68)	0.38 (0.12, 0.64)
Mx	0.24 (0.33, 0.56)	0.54 (0.21, 0.74)	0.80 (0.65, 0.88)	0.42 (-0.01, 0.67)
NL	0.64 (0.38, 0.79)	0.60 (0.30, 0.77)	0.75 (0.57, 0.86)	0.35 (-0.13, 0.63)
MxW	0.34 (-0.14, 0.62)	0.56 (0.24, 0.75)	0.69 (0.47, 0.82)	0.40 (-0.04, 0.65)
<b>PVP/</b>				
WL	0.81 (0.67, 0.89)	0.60 (0.31, 0.78)	0.84 (0.72, 0.91)	0.37 (-0.09, 0.64)
Mx	0.47 (0.08, 0.70)	0.43 (0.01, 0.67)	0.51 (0.14, 0.72)	0.49 (0.11, 0.71)
NL	0.78 (0.61, 0.87)	0.46 (0.06, 0.69)	0.81 (0.68, 0.89)	0.38 (-0.08, 0.64)
MxW	0.57 (0.25, 0.75)	0.18 (-0.44, 0.53)	0.37 (-0.09, 0.64)	0.72 (0.51, 0.84)
<b>HPI/</b>				
WL	0.46 (0.07, 0.69)	0.78 (0.62, 0.88)	0.75 (0.57, 0.86)	0.62 (0.34, 0.78)
Mx	0.74 (0.54, 0.85)	0.77 (0.61, 0.87)	0.85 (0.71, 0.91)	0.72 (0.52, 0.84)
NL	0.58 (0.28, 0.76)	0.65 (0.40, 0.80)	0.78 (0.62, 0.87)	0.61 (0.31, 0.78)
MxW	0.71 (0.49, 0.83)	0.62 (0.33, 0.72)	0.68 (0.45, 0.82)	0.71 (0.50, 0.83)

All ROIs are given separately.

ICC, intraclass correlation coefficient; CI, confidence interval; ROI, region of interest; BF, blood flow; WL, whole liver; Mx, metastasis; NL, normal liver; MxW, metastasis wall; BV, blood volume; ALP, arterial liver perfusion; PVP, portal venous perfusion; HPI, hepatic perfusion index.

of 16 colorectal adenocarcinomas, two pancreatic adenocarcinomas, one pancreatic neuroendocrine tumor, one malignant melanoma, and one pheochromocytoma (Table 1). All perfusion scans were performed successfully and analyzed by the software. The mean effective dose of all perfusion studies was 2.9 mSv, calculated as the dose-length product (DLP) multiplied by a tissue weighting factor for the abdomen ( $k=0.015$ ) (17). DLP was obtained from the dose report of each CT scan.

Intra- and interobserver agreements for pCT measurements are shown in Table 2. The mean ICCs between readers were  $0.91\pm 0.07$ ,  $0.93\pm 0.05$ ,  $0.86\pm 0.09$ ,  $0.45\pm 0.15$ ,  $0.53\pm 0.20$ , and  $0.66\pm 0.11$  for BV, BF, permeability, ALP, PVP, and HPI. The mean ICCs between readings were  $0.86\pm 0.13$ ,  $0.91\pm 0.08$ ,  $0.81\pm 0.14$ ,  $0.53\pm 0.18$ ,  $0.56\pm 0.20$ , and  $0.71\pm 0.08$  for BV, BF, permeability, ALP, PVP, and HPI. The least variable parameters were BF and BV between the readings and as well as between the readers for all ROIs as demonstrated in Table 3. Intra- and interobserver agreements were very weak for ALP, PVP, and HPI. Moreover, there was greater agreement on the parameters measured for the whole liver and whole metastasis than the parameters measured for normal-looking liver and metastasis wall respectively, as summarized in Table 4. An example of Bland-Altman analysis for BV measurements and reader agreement on four ROIs are given in Figs. 1 and 2.

## Discussion

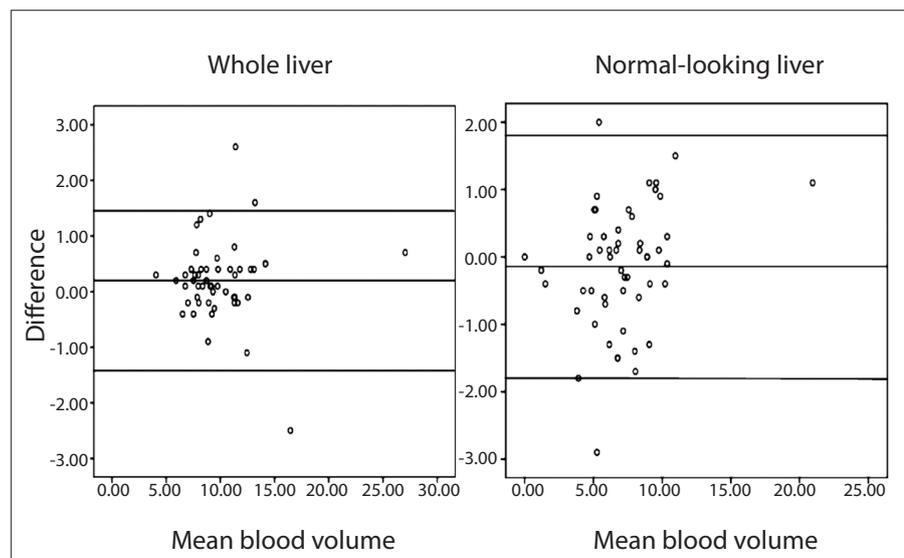
We found BF and BV to be the most reproducible and the least variable parameters independent of ROI localizations using very low dose pCT in metastatic liver disease. Goh et al. (18) and Petralia et al. (14) reported similar high ICCs for BF and BV between readers and readings in colorectal cancer and hepatocellular carcinoma, respectively. The reproducibility of measurements may be affected by how the ROIs are drawn (19). Goetti et al. (4) reported the feasibility and image quality of hepatic pCT for liver, metastasis, metastasis border, and normal tissue with variable pitch. However, to the best of our knowledge there was no study evaluating the reproducibility of perfusion parameters separately for whole liver, normal liver, whole metastasis, and metastasis wall. Our study demonstrated that the reproducibility and variability of pCT parameters can differ depending on where the ROIs are drawn. The perfusion parameters of the whole liver were less variable compared with normal-looking liver, and the

perfusion parameters of the whole metastasis were less variable compared with the metastasis wall. This was not too surprising because ROIs for the whole liver and whole metastasis did not differ between readers and readings. However, ROIs for metastasis wall and normal-looking liver differed on

every evaluation, even on the second analysis of the same reader. Thus, as the ROI gets smaller, the reproducibility of perfusion parameters is declined.

One of the most important limitations for routine clinical utilization of pCT is the high radiation dose (20). Radiation is becoming

more of an issue, particularly for patients in need of repeated pCT examinations for monitoring therapy response (21). In addition to pCT, routine chest and abdominal CTs also increase the total radiation burden. The effective doses of hepatic pCT are twice or triple the effective doses of conventional abdominal CTs (20). Total scan time, scan length, temporal interval between cine acquisitions and tube current/voltage are the main data affecting DLP of all pCT (22). Several ways were described to reduce the total dose (1, 21, 23–26). Considering very high radiation doses measured in most of the previous studies (7–30.7 mSv) (4, 8, 10–12, 20), the effective dose of our pCTs remains very low at 2.9 mSv. In our study, a very short scan length (2 cm), very low tube current/voltage (as little as possible; 80 kVp, 80 mA), and decreased scan time (48 s) were the main reasons for diminished radiation without sacrificing satisfactory perfusion calculations as recommended by Miles et al. (19). Goetti et al. (4) reported that by increasing the scan length only two-fold, the effective dose will be doubled. Thus, as there is no proven standard technique for hepatic pCT, we decreased the scan length as much as possible to lessen the dose without leading to erroneous results, and investigated whether the reproducibility of perfusion parameters necessitates an enlarged field of view. However, it should be noted that a 2 cm scan length may not be enough to monitor therapy response in a clinical relevance study and it can be extended to guarantee inclusion of the relevant parts of the tumors in the field of view. In a study by Watanabe et al. (27), an ultralow tube current of 20 mA was used for hepatic pCT; however, this could only be achieved during catheter angiography, which is an invasive procedure. Wang et al. (13) used 50 mA for hepatic pCT in nine healthy volunteers but the total effective dose was as high as 7 mSv.



**Figure 1.** Bland-Altman analysis of blood volume measurements and observer agreement for whole liver and normal-looking liver. Agreement plots of blood volume measurements for whole liver and normal-looking liver by readers 1 and 2 are shown. Plots show the difference between readers' measurements and mean measurements. Top and bottom lines show the 95% limits of agreement; midline shows the mean difference.

**Table 3.** Mean ICCs (95% CI) between readers and readings

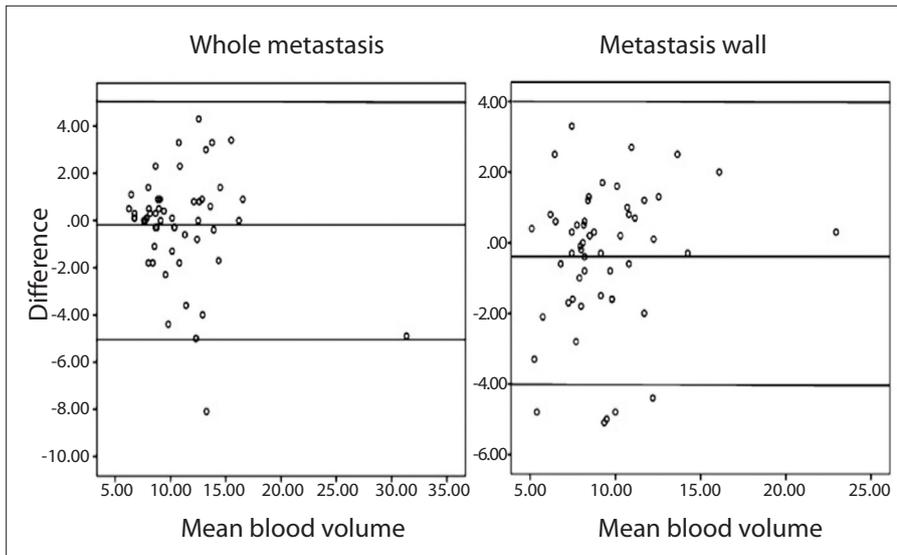
Perfusion parameter	Mean ICCs between readers	Mean ICCs between readings
BF	0.93 (0.90, 0.96)	0.86 (0.77, 0.95)
BV	0.91 (0.86, 0.96)	0.91 (0.85, 0.97)
Permeability	0.86 (0.80, 0.92)	0.81 (0.71, 0.91)
ALP	0.45 (0.35, 0.55)	0.53 (0.41, 0.65)
PVP	0.53 (0.39, 0.67)	0.56 (0.42, 0.70)
HPI	0.66 (0.58, 0.74)	0.71 (0.65, 0.77)

ICC, intraclass correlation coefficient; CI, confidence interval; BF, blood flow; BV, blood volume; ALP, arterial liver perfusion; PVP, portal venous perfusion; HPI, hepatic perfusion index.

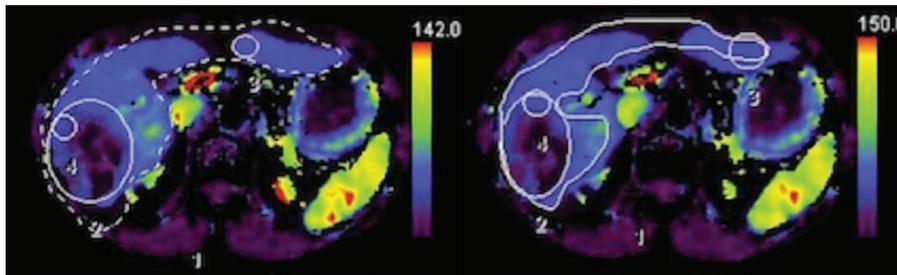
**Table 4.** Mean ICCs (95% CI) for whole metastasis vs. the metastasis wall and whole liver vs. normal-looking liver

Perfusion parameter	Mean ICCs for whole metastasis	Mean ICCs for metastasis wall	Mean ICCs for whole liver	Mean ICCs for normal-looking liver
BF	0.92 (0.87, 0.97)	0.87 (0.83, 0.91)	0.97 (0.96, 0.98)	0.77 (0.63, 0.91)
BV	0.94 (0.91, 0.97)	0.88 (0.83, 0.93)	0.99 (0.98, 1.00)	0.87 (0.83, 0.91)
Permeability	0.89 (0.85, 0.93)	0.76 (0.65, 0.87)	0.92 (0.88, 0.96)	0.77 (0.62, 0.92)
ALP	0.50 (0.27, 0.73)	0.49 (0.34, 0.64)	0.39 (0.33, 0.45)	0.59 (0.42, 0.76)
PVP	0.47 (0.44, 0.50)	0.46 (0.23, 0.69)	0.66 (0.44, 0.87)	0.61 (0.40, 0.82)
HPI	0.77 (0.71, 0.83)	0.68 (0.64, 0.72)	0.65 (0.51, 0.80)	0.66 (0.57, 0.74)

ICC, intraclass correlation coefficient; CI, confidence interval; BF, blood flow; BV, blood volume; ALP, arterial liver perfusion; PVP, portal venous perfusion; HPI, hepatic perfusion index.



**Figure 2.** Bland-Altman analysis of blood volume measurements and observer agreement for the whole metastasis and metastasis wall. Agreement plots of blood volume measurements for whole metastasis and metastasis wall by readers 1 and 2 are shown. Plots show the difference between readers' measurements and mean measurements. Top and bottom lines show the 95% limits of agreement; midline shows the mean difference.



**Figure 3.** Perfusion maps of BF in a 66-year-old woman with a hepatic metastasis of colonic adenocarcinoma. ROIs, particularly ROI-3 and ROI-4, were slightly different in size and location between reader 1 (on the left) and reader 2 (on the right). However, BFs were quite variable between readers. ROI-1, whole liver; ROI-2, whole metastasis; ROI-3, normal liver; and ROI-4, metastasis wall.

Previous studies reported that lower scan times in hepatic pCT are not reliable and reproducible, particularly for permeability (20, 23, 28). Ng et al. (28) proposed that at least 590 s were required for permeability with moderate confidence. In the current study, there was less agreement on permeability, as well as ALP, PVP, and HPI between readings and readers. This was not surprising since ALP, PVP, and HPI are related to portal perfusion and a total of 48 s was not enough for portal perfusion to end. In this study we specifically used a lower scan time to decrease the radiation dose and we aimed to identify those parameters that are reproducible even at the lowest doses. Several authors have discussed that shortening of the scan time can alter the reproducibility of perfusion measurements although it reduces the radiation dose (20, 29), motion artifacts, and provides more rapid post-

processing (20). Therefore, there must be a balance between the radiation burden and the reliability of measurements. Kambadakone et al. (20) proposed that 45–50 s of acquisition time is satisfactory for reliable BF measurements, but not for BV. However, in the current study with a total scan time of 48 s, BF and BV were the most reproducible parameters. We attributed this finding, first of all, to the decreased sampling interval during the first pass of contrast material. Thus, despite the short scan time, BF and BV measurements remained reproducible. Second, the difference may be due to the group of patients studied. In our study, patients with liver metastasis were included for pCT, whereas patients with rectal and retroperitoneal tumors were included in the study of Kambadakone (20).

Temporal interval between the cine acquisitions is another important factor in-

fluencing the dose. In our study the cycle time after the first 20 s (which is the most important part of the perfusion imaging so-called “first pass study” and 1 s was the cycle time for that part) was increased to 2 s for the next 16 s and was further increased to 3 s for the last 12 s. Miles et al. (19) proposed that during the first pass of contrast material, the image cycle time must not be greater than 2 s. Goh et al. (24) recommended a maximum temporal interval of 3 s in order to avoid inaccurate assessment. Ng et al. (28) reported that an optimal perfusion data might be based on high temporal sampling for the first 30 s and low temporal sampling for the second phase. Several other studies also have found that sampling interval up to 2 s can allow reproducible pCT parameters (20, 25, 30). Thus, we kept the cycle time as low as possible (1 s) for the first 20 s and then gradually increased.

Miles et al. (19) proposed that a maximum effective dose of 20 mSv for a 4 cm scan length was enough for adequate perfusion calculations. However, for the purpose of monitoring therapy response in cancer patients with liver metastasis requiring multiple pCTs, that amount of radiation may not be acceptable. pCT with an effective dose of 2.9 mSv, on the other hand, may be utilized many times for this group of patients.

In addition, in most of the previous perfusion studies, the least variable or the most reliable parameters were found to be BF and BV (14, 18, 27, 31). Our results showed BF and BV to be the most reproducible parameters for very low dose hepatic pCT. Thus, extra radiation may be unnecessary if the most reproducible and the least variable parameters will be the same in both pCT with high radiation and pCT with low radiation. Moreover, pCT with low radiation has the advantage of enabling recurrent pCT examinations as safely as possible in cancer patients.

There were several limitations in our study. First, very low tube voltage and tube current (80 kVp/ 80 mA) were insufficient in some obese patients leading to increase in the attenuation and inevitably to noise. Second, ROIs were not uniform in size and differed between readings and readers which means the target metastatic lesion and normal liver tissue were different in some patients, particularly in those having more than one metastasis. In addition, the ROIs for metastasis wall were also varied and located at different parts of the wall (Fig. 3). Third, sample size was relatively small and it remains to be determined whether our

results can be confirmed in larger prospective series. Finally, the current study included both hypovascular and hypervascular metastases and this mixture could lead to alterations in measurements. However, despite these limitations, we suggest that the present study may have important implications regarding the potential of very low dose hepatic pCT in clinical practice, particularly in patients needing repeated perfusion examinations.

In conclusion, our results demonstrated that there is greater intra- and interobserver agreement for BF and BV than for permeability, ALP, PVP, and HPI at very low dose hepatic pCT. Permeability, ALP, PVP, and HPI parameters cannot be used in clinical practice for hepatic pCT with an effective dose of 2.9 mSv. It should also be emphasized that the results of the current study are specific to hepatic pCT, analytic method, tube current/voltage, and injection rate and volume.

#### Conflict of interest disclosure

The authors declared no conflicts of interest.

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