Hepatic CT Perfusion Measurements: Effects of Radiation Dose Reduction and New Image Reconstruction Method

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Authors: N. Negi¹, T. Yoshikawa¹, Y. Ohno¹, Y. Somiya², T. Sekitani², T. Kanda², T. Murakami², H. Kawamitsu¹, K. Sugimura¹; ¹Kobe/JP, ²Kobe /JP

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Purpose

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. Different imaging techniques, such as xenon-enhanced computed tomography (CT), 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 relatively new 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], assessment of hepatic tumor perfusion [4], prediction of tumor response to therapies [5], and evaluation of hepatic perfusion changes after surgical [6] or radiological [7] interventions. However, it reportedly requires 1-2 times the dose used for routine abdominal CT [8]. And the relatively high radiation dose has prevented it from being used in routine clinical practice.

To date, many techniques have been used to reduce body CT, such as modification of tube current or voltage, helical pitch, individualization of scanning parameters, automatic exposure control (AEC) and image filters [9]. One of image filters is known as quantum denoising (QDS) [10, 11]. However, no published study has assessed these techniques in the field of hepatic CTP. Furthermore, a new generation of image reconstruction methods for CT has become clinically available during the past several years [12 - 18]. 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. One of these methods is adaptive iterative dose reduction (AIDR) processing [12]. However, there has been no report of its use in hepatic CTP, which can be expected to gain major benefits from these new techniques.

Purpose

The purpose of this study was thus to assess the effects of reduction of radiation dose, conventional image filter, and AIDR on hepatic CTP measurements with the aim of successfully reducing radiation dose.
Methods and Materials

Patients

We selected 60 consecutive patients at high risk of malignant liver or upper abdominal tumors (57 strongly suspected of having lung cancer, 2 strongly suspected of having intrathoracic mesothelioma, and 1 with atypical carcinoid in the lung) and 10 suspected of having primary liver tumor for inclusion in this study. Before their enrolment, 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 were one because of allergy to iodinated contrast medium. Three patients had liver metastases from histologically proved lung cancer and 3 had histologically proved hepatocellular carcinomas. Another had hepatic hemangiomas confirmed by follow-up imaging 6-12 months after the initial CTP. These 7 patients were excluded from the study population because overt hepatic tumors can have a significant effect on hepatic perfusion. The remaining 60 patients (44 men and 16 women; age: 51 - 83 years, mean 69.2 years), whose charts, laboratory data or imaging modalities, including those obtained at follow-up examinations, showed no indications of pathologic conditions in the upper abdomen, were considered eligible for this study and were randomly divided into two groups (standard and low radiation dose groups).

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 liver. A 20-gauge catheter was placed in the antecubital vein and 30ml of nonionic contrast material (Iopamiron 370; Bayer HealthCare, Osaka, Japan) was administered at a rate of 5 ml/s with a power injector (Dual Shot GX; Nemoto Kyorindo Co. Ltd., Tokyo, Japan), followed by 20ml of saline chaser. Dynamic scans were performed 7 to 120 seconds after injection of contrast material during breathholds. Images were acquired with the following parameters: 0.5 mm thickness, 320 slices, 512 × 512 matrices, 80 kV, 210 or 250 mA for the standard dose group and 120 or 140 mA for the low dose group, 0.5 sec/rot. Fields of view was set depending on the body size and ranged from 290 to 380 mm. An X-ray cube current of 140 or 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 seconds during one breathhold. Next, after a 9.6-second rest, three scans were performed every 7 seconds during one breathhold, and this procedure was repeated after another 9.6-second rest. A delayed-enhanced abdomino-pelvic scan was acquired 135 seconds after additional injection of 70ml of contrast material at a rate of 3 ml/sec.
To assess radiation exposure for patients undergoing CTP, the volume computed tomographic dose index (CTDvol) and dose-length product (DLP) for CTP, estimated on the CT scanner's console, were recorded for each of the patients.

**Image reconstruction**

CT images for each of the patients were reconstructed by using FBP, QDS, and AIDR processing. Examples of CT images reconstructed with the three methods are shown in Figure 1.

QDS is one of imaging filters [10, 11]. With this image-data based processing, the edge elements are extracted from the source images by using the edge detection filter and then used to calculate a suitable blending ratio (0 - 1) for smoothed and sharpened images on the basis of the edge-sensitivity curve. The input image is smoothed by using low-pass filtering to attenuate noises on the image, while the input image is sharpened with high-pass filtering to enhance the fine structures. Noises in areas with low edge intensity are reduced by increasing the blending ratio of the smoothed image, while resolution in areas with high edge intensity is maintained by increasing the blending ratio of the sharpened image. The edge-sensitivity curve is then used to adjust the blending ratio. Each of the processes is applied to 3-dimensional data.

AIDR processing is one of newly developed image reconstruction methods for CT, which has become clinically available in the past several years [12 - 18]. This method can reduce noises on the images, thus preserving CT values on images and image quality, so that radiation doses can be reduced compared to those required for the conventional FBP method. In this process, noises on the image are selectively extracted from the reconstructed data and iteratively eliminated by using three-dimensional information. Combining the resultant data with the original data contributes to maintaining the noise granularity. Thus, AIDR improves signal-to-noise ratio (SNR) while preserving the spatial resolution and natural appearance. The flow diagram for AIDR is shown in Figure 2.

**Image analysis**

The CT images were analyzed using software (Body Perfusion; Toshiba Medical Systems), which compensated automatically for respiratory misregistrations. 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 to generate time-density curves (TDC). Next, hepatic arterial and portal perfusions (HAP and HPP; ml/min/100ml) and arterial perfusion fraction (APF, %) were calculated with the two-input maximum slope method, and CT values and image noises (standard deviations of CT value, SD) were measured on the source CT images.

Liver ROIs for perfusion measurement were placed on each of the liver subsegments on the perfusion maps and made with a diameter larger than 2 cm while avoiding large vessels. Images near the hepatic hilum were chosen for measurement because there
was less likelihood of data degradation due to various artifacts. All ROI were placed according to a consensus opinion of two experienced abdominal radiologists (T. Y., N.K.). An example of perfusion maps for one patient is shown in Figure 3.

**Statistical analysis**

CT value, image noise, HAP, HPP, and APF for each image reconstruction method and the two groups were compared by means of one-way analysis of variance (ANOVA) and the Scheffé criterion. CT value, image noise, HAP, HPP, and APF for each group were compared with the unpaired t-test, which was also used for comparisons of demographic features of the groups.

StatView version 5.0 (SAS Institute, Cary, NC, USA) was used for all statistical analyses. Quantitative variables were expressed as mean ± SD, and statistical significance was established at a p value of < 0.05.
**Fig. 1.** Source CT images with a thickness of 0.5mm of a 57-year-old man in the standard dose group (a, b, and c) and a 64-year-old man in the low dose group (d, e, and f).
Fig. 2. Flow Diagram for AIDR

Fig. 2

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Fig. 3. Hepatic CT perfusion maps of a 60-year-old man in the low dose group with histopathologically diagnosed right lung cancer without abdominal metastasis. CT hepatic arterial (a), portal perfusion (b) and arterial perfusion fraction (c) maps were calculated from source CT images (d) reconstructed with AIDR.
Results

There were no significant differences in demographic features between the standard and low radiation dose groups (Table 1, Fig. 4). Mean CT values, image noises, HAPs, HPPs, and APFs for the standard and low dose groups are shown in Table 2 (Fig. 5). There were no significant differences in these values between the groups or among the image reconstruction methods. However, mean SDs of the standard dose group were significantly lower than those of the low dose group (p<0.0001), and mean SDs of AIDR were significantly lower than those of the original method for both groups (p=0.0006 and 0.013).

Mean CTDIvol and DLP for CTP were 53.8 ± 6.4 (mGy) and 853.0±102.3 (mGy cm) for the standard dose group and 29.3±4.6 (mGy) and 467.6±77.3 (mGy cm) for the low dose group, respectively. CTDIvol and DLP for the low dose group were significantly lower than those for the standard dose group (p<0.0001). Dose reductions for the low dose group were 45.5% and 45.2%, respectively.

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, above all the relatively high radiation dose associated with this technique, which has prevented it from being used in routine clinical practice.

To date, many techniques have been used to reduce CT, such as modification of tube current or voltage or of helical pitch, individualization of scanning parameters, automatic exposure control (AEC) and imaging filters [9], one of which is known as QDS [10,11]. With this processing, noises in areas with low edge intensity are reduced, while resolution in areas with high edge intensity is maintained. However, there have been no reported studies which assessed these techniques in the field of hepatic CTP. In the past several years, newly developed image reconstruction methods for CT have become clinically available [12-18]. These new methods can reduce noises on the images, thus preserving CT values on images and image quality, so that radiation doses can be reduced compared to those required for the conventional FBP method. One of these new methods is AIDR processing [12]. However, we have not been able to find any reports on employment of these techniques for CTP of the abdomen, which can be expected to gain major benefits from these new techniques.
Our results showed no significant differences in mean HAP, HPP, APF, and CT values between the groups or among the image reconstruction methods. These findings indicate that estimated perfusion values are nearly stable and quite reliable for the two tube current ranges and three image reconstruction methods. Mean SDs for the standard dose group were significantly lower than those for the low dose group, and mean CT Dvol and DLP for the low dose group were significantly lower than those for the standard dose group. This indicates that noises on the CTP images increased in proportion to reduction of radiation dose without the estimated hepatic perfusion values being affected. Mean SDs of AIDR were significantly lower than those of the FBP for both groups, indicating that further reduction in the CTP radiation dose might be possible with AIDR.

QDS is a kind of smoothing filter that can obscure edges of fine structures with low contrast, which can be a problem because some types of focal hepatic lesions have small contrast differences compared to surrounding liver. AIDR, on the other hand, preserves the structures on the image more efficiently, thus making it superior to QDS in this respect. Our results also indicate that AIDR is superior to QDS in terms of noise reduction. For hepatic CTP, AIDR is thus the recommended image reconstruction method.

Another problem of hepatic CTP is standardization of analytic methods [8]. In this study, we used only the maximum slope method, but the compartment model and deconvolution methods have also been proposed as valid methods. Because of their complicated calculation procedures, the compartment model and deconvolution methods can be more sensitive to image noises than the maximum slope method. Thus, our results may underestimate the effects of image noise and further studies are needed using analytic methods other than the ones we employed.

Previous researches using new image reconstructions for abdominal CT indicated that 25-50 % radiation dose reduction could be achieved while maintaining image quality [13 - 18], and our low-dose protocol achieved a reduction of approximately 45%. Changes in image quality due to the use of new image reconstructions have been reported [14], but this drawback do not affect hepatic CTP because only CT values on images are used in the calculation procedures for hepatic CTP. Thus, further radiation dose reduction for hepatic CTP may be possible with these image reconstruction methods.

The most recent image reconstruction methods have been introduced during the past two years [19, 20]. These new techniques use scanner models and/or statistical noise models which take both photon and electrical noise into account and selectively extract and eliminate noise iteratively from the image reconstruction data while maintaining noise granularity, thus improving SNR without any substantial loss in spatial resolution or the natural appearance of structures on the image. Our preliminary results for AIDR suggest that these new techniques may make it possible to further reduce the radiation dose for hepatic CTP.

There are some limitations to this study. First, our sample size was relatively small which limits the statistical significance of the findings, so that further studies with a larger
population are needed to verify our results. Second, we evaluated only patients without hepatic diseases, thus making further studies including subjects with focal and diffuse diseases necessary. Third, our study was limited to hepatic perfusion measurement. In other abdominal organs, such as pancreas, spleen, stomach, and adrenal glands, perfusion measurements were reportedly useful for assessment of organ function, diagnosis of focal lesions, and evaluation of therapeutic effects. Finally, AEC was not used in our study because the optimal SNR for hepatic CTP images was unknown and remains so now. Further studies are thus needed to determine optimal SNR and assess its effects on estimated perfusion values.
Table 1. Demographic features of the two groups

<table>
<thead>
<tr>
<th></th>
<th>Standard Dose Group (n = 30)</th>
<th>Low Dose Group (n = 30)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>69.1 ± 8.7 (51 - 83)</td>
<td>69.3 ± 8.0 (55 - 81)</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Sex</td>
<td>19 men and 11 women</td>
<td>25 men and 5 women</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>162.1 ± 9.3 (144 - 179)</td>
<td>161.5 ± 6.6 (148 - 178)</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>58.6 ± 9.7 (39 - 81)</td>
<td>58.4 ± 10.5 (42 - 81)</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Presence of liver diseases</td>
<td>0</td>
<td>0</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Presence of cardiovascular</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>diseases</td>
<td>6 (AP;3, AF;2, PSVT;1)</td>
<td>6 (AP;4, AF;1, PSVT;1)</td>
<td>&gt;0.05</td>
</tr>
</tbody>
</table>

AP: angina pectoris, AF: atrial fibrillation, PSVT: paroxysmal supraventricular tachycardia

Fig. 4

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Table 2. Mean CT values, image noises, hepatic arterial and portal perfusions, and arterial perfusion fractions for the two groups by image reconstruction method

<table>
<thead>
<tr>
<th></th>
<th>Standard Dose Group (n = 30)</th>
<th>Low Dose Group (n = 30)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CT value (HU)</td>
<td>FBP 52.6 ± 7.0</td>
<td>54.7 ± 8.8</td>
</tr>
<tr>
<td></td>
<td>QDS 52.6 ± 7.1</td>
<td>54.7 ± 8.7</td>
</tr>
<tr>
<td></td>
<td>AIDR 52.6 ± 7.1</td>
<td>54.7 ± 8.8</td>
</tr>
<tr>
<td>Image noise (SD)</td>
<td>FBP 20.6 ± 5.4(^a)</td>
<td>28.2 ± 6.6</td>
</tr>
<tr>
<td></td>
<td>QDS 18.5 ± 4.8(^a)</td>
<td>26.1 ± 5.7</td>
</tr>
<tr>
<td></td>
<td>AIDR 15.5 ± 4.5(^a,b)</td>
<td>23.5 ± 6.0(^c)</td>
</tr>
<tr>
<td>HAP (ml/min/100ml)</td>
<td>FBP 27.0 ± 6.6</td>
<td>28.9 ± 9.1</td>
</tr>
<tr>
<td></td>
<td>QDS 26.7 ± 6.8</td>
<td>28.5 ± 9.1</td>
</tr>
<tr>
<td></td>
<td>AIDR 26.2 ± 6.8</td>
<td>28.3 ± 9.1</td>
</tr>
<tr>
<td>HPP (ml/min/100ml)</td>
<td>FBP 107.4 ± 32.9</td>
<td>107.4 ± 31.7</td>
</tr>
<tr>
<td></td>
<td>QDS 107.8 ± 37.7</td>
<td>111.3 ± 40.1</td>
</tr>
<tr>
<td></td>
<td>AIDR 104.4 ± 34.2</td>
<td>108.3 ± 33.2</td>
</tr>
<tr>
<td>APF (%)</td>
<td>FBP 22.4 ± 6.7</td>
<td>23.5 ± 7.1</td>
</tr>
<tr>
<td></td>
<td>QDS 22.4 ± 7.4</td>
<td>23.0 ± 7.7</td>
</tr>
<tr>
<td></td>
<td>AIDR 22.3 ± 7.4</td>
<td>23.1 ± 8.0</td>
</tr>
</tbody>
</table>

AIDR: adaptive iterative dose reduction, APF: arterial perfusion fraction, HAP: hepatic arterial blood flow, HPP: hepatic portal perfusion, QDS: quantum de-noising

\(^a\)Mean image noises were significantly lower than those in the low dose group (p < 0.0001).
\(^b\)Mean image noise was significantly lower than that for FBP (p = 0.0006).
\(^c\)Mean image noise was significantly lower than that for FBP (p = 0.013).

Fig. 5

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Conclusion

Reductions in radiation dose associated with QDS and AIDR did not affect estimated hepatic perfusion values in our study. AIDR also significantly reduced images noises and thus may make it possible to further reduce the radiation dose for hepatic CTP.
References


