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ORIGINAL ARTICLE

Clinical Value of Dual-energy CT in Detection of Pancreatic Adenocarcinoma: Investigation of the Best Pancreatic Tumor Contrast to Noise Ratio

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Key words: pancreatic adenocarcinoma; dual-energy; contrast to noise ratio; non-linear blending

Objective To quantitatively compare and determine the best pancreatic tumor contrast to noise ratio (CNR) in different dual-energy derived datasets.

Methods In this retrospective, single center study, 16 patients (9 male, 7 female, average age 59.4 ± 13.2 years) with pathologically diagnosed pancreatic cancer were enrolled. All patients received an abdominal scan using a dual source CT scanner 7 to 31 days before biopsy or surgery. After injection of iodine contrast agent, arterial and pancreatic parenchyma phase were scanned consequently, using a dual-energy scan mode (100 kVp/230 mAs and Sn 140 kVp/178 mAs) in the pancreatic parenchyma phase. A series of derived dual-energy datasets were evaluated including non-linear blending (non-linear blending width 0-500 HU; blending center -500 to 500 HU), mono-energetic (40-190 keV), 100 kVp and 140 kVp. On each datasets, mean CT values of the pancreatic parenchyma and tumor, as well as standard deviation CT values of subcutaneous fat and psoas muscle were measured. Regions of interest of cutaneous fat and major psoas muscle of 100 kVp and 140 kVp images were calculated. Best CNR of subcutaneous fat (CNR_F) and CNR of the major psoas muscle (CNR_M) of non-linear blending and mono-energetic datasets were calculated with the optimal mono-energetic keV setting and the optimal blending center/width setting for the best CNR. One Way ANOVA test was used for comparison of best CNR between different dual-energy derived datasets.

Results The best CNR_F (4.48 ± 1.29) was obtained from the non-linear blending datasets at blending center -16.6 ± 103.9 HU and blending width 12.3 ± 10.6 HU. The best CNR_F (3.28 ± 0.97) was obtained from the mono-energetic datasets at 73.3 ± 4.3 keV. CNR_F in the 100 kVp and 140 kVp were 3.02 ± 0.91 and 1.56 ± 0.56 respectively. Using fat as the noise background, all of these images series showed significant differences ($P < 0.01$) except best CNR_F of mono-energetic image sets vs. CNR_F of 100 kVp image ($P = 0.460$). Similar results were found using muscle as the noise background (mono-energetic image vs. 100 kVp image: $P = 0.246$; mono-energetic image vs. non-linear blending image: $P = 0.044$; others: $P < 0.01$).

Conclusion Compared with mono-energetic datasets and low kVp datasets, non-linear blending image at automatically chosen blending width/window provides better tumor to the pancreas CNR, which might be beneficial for better detection of pancreatic tumors.

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PANCREATIC cancer occurs in 11.7 per 100 000 people every year.¹ Globally around 240 000 people have died from pancreatic cancer every year making it the 8th most fatal malignant tumor type.² Early surgical therapy offers the only cure opportunity for pancreatic adenocarcinoma patients. To improve the outcome of clinical treatment, early diagnosis, accurate staging and evaluation for surgical resection has become the main objective of radiological diagnosis of pancreatic cancer. Computed tomography (CT) is now regarded as the main imaging technique for such clinical purpose. To the state of the art, using multi-detector CT can yield 76%-92% sensitivity.³⁻⁵ Imaging in the pancreatic phase, with 40-70 seconds delay after contrast media injection, can result in larger attenuation differences between pancreatic tumor and adjacent normal pancreatic parenchyma.^{6, 7} However, there are still up to 11% of pancreatic adenocarcinomas appearing isoattenuated and exhibiting less conspicuity than the surrounding pancreatic parenchyma, making them difficult to be detected.⁸

Recent studies have been performed using dual energy CT to evaluate the clinical merit of 80 kVp images for increased conspicuity of pancreatic tumors.⁹⁻¹¹ Images with 80 kVp (roughly equal to 56 keV) had a better contrast to noise ratio (CNR) than the routine 120 kVp images and the linear blended M0.3 images.

However, the improved iodine contrast from low tube potential has to be offset with the increasing image noise. Recently, Holmes *et al*¹² described a non-linear (moldal) image blending method for data acquired at two energies. Different to the linear blending method which applies the same mixing ratio across all the pixels, non-linear blending methods apply a mixing ratio calculated at each pixel by a specific formula using a Hounsfield unit (HU) value as a variable. In the non-linear blending method voxels with low attenuation values are preferentially obtained from the high tube voltage data set to minimize noise, whereas voxels with high attenuation values are extracted from the low tube voltage data to maximize contrast enhancement. Therefore, non-linear blending has the potential for better density differentiation while reducing image noise in the resulting image.

What's more, dual energy CT also provides a chance to generate a range of mono-energetic images at every effective voltage level from 40 to 190 keV which also covers the 80 kVp image outcome. It is good chance for us to find out whether 80 kVp (roughly equal to 56 keV) is the best choice for pancreatic tumor detection or not.

To the best of our knowledge, there are no reports on the image quality and the tumor-normal tissue contrast of

both non-linear blending images and mono-energetic images using dual-energy CT technique. Our study was carried out to quantitatively compare and determine the best pancreatic tumor CNR in different dual-energy derived datasets including non-linear blending images and mono-energetic images.

PATIENTS AND METHODS

Patients

From October 2010 to March 2011, 16 patients (9 male and 7 female, age range 38-79 years, with an average age of 59.4 ± 13.2 years) diagnosed with pathologically confirmed pancreatic adenocarcinoma in Peking Union Medical College Hospital were enrolled. Totally, 10 of the patients received final needle biopsy surgery and 6 received Whipple surgery. Final pathological results confirmed pancreatic adenocarcinoma for all 16 patients. Dual-energy CT scan was performed 7-31 days (average 12 days) prior to surgery.

Image acquisition

Patients were required to fast 6-8 hours prior to the CT scan, and 500 mL water as oral negative contrast agent was given for the gastrointestinal tract dilation 30 minutes before the CT examination. All CT scans were performed using a dual source CT scanner (Somatom Definition Flash, Siemens Healthcare, Forchheim, Germany). Scans were performed in the craniocaudal direction and supine position. Non-contrast phase, early arterial phase and pancreatic parenchyma phase were scanned consequently. The contrast enhanced scan was triggered by the bolus tracking technique, region of interest (ROI) was put inside the descending aorta at the level of 11th thoracic vertebrae, and threshold for starting the enhancement scan was 100 HU. Delay time was 4 seconds for arterial phase and 35 seconds for the pancreatic parenchyma phase respectively. The scanner was set to Dual-Energy mode for the pancreatic parenchyma phase scan, using 140 kVp/178 mAs (tube B) and 100 kVp/230 mAs (tube A). To further harden the 140 kVp spectrum and improve the spectral separation, a 0.4 mm tin filter was applied to tube B during the scan. Automatic tube current modulation (CARE Dose 4D technique from Siemens Healthcare) was used to compensate for the variable attenuation of different projections. System settings were collimation $0.6 \times 64 \times 2$ mm, rotation time 0.5 second, pitch 0.9, and field of view (FOV) 33 cm. The scanning direction was craniocaudal, and the scanning range was from the superior margin of the liver to the upper part of the iliac crest. And 90-100 mL non-ionic iodine contrast medium (iopromide injection, Ultravist pro-

duced by Bayer Schering, 300 mgI/mL or iohexol, Omnipaque produced by GE Amsham, 300 mgI/mL) was injected at 4.0 mL/s through the medial cubital vein with a high-pressure auto-injector. The 100 kVp and 140 kVp images were obtained directly after the scanning with slice thickness of 1.0 mm, reconstruction interval of 1.0 mm and kernel of S30f. Dual Energy images (Mixed factor 0.5) were obtained with slice thickness of 1.0 mm, reconstruction interval of 1.0 mm, and kernel of D30f.

Post processing

Non-linear blending dataset The 100/140 kVp dual energy data was post-processed with homemade software based on Matlab platform (Version 7, MathWorks, USA). Series of non-linear blending images were generated with blending center ranged from -500 to 500 HU and blending width from 0 to 500 HU. The value of blending center and blending width changed 1 HU every other image series.

Mono-energetic dataset The 100/140 kVp dual energy data was post-processed with homemade software based on Matlab platform (Version 7). Series of mono-energetic images were generated from 40 keV to 190 keV. The value of keV value changed 1 keV every other image series.

Image analysis and measurement

Two radiologists did the tumor definition and the measurements in consensus together. For one patient, 100 kVp, 140 kVp, non-linear blending and mono-energetic image series were input into homemade software based on the Matlab platform (Version 7).

The ROI of the normal pancreatic parenchyma (ROI_P) and pancreatic tumor (ROI_T) were drawn on the 100 kVp image with a minimum area of 60 mm² (averagely voxels) and 40 mm² (averagely voxels) respectively (Fig. 1). The ROI of both cutaneous fat (ROI_F) and major psoas muscle (ROI_M) were placed with a minimum area of 100 mm².

Those ROIs were automatically duplicated onto the 140 kVp, non-linear blending and mono-energetic image series at the same position. Mean CT attenuations of the pancreatic parenchyma and the tumor, as well as standard deviation (SD) value of cutaneous fat from anterior abdominal wall and the major psoas muscle, were measured in 3 different layers on each image series. The average mean CT attenuation and SD value of each collected data was calculated. Pancreatic tumor CNR was calculated as the followed formulas: $CNR_F = (ROI_P - ROI_T) / \sigma(ROI_F)$ and $CNR_M = (ROI_P - ROI_T) / \sigma(ROI_M)$, where ROI is the mean value and $\sigma(ROI)$ is the SD (Fat and muscle were taken as alternative noise level measurements.).

For the non-linear blending images and mono-energetic images of each patient, the best CNRs were automatically detected respectively, and the values of corresponded blending center/blending width and keV were recorded as well.

Statistical analysis

Statistical analysis was performed using SPSS 17.0, Paired One Way ANOVA *t*-test was used for comparison of the best CNR values in mono-energetic images, best CNR values in non-linear blending images, CNR values of 100 kVp images and CNR values of 140 kVp images respectively. A *P* value less than 0.05 was considered statistically significant.

RESULTS

The best CNR results were, in order best to worst: non-linear blending images, mono-energetic images, 100 kVp images and 140 kVp images with either fat noise or muscle noise background. When fat was used as the noise background, all of these images series showed significant differences ($P < 0.01$) except best CNR_F of mono-energetic image sets vs. CNR_F of 100 kVp image ($P = 0.460$). Similar

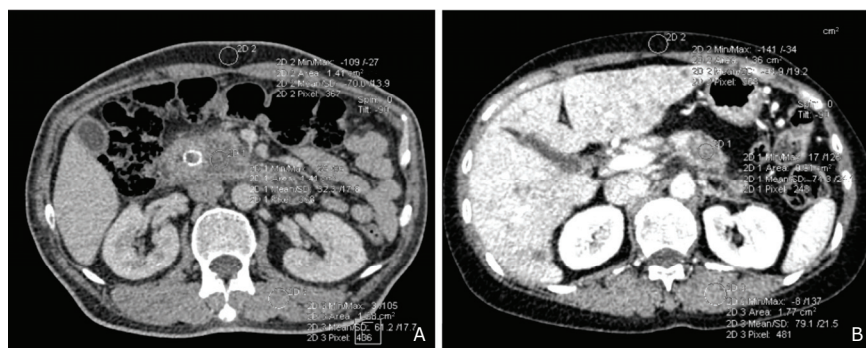


Figure 1. Axial image sets in two pancreatic adenocarcinomas.

The 140 kVp (A) and 100 kVp (B) images obtained from pancreatic parenchyma phase show freehand regions of interest (ROIs) manually drawn at pancreatic adenocarcinoma as well as circular ROIs on cutaneous fat from anterior abdominal wall and the major psoas muscle. The minimal, maximum, mean and standard deviation (SD) attenuation values of the selected ROI are automatically measured and exhibited.

results were found using muscle as the noise background (mono-energetic image vs. 100 kVp image: $P=0.246$; mono-energetic image vs. non-linear blending image: $P=0.044$; others: $P<0.01$).

Either using fat or muscle as the noise background, the best CNRs were found in 73-74 keV mono-energetic images, a paired t -test showed no significant difference between their CNRs ($t=-1.634$, $P=0.123$). While for non-linear blending images, blending center/width settings that yielded best CNRs depended on the choice of the noise background setting (Table 1). Figure 2 shows the mono-energetic curve of pancreatic parenchyma, pancreatic cancer and the best CNR curve of pancreatic tumor to parenchyma.

In the non-linear blending image, voxel CT values with

low density mainly derived from 140 kVp, while voxel CT values with high density mainly derived from 100 kVp. Fat and muscle were both low density tissue, and datasets of their SD value were mainly derived from 140 kVp, thus resulted in lower SD value. Interestingly, when fat was used as background noise, blending center showed great variance (-16.6 ± 103.9 HU), and high CNR value area distributed as a "V" shape (Fig. 3A). In different patient, best CNR can be achieved at either acme of the "V". However, when muscle was used as background noise, blending center showed great consistency, and high CNR value area distributed as a dot shape (Fig. 3B). So in different patient, best CNR can be achieved at almost the same blending center (122.5 ± 11.3 HU).

Table 1. Comparison of CNR values between images derived from dual energy scan[§] ($n=16$)

Group	CNR _F	Condition	CNR _M	Condition
Mono-energetic image	3.28 ± 0.97	73.3 ± 4.3 keV	2.73 ± 0.76	74.4 ± 2.80 keV
Non-linear blending image	4.48 ± 1.29	-16.6 ± 103.9 HU (center) 12.3 ± 10.6 HU (width)	3.25 ± 0.93	122.5 ± 11.3 HU (center) 1.6 ± 2.4 HU (width)
100 kVp image	3.02 ± 0.91	—	2.44 ± 0.65	—
140kVp image	1.56 ± 0.56	—	1.25 ± 0.43	—
P value	<0.001	—	<0.001	—

§: Plus-minus values are means $\pm$ SD.

CNR: contrast to noise ratio; CNR_F: CNR of cutaneous fat; CNR_M: CNR of major psoas muscle; —: none.

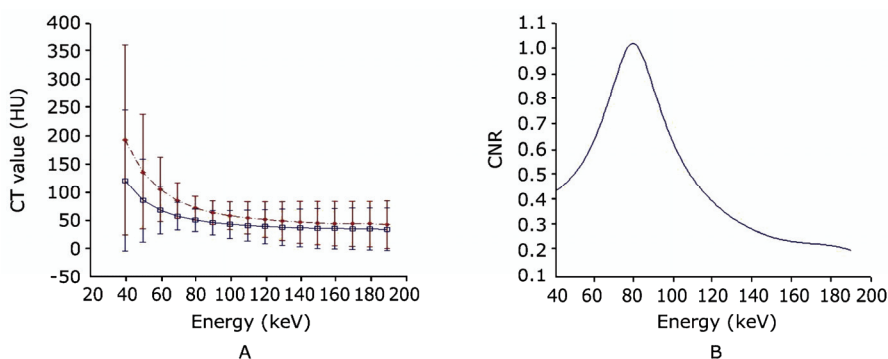


Figure 2. Mono-energetic curve (A) of pancreatic parenchyma (red curve) and pancreatic cancer (blue curve) and the best CNR curve (B) of pancreatic tumor to parenchyma. ($n=16$)

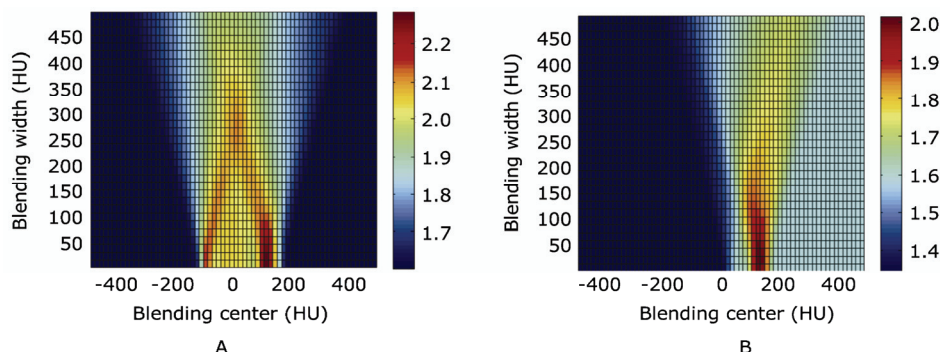


Figure 3. In non-linear blending images, CNR distribution map of optimal contrast image sets using fat as noise background (A); CNR distribution map of optimal contrast image sets using muscle as noise background (B). The red means larger CNR value and blue means lower CNR value. ($n=16$)

DISCUSSION

Our study results demonstrated that the non-linear blending dual-energy images yielded a significant improved image quality for pancreatic cancer in the pancreatic parenchyma phase.

Our findings have important clinical implications. Using dual energy scanning mode, different image sets and the individualized best CNR can be obtained. In the previous studies, 80 kVp was most applied in the clinical settings. It was found that 80 kVp could give the best CNR not only for pancreatic tumor but also for abdominal organ parenchyma. Yet, the mean photon energy is about 54 keV at 80 kVp, we have shown in the mono-energetic image datasets, it was not 54 keV mono-energetic image but 73-74 keV images yielded the best CNR. And according to our study, compared with the mono-energetic image of 73 keV, non-linear blending method can obtain better CNR. In the meantime, the image quality of mono-energetic images of 69 keV matches the mean energies of standard 120 kVp.

In our study, 100 kVp was used as the lower tube voltage instead of 80 kVp. First, we used tin filter for 140 kVp, as for Sn 140 kVp, which can further harden the 140 kVp voltage and yield higher energy as 92 keV (with tin filter) instead of 76 keV (without tin filter), so the energy difference between low and high energy are still large enough for dual energy analysis. Second, CT abdominal image quality with 80 kVp could be acceptable for smaller size patient, but for large size patient, tube current should be increased in order to gain reasonable image quality. Thus, 100 kVp with lower tube current (generally about 230 mAs) would yield similar dose as 80 kVp with higher tube current (generally 458 mAs).

Pancreatic parenchyma SD was planned to be used as background noise in our study design, but due to its density heterogeneity and individually various enhancement degrees, both fat and muscle were decided to be taken as the noise background. Although better CNR can be obtained using fat SD, muscle as a soft tissue could better represent pancreatic parenchyma or tumor situation. From our study, the best CNRs taking fat as noise background were better than muscle noise background in all the four post processing means.

In the non-linear blending image, the best CNR value curves with different blending center and blending width were quite dissimilar under different tissue as background noise. Although taking fat as noise background noise can achieve better CNR value, taking muscle as background noise got great consistency in blending center. It is still

under discussion about the influence of the 2 type curves of best CNR value.

Limitations of our study include the followings. First, we did not use 80 kVp voltage as the low voltage image. Although the image will be noisy, but better enhancement contrast and better CNR would be further beneficial. Also, with the use of iterative reconstruction in image space (IRIS) or sinogram-affirmed iterative reconstruction (SAFIRE) technique, 80 kVp images in the dual energy scan would be less noisy and more ready for optimum contrast assessment. Third, the enrolled patient cohort is still limited to a small number. Large sample will be done in the future and multi-center study.

In a summary, dual energy CT may allow individual image quality optimization which can be performed retrospectively and automatically with better identification of pancreatic parenchyma and the pancreatic tumor.

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