

Perfusion measurement of the whole upper abdomen of patients with and without liver diseases: Initial experience with 320-detector row CT

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ABSTRACT

Objectives: To report initial experience of upper abdominal perfusion measurement with 320-detector row CT (CTP) for assessment of liver diseases and therapeutic effects.

Materials and methods: Thirty-eight patients who were suspected of having a liver disease underwent CTP. There were two patients with liver metastases, two with hemangiomas, and four with cirrhosis (disease group). CTP was repeated for four patients with cirrhosis or hepatocellular carcinoma (HCC) after therapy. Hepatic arterial and portal perfusion (HAP and HPP) and arterial perfusion fraction (APF), and arterial perfusion (AP) of pancreas, spleen, stomach, and intra-portal HCC were calculated. For disease-free patients (normal group), the values were compared among liver segments and among pancreatic and gastric parts. The values were compared between groups and before and after therapy.

Results: No significant differences were found in the normal group except between APFs for liver segments 3 and 5, and fundus and antrum. Mean HAP and APF for the disease group were significantly higher than for the normal group. APF increased after partial splenic embolization or creation of a transjugular intrahepatic portosystemic shunt. HPP increased and AP of intra-portal HCC decreased after successful radiotherapy.

Conclusions: 320-Detector row CT makes it possible to conduct perfusion measurements of the whole upper abdomen. Our preliminary results suggested that estimated perfusion values have the potential to be used for evaluation of hepatic diseases and therapeutic effects.

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1. Introduction

Because various liver diseases lead to significant changes in hepatic microcirculation, quantification of hepatic perfusion can improve the assessment and management of liver diseases. Various imaging techniques, such as xenon-enhanced computed tomography (CT), non-contrast or contrast-enhanced magnetic resonance imaging (MRI), isotope scintigraphy, and Doppler ultrasound, as well as positron emission tomography using oxygen-15 labeled

water, have been used for evaluation of hepatic perfusion. However, their acceptance and clinical application are limited due to high cost, low spatial resolution, or poor reproducibility [1].

CT perfusion (CTP) with cine imaging and administration of contrast media is a method of perfusion analysis in which quantitative maps of tissue perfusion can be created from cine CT data and displayed by using a color scale, which allows for quantification of perfusion in absolute units at high spatial resolution [1,2]. This method is reportedly useful for evaluation of liver damage or severity of hepatic fibrosis associated with chronic liver disease [3,4], assessment of hepatic tumor perfusion [5,6], prediction of tumor response to therapies [7,8], and evaluation of hepatic perfusion changes after surgical [9,10] or radiological [11,12] interventions. This method is also reportedly useful for evaluation of various diseases and conditions in other upper abdominal organs, such as pancreas [13,14], spleen [15–17], and stomach [18–20]. However, some problems remain with using this method, such as limited cranio-caudal scan range, additional radiation exposure,

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long breathholding for portal flow measurement, separation of arterial and portal blood flow, standardization of analytic methods, and unknown effects of extra-hepatic factors [1,2]. Our study dealt with the first problem.

Recently, a new generation of CT systems with 320-detector rows has become clinically available and is capable of performing volumetric imaging. These systems provide a single rotational acquisition, which covers 16 cm in the z-direction, and almost the whole upper abdomen can be appraised by means of serial rotational acquisitions at a single location in the z-direction.

The purpose of this study was thus to report our initial experiences of upper abdominal CTP with 320-detector row CT for assessment of liver diseases and therapeutic effects.

2. Materials and methods

2.1. Patients

We selected 42 consecutive patients at high risk of malignant liver or upper abdominal tumor (34 highly suspected to have lung cancer, 2 highly suspected to have intrathoracic mesothelioma, and 1 with atypical carcinoid in the lung) or portal hypertension (5 with chronic liver disease) for inclusion in this study. Before being enrolled, all subjects gave their informed consent after the nature of the procedure had been fully explained in accordance with the regulations of the institutional review board that approved our study. Two patients were excluded from the study population because a 20-gauge catheter could not be placed properly in the peripheral vein, as was one because of allergy to iodinated contrast medium. Eventually, 38 patients (27 men and 11 women, age: 43–83 years, mean 63.6 years) were considered eligible for this study.

Two patients had liver metastases from histologically proved lung cancer and another two had hepatic hemangiomas confirmed by follow-up imagings in 6–12 months after the initial CTP. There were four other patients with cirrhosis and portal hypertension due to type C hepatitis virus infection; one of them was classified as Child-Pugh B and three as Child-Pugh C. These eight patients constituted the disease group. One of them had hepatocellular carcinomas (HCC) and subsequently underwent transcatheter arterial chemoembolization for intra-hepatic lesions and radiation therapy for an intra-portal lesion. Two of these patients were treated with transjugular intrahepatic portosystemic shunt (TIPS) and one with partial splenic embolization (PSE). All of the four patients with cirrhosis underwent CTP before and after therapy. The follow-up CTPs were performed within 10 days after the end of therapy (mean 4 days, range: 2–10). None of them were previously treated with cytotoxic or anti-angiogenic therapy at the time of the initial CTP. The remaining 30 patients, who did not have any indications of pathologic conditions in the upper abdomen on their chart or among laboratory data or imaging modalities, including followed-up examinations, constituted the normal group. One patient in this group had undergone distal gastrectomy due to benign gastric ulcer 30 years before CTP.

2.2. CT examinations

All examinations were performed with a 320-detector row CT (Aquilion ONE; Toshiba Medical Systems, Ohtawara, Japan). Slices for CT perfusion were selected from pre-contrast abdomino-pelvic helical scans and included images as large as possible of the upper abdominal organs comprising the liver, spleen, pancreas, and stomach. A 20-gauge catheter was placed in the antecubital vein and 30 ml of nonionic contrast material (Iopamiron 370; Bayer HealthCare, Osaka, Japan) was administered at a rate of 5 ml/s with a power injector, followed by 20 ml of saline chaser. Dynamic scans

were performed 7–120 s after injection of contrast material under breathholding. Images were acquired with the following parameters: 0.5 mm thickness, 320 slices, 512×512 matrices, 80 kV, 210 or 250 mA, 0.5 s/rot. X-ray tube current of 250 mA was selected for larger patients with a field of view of more than 330 mm. The first 10 scans were performed every 3 s during one breathhold. Next, after a 9.6-s rest, three scans were performed every 7 s during one breathhold, and this procedure was repeated after another 9.6-s rest. A delayed-enhanced abdomino-pelvic scan was acquired 135 s after additional injection of 70 ml of contrast material at a rate of 3 ml/s.

To assess radiation exposure for patients undergoing CTP, volume computed tomographic dose index (CTDIvol) and dose-length product (DLP) for CTP, estimated on the console of CT scanner, were recorded for each of the patients.

2.3. Image analysis

The CT images were then transferred to a prototype workstation (Toshiba Medical Systems), and a prototype software was used for analysis. Respiratory misregistrations were compensated for first manually and then automatically with the software. Regions-of-interest (ROIs) were then placed on the abdominal aorta at the level of the celiac axis, the main portal vein, and the liver, spleen, pancreas, and stomach wall to generate time–density curves (TDC). Subsequently, hepatic arterial and portal perfusions (HAP and HPP; ml/min/100 ml) and arterial perfusion fraction (APF, %) were calculated with the two-input maximum slope method and arterial perfusions (AP, ml/min/100 ml) of pancreas (head, body and tail), spleen, gastric wall (fundus and antrum) were calculated using the one-input maximum slope method.

For the normal group, liver ROIs for perfusion measurement were placed on each liver subsegment on the perfusion maps and made as large as possible while avoiding large vessels. For the disease group, liver ROIs were made as large as possible to cover the entire hepatic normal parenchyma on the slice including the hepatic hilum while avoiding large vessels and focal liver lesions if these were present. For all patients, oval ROIs for perfusion measurement were placed on the spleen at the level of the splenic hilum and on every pancreatic or gastric part on the perfusion maps and made as large as possible while avoiding large vessels and ducts. Then, ROIs in the gastric wall included mucosal, muscle, and serosal layers. For intra-portal HCC, oval ROIs were also made as large as possible. All ROI placements were performed by two experienced radiologists (T.Y., N.K.), who were asked to make a consensus opinion.

2.4. Statistical analysis

HAP, HPP, and APF for each liver segment and AP for each part of the pancreas of the normal group were compared by means of one-way analysis of variance (ANOVA) and the Scheffé criterion. APs for two gastric parts were compared with the unpaired *t*-test, which was also used for comparisons between the normal and disease groups. HAP, HPP, and APF of liver segment 6 of the normal group was selected for comparison between normal and disease groups because of its location near the hepatic hilum where there was less likelihood of data degradation due to various artifacts.

StatView version 5.0 (SAS Institute, Cary, NC, USA) was used for all statistical analyses. Quantitative variables were expressed as mean \pm SD, and statistical significance was established at a *p* value of <0.05 .

3. Results

Mean HAPs, HPPs, APFs, and APs for the normal patient group are shown in Tables 1 and 2. No significant differences were found

Table 1
Estimated perfusion values of the liver of normal and disease groups.

| | HAP (ml/min/100 ml) | HPP (ml/min/100 ml) | APF (%) |
|--------------------------|-------------------------|------------------------|--------------------------|
| Normal group (n = 30) | | | |
| Subsegment | | | |
| 1 | 30.3 ± 10.1 | 131.4 ± 61.1 | 21.5 ± 10.2 |
| 2 | 28.5 ± 10.3 | 107.3 ± 45.5 | 25.0 ± 10.8 |
| 3 | 29.3 ± 11.4 | 95.6 ± 36.5 | 26.4 ± 9.2 ^a |
| 4 | 25.0 ± 11.2 | 116.3 ± 53.2 | 21.0 ± 10.5 |
| 5 | 23.3 ± 8.5 | 118.7 ± 39.3 | 18.6 ± 8.0 ^a |
| 6 | 24.1 ± 8.5 ^b | 116.7 ± 40.1 | 19.3 ± 7.3 ^c |
| 7 | 23.2 ± 7.4 | 114.0 ± 42.7 | 19.5 ± 7.4 |
| 8 | 24.0 ± 8.5 | 118.3 ± 42.3 | 19.6 ± 8.9 |
| Disease group (n = 8) | 31.0 ± 5.9 ^b | 80.7 ± 39.2 | 37.2 ± 19.0 ^c |

APF, arterial perfusion fraction; HAP, hepatic arterial blood flow; HPP, hepatic portal perfusion.

^a Mean APF of subsegment 3 was significantly higher than that of subsegment 5 ($p < 0.01$).

^b Mean HAP in the disease group was significantly higher than that in the normal group ($p < 0.05$).

^c Mean APF in the disease group was significantly higher than that in the normal group ($p < 0.0005$).

Table 2
Estimated arterial perfusion values of spleen, pancreas, and stomach of normal and disease groups (ml/min/100 ml).

| | Normal group | Disease group |
|----------|-----------------------------------|----------------------|
| Spleen | 130.2 ± 34.6 (n = 30) | 106.2 ± 30.0 (n = 8) |
| Pancreas | | |
| Head | 85.3 ± 27.5 (n = 30) | 82.3 ± 39.3 (n = 8) |
| Body | 92.5 ± 29.0 (n = 30) | 81.9 ± 26.5 (n = 8) |
| Tail | 92.9 ± 24.1 (n = 30) | 80.4 ± 21.6 (n = 8) |
| Stomach | | |
| Fundus | 67.5 ± 21.0 ^a (n = 30) | 62.9 ± 23.8 (n = 8) |
| Antrum | 51.2 ± 21.2 ^a (n = 29) | 60.6 ± 17.6 (n = 8) |

^a Mean arterial perfusion of gastric fundus was significantly higher than that of antrum ($p < 0.001$).

for HAP, HPP, or APF among liver subsegments except for APF for liver segments 3 and 5 ($p < 0.01$). No significant differences were detected among pancreas head, body and tail, either, but a significant difference was found between gastric fundus and antrum ($p < 0.001$).

Mean HAP and APF for the disease group were significantly higher than for the normal group ($p < 0.05$ and < 0.0005) (Table 1). The disease group tended to have lower mean APs than the normal group except for the gastric antrum (Table 2). APF increased after PSE (27.7–47.3) and TIPS (27.6–47.2 and 25.3–45.8), while HPP increased (80.8–105.8) and AP of intra-portal HCC decreased (62.4–35.6) after successful radiation therapy. Representative cases are shown in Figs. 1 and 2.

Mean CTDIvol and DLP for CTP were 54.1 ± 6.6 (mGy, range: 46.0–59.5) and 856.2 ± 99.0 (mGy cm, range: 743.0–942.7), respectively.

4. Discussion

Perfusion imaging can detect regional and global changes in organ perfusion and is an effective method for detecting hemodynamic characteristics of various diseases. Of the various techniques in use, CT perfusion is the least invasive method and has the advantage of providing highly reliable quantification of perfusion in abdominal organs and lesions at low cost [1]. Although many researchers have stressed the clinical usefulness of this technique, some problems remain. One of the major limitations of this technique is the cranio-caudal scan range. In most previous studies, the

perfusion data was obtained with single-level dynamic CT, which means that estimated perfusion values are biased by slice selection and only one major lesion can be evaluated. In the liver, perfusion can be estimated only in hepatic hilum slices because placement of ROIs over the portal vein cannot be avoided. Moreover, respiration-related motion artifacts also pose a significant problem [1,4].

In contrast, the 320-detector row CT system supports dynamic scanning over a cranio-caudal range of approximately 16 cm and can provide a larger amount of perfusion-related data compared to conventional CT systems with a maximum range of 32 mm. With this system, perfusion in multiple organs can be assessed with a single cine imaging protocol. However, a previous study using this system was restricted to specific organs [13]. To the best of our knowledge, no study has been conducted to assess whole upper abdominal perfusion measurement obtained with the 320-detector row CT system as we did in this study. Such an assessment is essential for effective routine clinical use of this technique.

Our results showed no significant differences for HAP, HPP, or APF among liver subsegments, except for APF segments 3 and 5, nor among pancreas head, body and tail. These findings indicate that estimated perfusion values are nearly stable and quite reliable throughout the cranio-caudal scan range. Possible explanations for the difference we found in the limited areas are the effects of artifacts due to respiration or gas in the intestine. Mean HAP and APF of the disease group were significantly higher than those of the normal group in our study. Many researchers have reported that chronic hepatitis, cirrhosis, and liver tumors can cause direct or relative increases in arterial perfusion [2,3], and our results are consistent with theirs.

Perfusion in the pancreatic head was lower than in the body or tail. Kandel et al. [13] reported similar findings in a study population with pancreatic cancer, although neither they nor we found any statistical significance. The disease group showed a tendency towards lower mean pancreatic APs than the normal group. No previous study on the relation between liver disease and pancreatic perfusion has been published and we did not find any statistically significant differences. Therefore, our results are not conclusive. Splenic arterial perfusion is reportedly reduced in patients with chronic hepatitis and cirrhosis [15–17], and our results are consistent with these previous findings. APs tended to be higher in the normal than in the disease group. This finding suggests that liver diseases can affect perfusion in other upper abdominal organs.

Several previous studies have investigated gastric CTP [18–20] and detected increased perfusion in gastric cancer compared to in normal gastric wall. We examined perfusion in two parts of the gastric wall and found a significant difference between fundus and antrum. Considering the differences in perfusion values in the spleen and pancreas between the two groups, perfusion values obtained in the antrum might not be reliable. Thin wall thickness and peristalsis of the antrum may have hampered accurate perfusion measurement in our study. The use of an anticholinergic agent is a possible solution for this, although it may affect perfusion in normal gastric wall.

CTP can play an important role in evaluation of therapeutic effects. Weidekamm et al. reported that portal venous perfusion remained almost unchanged and hepatic arterial perfusion increased after TIPS therapy [11]. In two of our patients, HAP and APF increased and HPP decreased after creation of TIPS and these findings are consistent with those previously reported. APF increased after PSE in our patients but no comparable findings could be found in the English literature. After successful radiation therapy for intra-portal HCC, HPP increased and AP of intra-portal HCC decreased, but again there are no previously reported comparable findings. While our results are not conclusive, CTP may well be useful for evaluation of therapeutic effects on various pathologic conditions.

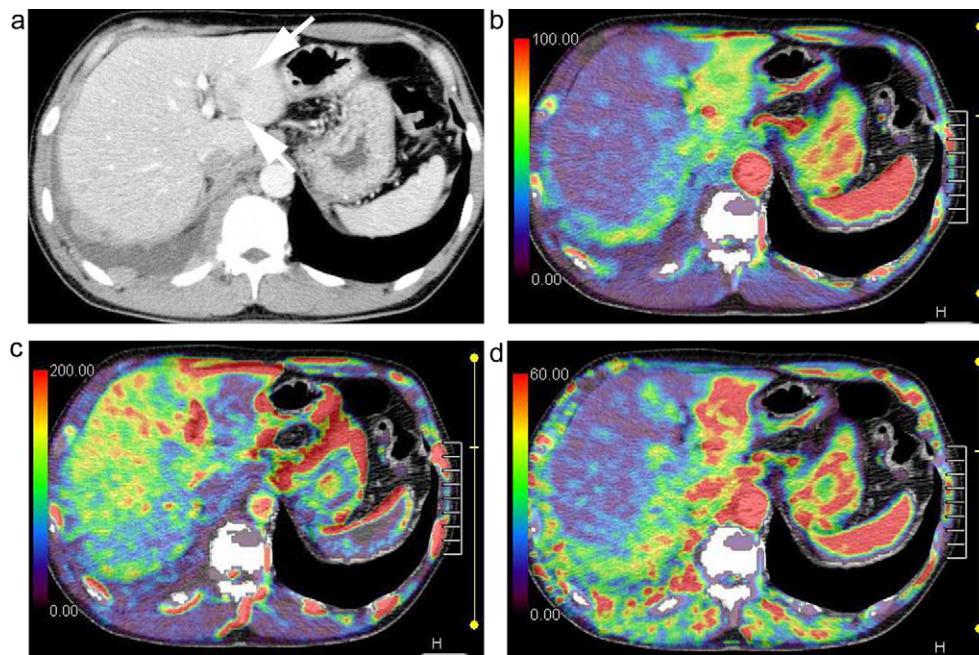


Fig. 1. A 57-year-old woman with histologically diagnosed right lung cancer accompanied by pleural invasion and liver metastases. On contrast-enhanced CT image, metastases are seen in the left lateral hepatic lobe (a) (arrows). CT hepatic arterial perfusion map (b) shows an increase in arterial perfusion in metastatic tumors as well as in surrounding non-cancerous parenchyma in the lobe. Portal perfusion map (c) shows a decrease in portal perfusion in the lobe. Arterial perfusion fraction map (d) also shows an increase in arterial perfusion.

Several benefits of CTP with wide scan ranges deserve to be considered. Simultaneous assessment of perfusion in multiple organs and/or lesions is possible, which is useful for conditions such as gastric cancer in combination with liver metastases and intra-hepatic and intra-vascular HCCs. Moreover, the effects of various pathologic conditions or focal lesions on other organs, such as cirrhosis

together with hypersplenism or gastric varices, or abnormal hemodynamics in the liver due to acute pancreatitis, can be evaluated. Assessments of therapeutic effects with a wide scanning range are also possible. A recently available newer CT technique, volume shuttle scan, can also offer greater cranio-caudal coverage. However, when using it, CT table is continuously moving during data

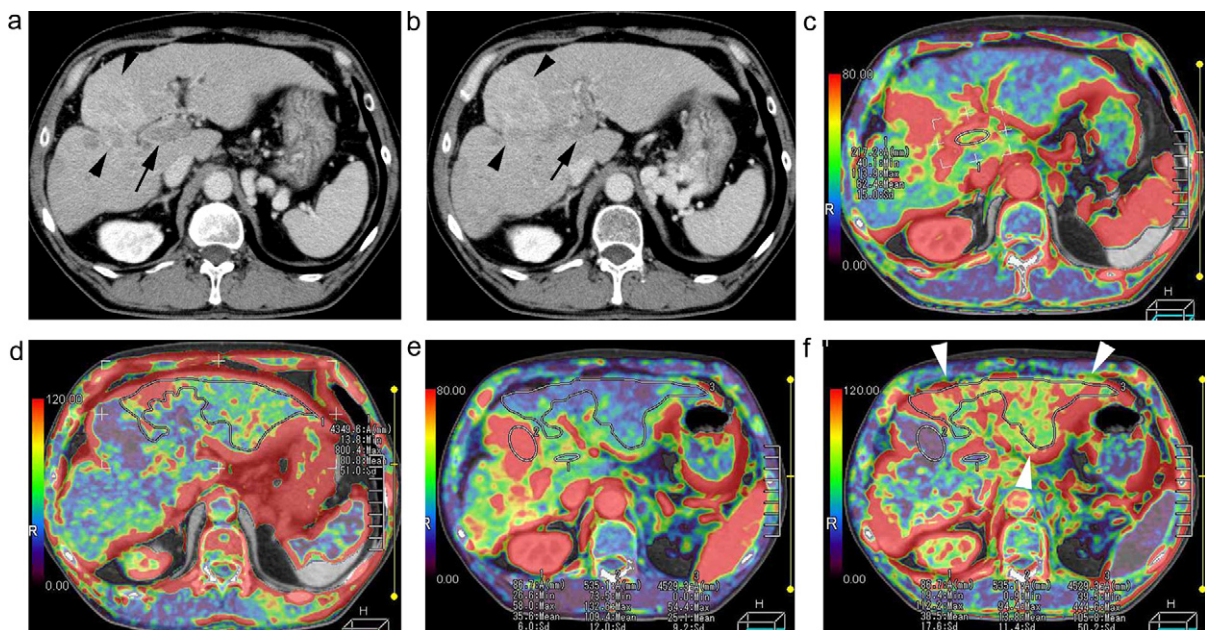


Fig. 2. A 60-year-old man with clinically diagnosed hepatocellular carcinoma accompanied by intra-portal tumor invasion. Contrast-enhanced CT images at time of the first CT perfusion are shown as (a) and (b). He received transcatheter chemoembolization for intra-hepatic tumors ((a) and (b), arrowheads) and radiation therapy for intra-portal tumor invasion ((a) and (b), arrows). CT hepatic arterial perfusion map (c) shows an increase in arterial perfusion in the intra-portal tumor and the portal perfusion map (d) shows a decrease in portal perfusion in the non-cancerous parenchyma. Following CT perfusion 1 week after the end of radiation therapy, the hepatic arterial perfusion map (e) shows a decrease in arterial perfusion in the intra-portal tumor and the portal perfusion map (f) shows recovery of portal perfusion, especially in left lobe of the liver (arrowheads).

acquisition and acquisition time points disperse in cranio-caudal direction. The effects of these factors on perfusion measurement have not been fully evaluated.

Compared to the previous studies, our CTDIvol were not reduced. And DLP was probably increased due to our wide cranio-caudal scan range. To date, many techniques have been used to reduce radiation exposure in body CT, such as modification of tube current or voltage, helical pitch, individualization of scanning parameters, automatic exposure control (AEC) and image filters. Furthermore, a new generation of image reconstruction methods for CT has become clinically available during the past several years, such as adaptive iterative dose reduction (AIDR). These new methods can reduce noises on the images while preserving CT values on images and image quality, so that radiation doses can be reduced compared to those used for the conventional filtered back projection (FBP) method and image filters. However, there has been no report of its use in abdominal CTP, which can be expected to gain major benefits from these new techniques. Further studies with new techniques are needed in this field.

There are some limitations to this study. First, our sample size was relatively small which restricts statistical significance, so that further studies with a larger population are needed to verify our results. Second, we evaluated patients with various diseases treated as one disease group, so that further studies limited to one specific disease or condition are needed. Third, the perfusion values obtained in our study were not compared to the gold standard. PET findings are regarded as the gold standard in the fields of neuroradiology and cardiology. However, manually obtained blood samples from the peripheral arteries are used for the estimation of arterial input, and this is a slightly invasive technique and the differences between peripheral and visceral arteries may lead to errors in perfusion estimates. In the case of the liver, arterial and portal perfusion values are estimated by using counts for the spleen and compartmental models. These drawbacks can make PET unreliable for the abdomen. Furthermore, perfusion values estimated by PET have not been compared to those obtained with microsphere study in the human liver. This means that currently there is no non-invasive modality which can be used as a gold standard. MRI is reportedly useful for perfusion measurements in abdominal organs. It is a non-invasive method, however, there is no proportional relation between signal intensity on the image and concentration of tracer. It could not be the gold standard in this study. Fourth, we employed the protocol with long breathholds. Our misregistration compensation software worked well and perfusion measurements could be done in all patients. However, it might affect our results. Finally, even with a 320-detector row CT, the cranio-caudal scanning range is limited to 16cm, which means that the entire liver of a significant proportion of our subjects could not be covered and this may have also affected our results.

5. Conclusion

With 320-detector row CT, it is possible to conduct perfusion measurements of the whole upper abdomen. Our preliminary results suggested that estimated perfusion values have the potential to be used for evaluation of hepatic diseases and therapeutic effects.

Conflict of interest

Takeshi Yoshikawa: Toshiba Corporation research grant and Koninklijke Philips Electronics NV research grant.

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