Application of Computed Tomography Virtual Noncontrast Spectral Imaging in Evaluation of Hepatic Metastases: A Preliminary Study

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Abstract

Objective: The objective was to qualitatively and quantitatively evaluate hepatic metastases using computed tomography (CT) virtual noncontrast (VNC) spectral imaging in a retrospective analysis.

Methods: Forty hepatic metastases patients underwent CT scans including the conventional true noncontrast (TNC) and the tri-phasic contrast-enhanced dual energy spectral scans in the hepatic arterial, portal venous, and equilibrium phases. The tri-phasic spectral CT images were used to obtain three groups of VNC images including in the arterial (VNCa), venous (VNCv), and equilibrium (VNCe) phase by the material decomposition process using water and iodine as a base material pair. The image quality and the contrast-to-noise ratio (CNR) of metastasis of the four groups were compared with ANOVA analysis. The metastasis detection rates with the four nonenhanced image groups were calculated and compared using the Chi-square test.

Results: There were no significant differences in image quality among TNC, VNCa and VNCv images ($P > 0.05$). The quality of VNCe images was significantly worse than that of other three groups ($P < 0.05$). The mean CNR of metastasis in the TNC and VNCs images was 1.86, 2.42, 1.92, and 1.94, respectively; the mean CNR of metastasis in VNCa images was significantly higher than that in other three groups ($P < 0.05$), while no statistically significant difference was observed among VNCv, VNCe and TNC images ($P > 0.05$). The metastasis detection rate of the four nonenhanced groups with no statistically significant difference ($P > 0.05$).

Conclusions: The quality of VNCa and VNCv images is identical to that of TNC images, and the metastasis detection rate in VNC images is similar to that in TNC images. VNC images obtained from arterial phase show metastases more clearly. Thus, VNCa imaging may be a surrogate to TNC imaging in hepatic metastasis diagnosis.

Key words: Contrast-to-noise Ratio; Hepatic Metastasis; Virtual Noncontrast Imaging

Introduction

Hepatic metastasis is the common malignancy of the liver; related primary cancers are frequently lung cancer, breast cancer, and gastrointestinal cancer.[1] Timely detection of hepatic metastasis has important clinical significance in helping the detection of primary cancer, the selection of therapy and the evaluation of prognosis. At present, there are many detection and qualification imaging methods for hepatic metastases, commonly ultrasonography, contrast-enhanced computed tomography (CT), contrast-enhanced magnetic resonance imaging, and positron emission tomography/CT.[2-4] Contrast-enhanced CT has high-density resolution, and the capabilities of acquiring the images of arterial, portal venous, and equilibrium phases, analyzing the hemodynamics of arteries and veins in hepatic metastases, and providing such important information as the size, number, enhancement degree, and distribution of metastases. However, ionizing radiation during CT scanning exposes patients to a certain health risk. Therefore, the minimal CT radiation dose with the maximal image quality becomes a popular concern in the medical circle.[5]

In spectral CT, iodine agent is separated from the contrast-enhanced image through iodine-water substance separation to give water and iodine density image pairs.[6] The water-based image contains no iodine and is regarded as a virtual noncontrast (VNC) image. VNC scan images can be used as a replacement for true noncontrast (TNC) scans, has been examined for use in pancreatic disease, renal disease, and colon disease.[7-9] However, the application of VNC detection of hepatic metastases is rarely reported. On such a basis, this study aimed to explore the feasibility of

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CT-VNC imaging as a substitution to TNC imaging in the diagnosis of hepatic metastases.

Methods

Patients

This study was approved by the ethics committee of our hospital, and all included patients provided the informed consent before examination. The images of 40 patients (25 males and 15 females, age range 30–84 years, with an average of 64 ± 11 years) with hepatic metastases who underwent spectral CT imaging in our hospital from January 2012 to December 2012 were retrospectively analyzed. Only primary tumors were analyzed, including six cases of lung cancer, four cases of breast cancer, nine cases of gastric cancer, seven cases of colonic cancer, eight cases of rectal cancer, four cases of pancreatic cancer, one case of cholangiocarcinoma, and one case of fallopian tube carcinoma. All primary tumors were confirmed either by operation or pathology. The diagnosis of hepatic metastases was based on (1) the metastasis was new compared with the previous CT image; and (2) the size of metastasis was increased or decreased after chemotherapy compared with the previous or subsequent CT image.[10] The follow-up time was 80 ± 40 days. Massive metastases with fused, unclear edges, and incapable to count were excluded. If there were >5 hepatic metastases, only the largest five metastases easily to be measured were evaluated.

Computed tomography imaging methods

All examinations were performed on spectral CT (GE Discovery HD750, USA), including the TNC imaging with 120 kVp tube voltage and the tri-phasic contrast-enhanced dual energy spectral scans in the hepatic arterial, portal venous, and equilibrium phases. The dual energy spectral CT imaging was performed with instantaneous (0.5 ms) switch of tube voltages 140 kVp and 80 kVp; pitch: 1.375. The scan range was from the diaphragmatic dome to the inferior boundary of the liver. The conventional TNC images were acquired first, and then iohexol (300 mg I/m1, GE Pharmaceutical, Shanghai of China) 80–100 ml was injected at 3.0–3.5 ml/s via a peripheral vein with a dual high-pressure syringe; at 25–30 s, 60 s and 120 s after injection, spectral imaging of the arterial, portal venous, and equilibrium phases was performed, respectively; and thereafter, the images were reconstructed with the standard algorithm and the slice thickness and slice interval of 5 mm.

Image postprocessing and evaluation

The image analysis and measurement were both performed on an AW4.5 workstation. VNC images in the arterial (VNCa), venous (VNCv), and equilibrium (VNCe) phase were obtained by the material decomposition process using water and iodine as a base material pair. Image quality of TNC, VNCa, VNCv, and VNCe images, contrast-to-noise ratio (CNR) of metastasis in relation to the liver parenchyma, and metastasis detection rate were evaluated and analyzed.

Image quality evaluation

The subjective evaluation on image quality of TNC and VNC images was performed by two radiologists (1 had 8 years of CT diagnostic experience [observer #1], and the other had 10 years of CT diagnostic experience [observer #2]). A 5-point scale was used on the basis of image noise, severity of artifacts (including linear high-density artifacts in renal pelvis), clarity of anatomic details for hepatic metastases, and its influence on diagnosis.[9,11] The specific scoring criteria were below: 5 (excellent) – The anatomic structures and details were highly visible and there were no significant noise and artifacts; 4 (good) – The anatomic structures and details were visible and there were some noise and artifacts; 3 (moderate) – Most anatomic structures were visible but the anatomic details were not clearly shown, and there were moderate but acceptable noise and artifacts; 2 (bad) – The anatomic structures were not clearly shown and the anatomic details were difficultly identified, and there were significant noise and artifacts; 1 (worst) – The anatomic structures were vague and the anatomic details were impossible to identify, and there were extremely high noise and artifacts. The images of ≥3 scores met the diagnostic requirements.

Contrast-to-noise ratio of metastasis-to-liver

All included hepatic metastases of each patient were selected as one region of interest (ROI). Three ROIs were placed on the normal liver parenchyma that has uniform density, few artifacts, and far away from great blood vessels. The ROIs for both the liver parenchyma and metastasis were at the same image-level to guarantee the consistent position, shape and size of ROIs in TNC and VNC images. The area of ROI was approximately 1.0 cm^2 [Figure 1] and was adjustable according to the metastasis size (not exceeding the metastasis size).

Contrast-to-noise ratio of metastasis-to-liver was calculated as following:[12,13]

$$CNR = \frac{|ROI_{metastasis} - ROI_{liver}|}{SD_{liver}}$$

For TNC images, $ROI_{metastasis}$ was the CT value of metastasis in ROI, ROI_{liver} was the mean CT value of liver averaged over the 3 ROIs, and SD_{liver} was the standard deviation of the mean CT value of liver; for VNC images, $ROI_{metastasis}$

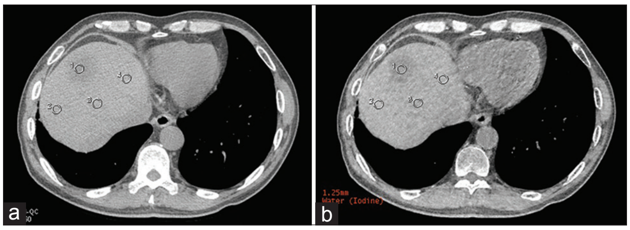

Figure 1: True noncontrast image (a) and virtual noncontrast arterial image; (b) one ROI was set at hepatic metastasis (arrow) when contrast-to-noise ratio was measured, and three consistent region of interests were set at normal liver.

was water density value of metastasis from the water-based material decomposition image, ROI_{liver} was mean water density value of liver parenchyma averaged over the 3 ROIs on the water-based material decomposition image, and SD_{liver} was standard deviation of the mean ROI_{liver} value.

Metastasis detection rate

Using the indication of metastases in tri-phasic images as a standard, the ability to identify metastasis in TNC, VNCa, VNCv, and VNCe images was evaluated by two observers with the 5-point scale (1: Normal, 2: Suspected normal, 3: Uncertain, 4: Suspected metastasis, 5: Metastasis). Metastases with 1–3 scores served as negative group, while metastases with 4–5 scores served as a positive group. In each group of images, the patients in both positive and negative groups were counted, and then the metastasis detection rate was calculated.

Statistical analysis

SPSS 17.0 (SPSS Inc., Chicago, IL, USA) statistical software was used for statistical analysis. Inter-observer agreement (the evaluation of image quality and the metastasis detection of four groups) was evaluated with Cohen's kappa test, and the interpretation of *K* value was as follows: <0.2 – Worse inter-observer agreement, 0.21–0.40 – Bad inter-observer agreement, 0.41–0.60 – acceptable inter-observer agreement, 0.61–0.80 – Good inter-observer agreement, and 0.81–1.00 – Excellent inter-observer agreement. If the inter-observer agreement was good, the scores made by the observer #2 were used for statistical analysis. ANOVA was used for comparisons of image quality score and CNR of metastasis-to-liver among four groups, and used Tukey–Kramer method as a *post-hoc* test to compare the results between any two groups. The Chi-square test for comparisons of metastasis detection rate among four groups. A difference with $P < 0.05$ was regarded to be statistically significant.

Results

Totally, 116 hepatic metastases from the 40 patients were included in the analysis, and the maximum tumor sizes were 6–70 mm; 22 metastases had the maximum size of <10 mm, 71 metastases had the maximum size of 10–30 mm, and 23 metastases had the maximum size of >30 mm.

Image quality evaluation

The image quality evaluation results of four groups by two observers and their comparison were shown in Tables 1 and 2, respectively.

The inter-observer agreement was good, $K > 0.600$.

No statistically significant difference in image quality was observed among TNC, VNCa and VNCv images ($P > 0.05$). The image quality of VNCe group was significantly worse than that of other three groups ($P < 0.05$). In VNCe images of all patients, linear high-density shadows were observed within renal pelvis and ureters.

Contrast-to-noise ratio of metastasis-to-liver

The mean CNR of metastasis-to-liver of four groups and their comparison results were shown in Table 3.

There was a statistically significant difference in CNR of metastasis-to-liver between VNCa images and TNC images ($P = 0.000$). There were no statistically significant differences in CNR of metastasis-to-liver among TNC, VNCv, and VNCe images ($P > 0.05$). The CNR of metastasis-to-liver in VNCa images was higher than that in TNC images.

Metastasis detection rate

Evaluation results of metastasis detection rate in four groups

Table 1: Image quality evaluation results of four groups by two observers and inter-observer agreement

Imaging mode	Observer number 1					Observer number 2					*K*
	1	2	3	4	5	1	2	3	4	5	
TNC	0	0	0	7	33	0	0	0	9	31	0.689
VNCa	0	0	0	8	32	0	0	0	11	29	0.658
VNCv	0	0	1	13	26	0	0	0	15	25	0.844
VNCe	0	0	15	25	0	0	0	14	26	0	0.838

TNC: True noncontrast; VNCa: Virtual noncontrast arterial; VNCv: Virtual noncontrast venous; VNCe: Virtual noncontrast equilibrium.

Table 2: Image quality evaluation results of four groups and their comparison

Imaging mode	TNC (A)	VNC			*P*					
		Arial phase (B)	Venous phase (C)	Equilibrium phase (D)	A versus B	A versus C	A versus D	B versus C	B versus D	C versus D
Score	4.78 ± 0.42	4.73 ± 0.45	4.63 ± 0.49	3.65 ± 0.48	0.630	0.149	0.000	0.335	0.000	0.000

VNC: Virtual noncontrast; TNC: True noncontrast.

Table 3: Mean CNR of metastasis-to-liver of four groups and their comparison results

Imaging mode	TNC (A)	VNC			*P*					
		Arial phase (B)	Venous phase (C)	Equilibrium phase (D)	A versus B	A versus C	A versus D	B versus C	B versus D	C versus D
CNR	1.86	2.42	1.92	1.94	0.000	0.692	0.604	0.001	0.002	0.902

VNC: Virtual noncontrast; TNC: True noncontrast; CNR: Contrast-to-noise ratio.

Table 4: Evaluation results of metastasis detection rate in four groups of images by two observers

Group	Observer number 1		Observer number 2		*K*
	Positive (*n*)	Negative (*n*)	Positive (*n*)	Negative (*n*)	
TNC	100	16	102	14	0.770
VNCa	107	9	103	13	0.700
VNCv	101	15	102	14	0.645
VNCe	96	20	98	18	0.811

TNC: True noncontrast; VNCa: Virtual noncontrast arterial; VNCv: Virtual noncontrast venous; VNCe: Virtual noncontrast equilibrium.

Table 5: Comparison of metastasis detection rate among four groups of images

Group	*n*	Appearance (*n*)		Detection rate (%)
		Negative group	Positive group	
TNC	116	102	14	87.93
VNCa	116	103	13	88.79
VNCv	116	102	14	87.93
VNCe	116	98	18	84.48
χ^2	1.146			
P	0.766			

TNC: True noncontrast; VNCa: Virtual noncontrast arterial; VNCv: Virtual noncontrast venous; VNCe: Virtual noncontrast equilibrium.

of images by two observers and their comparison were shown in Tables 4 and 5, respectively.

The inter-observer agreement was good, K > 0.600.

There were no statistically significant differences in metastasis detection rate among four groups ($P = 0.766$).

Discussion

Since X-ray absorption coefficient of any two substrates can determine that of one substance, the attenuation of one substance can be converted into the density of two substances with the same attenuation, which can realize substance separation and composition analysis.[14,15] In spectral CT, iodine agent is separated from the contrast-enhanced image through iodine-water substance separation to give water and iodine density image pairs. The water-based image is regarded as a VNC image. The water density of ROI is defined as water content per unit area and presented as a concentration in the unit of mg/ml,[16] and it can be measured in VNC images. The patients were exempted from one scan because TNC was not performed, thus effectively reducing the radiation dose.[17,18] Besides, the scan time was shortened, thus accelerating the throughput of patients.[19]

This study showed no differences in subjective score among spectral CT VNCa, VNCv, and TNC images, and clear visualization of anatomic details like hepatic hilar region. The visualization degree of hepatic metastases in CT images can be objectively evaluated with image noise and CNR.[20,21] A lower noise and a higher CNR of images corresponds to a higher identification capacity of hepatic metastases and better image quality. Our study results suggested that the CNR of metastasis-to-liver in spectral CT VNCa images was greater than that in TNC images, indicating spectral CT VNCa imaging is superior to TNC imaging in visualizing hepatic metastases to a certain extent. This may be because iodine is not removed completely during water-iodine separation of contrast-enhanced CT arterial phase images, and the resultant VNC images are similar to slightly contrast-enhanced images.[9] The use of adaptive statistical iterative reconstruction (ASIR) may effectively reduce image noise,[22,23] thus further increasing the CNR of VNC images, but the evaluation of ASIR in spectral CT is beyond the scope of this study and will be studied in the future.

In this study, the subjective evaluation of image quality and metastasis detection rate was performed by two observers at the same time, and then the inter-observer agreement was tested. The study findings proved that there was good inter-observer agreement. It indicated that the subjective evaluation of image quality and detection rate in this study was objective and feasible. There was no difference in metastasis detection rate between the tri-phasic VNC images and TNC images; in the tri-phasic VNC images, hepatic metastases with a small size were also displayed, achieving an effect similar to TNC images. In this study, the smallest hepatic metastasis detected was about 6 mm in diameter. It was found in this study that there were linear high-density artifacts within renal pelvis and ureters in VNCe images, which might be because a big proportion of contrast was excreted through renal pelvis in equilibrium phase and thus led to a high concentration of iodine in renal pelvis and ureters which exceeded the threshold of iodine to be removed during water-iodine separation, so that the high concentration of iodine in renal pelvis and ureters was incapable to be identified. These artifacts had no influence on the evaluation of metastasis detection rate, though they affected the subjective evaluation on the quality of VNCe images.

This study has its own limitations. First, the cases included in this study were all hepatic metastases of extrahepatic origin, and the liver cancer patients with hepatic metastases and the patients with hepatic metastases and concomitant hepatic hemangioma or cyst were excluded, thus it is necessary to conduct the subsequent study of VNC imaging in the diagnosis of hepatic metastases with other liver diseases. Second, the sample size used in this study is smaller relative to the hepatic metastasis group, and no comparison with other imaging examination results was performed. These will be further discussed and studied.

In a summary, there are no differences in image quality among TNC images and spectral CT VNCa and VNCv images; the metastasis detection rate of VNC images is similar to that of TNC images, and the visualization of hepatic metastases in VNCa images is clearer than that in TNC images. Therefore, VNCa imaging can exempt patients from TNC imaging in the detection of hepatic metastases.

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