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FULL PAPER

Subtraction CT angiography in head and neck with low radiation and contrast dose dual-energy spectral CT using rapid kV-switching technique

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Objective: To investigate the application of low radiation and contrast dose spectral CT angiography using rapid kV-switching technique in the head and neck with subtraction method for bone removal.

Methods: This prospective study was approved by the local ethics committee. 64 cases for head and neck CT angiography were randomly divided into Groups A ($n = 32$) and B ($n = 32$). Group A underwent unenhanced CT with 100 kVp, 200 mA and contrast-enhanced CT with spectral CT mode with body mass index-dependent low dose protocols. Group B used conventional helical scanning with 120 kVp, auto mA for noise index of 12 HU (Hounsfield unit) for both the unenhanced and contrast-enhanced CT. Subtraction images were formed by subtracting the unenhanced images from enhanced images (with the 65 keV-enhanced spectral CT image in Group A). CT numbers and their standard deviations in aortic arch, carotid arteries, middle cerebral artery and air were measured in the subtraction images. The signal-to-noise ratio and contrast-to-noise ratio for the common and internal carotid arteries and middle cerebral artery were calculated. Image quality in terms of bone removal effect was evaluated by two experienced radiologists independently and blindly using a 4-point system. Radiation dose and total iodine load were

recorded. Measurements were statistically compared between the two groups.

Results: The two groups had same demographic results. There was no difference in the CT number, signal-to-noise and contrast-to-noise ratio values for carotid arteries and middle cerebral artery in the subtraction images between the two groups ($p > 0.05$). However, the bone removal effect score [median (min-max)] in Group A [4 (3-4)] was rated better than in Group B [3 (2-4)] ($p < 0.001$), with excellent agreement between the two observers ($\kappa > 0.80$). The radiation dose in Group A (average of 2.64 mSv) was 57% lower than the 6.18 mSv in Group B ($p < 0.001$). The total iodine intake in Group A was 13.5g, 36% lower than the 21g in Group B.

Conclusion: Spectral CT imaging with rapid kV-switching in the subtraction angiography in head and neck provides better bone removal with significantly reduced radiation and contrast dose compared with conventional subtraction method.

Advances in knowledge: This novel method provides better bone removal with significant radiation and contrast dose reduction compared with the conventional subtraction CT, and maybe used clinically to protect the thyroid gland and ocular lenses from unnecessary high radiation.

INTRODUCTION

CT examinations have increased dramatically over the past few decades due to the rapid advances in CT technology.^{1,2} CT angiography (CTA) of brain-supplying arteries is frequently used in clinical routine, such as in patients undergoing CT for ischemic stroke imaging. However, the complex osseous structures of the skull base and neck, as well as the proximity of blood vessels to the bones, significantly affect the

clarity and accuracy of displaying the blood vessels and their stenosis in the threshold-based method in conventional CT to separate blood vessels from bones. Subtraction CT angiography (sCTA) in the head and neck has therefore emerged recent years to improve the separation between blood vessels and bones and has shown good results.³⁻⁷ In a typical sCTA, iodine doses of 21-27g are commonly used to ensure sufficient opacity in the vessels and good image quality.⁶⁻⁸

With the increased application of head and neck CTA clinically, potential radiation damage has become more of a concern with the subtraction CTA since it is a two-scan approach. Another concern is the potential risk of nephropathy due to the use of contrast medium. Although necessary and the clinical risks are not conclusive, the consensus is that the use of high contrast dose may produce toxic effects. Recently, there has been a lot of effort to reduce the total iodine load to patients.^{9,10} How to reduce the radiation dose and contrast dose (iodine dose) at the same time to meet the requirements of clinical diagnosis has become an imaging focus. Dual-energy CT, with its ability to produce images at lower photon energies, has demonstrated the advantages of improving the contrast resolution of contrast agent.^{11,12} Therefore, the purpose of this study was to investigate the application of using low radiation dose, rapid kV-switching dual-energy spectral imaging mode in the sCTA in the head and neck for better bone removal and contrast dose reduction, using the conventional subtraction CT method as the reference of standard.

METHODS AND MATERIALS

General information

This prospective study was approved by the Ethics Committee of our hospital, and all patients signed the informed consent form. From March 2015 to June 2016, 68 patients with head and neck CTA examination for clinical indications were prospectively enrolled. Indications for CTA were the detection of aneurysms of the extra-and intracranial arteries ($n = 4$), evaluation of vascular infiltration of a head and neck cancer ($n = 2$), subordinately preoperative diagnostic ($n = 3$) and assessment of occlusive cerebrovascular disease ($n = 59$). The exclusion criteria included a

history of head and neck surgery, hyperthyroidism, asthma, heart failure, renal insufficiency (estimated glomerular filtration rate <30 ml min 1.73 m²) and iodine allergy. Four (5.9%) of the 68 patients were excluded for the following reasons: One patient had a history of head and neck surgery; three patients declined participation after reviewing the informed consent.

Finally, 64 cases were included in the study and were randomly divided into A and B groups (each group had 32 cases) using a simple, equal-probability randomization scheme. There were 31 males and 33 females, aged 45 to 76 years old. The patient's general data are shown in Table 1.

Methods

All scans were performed on a 64-slice Discovery CT 750 HD scanner equipped with rapid kV-switching dual-energy spectral imaging mode (GE Healthcare, Waukesha, WI). The scan range was from the aortic arch to the top of the head.

For patients in Group A, the unenhanced scan was performed using the conventional single tube voltage (kVp) scan mode and contrast-enhanced scan was performed using the rapid kV-switching dual-energy spectral imaging mode. The conventional scan parameters were large body bowtie, 100 kVp tube voltage, 200 mA tube current, 0.5 s gantry rotation speed, 0.984:1 helical pitch, and 0.625 mm scan slice thickness; the contrast-enhanced scan was performed with the dual-energy spectral CT imaging mode using the instantaneous tube voltage switching between 80 kVp and 140 kVp for any detection view during gantry rotation. Patient body mass index (BMI)-dependent gemstone

Table 1. Patient demographics

	Group A	Group B	Statistic value	<i>p</i> value
Patient number	32	32		
Sex (M/F)	17/15	14/18	0.56 ^c	0.45
Age (years) ^a	58.94 ± 8.40	59.13 ± 8.44	0.09 ^d	0.93
Weight (kg) ^a	62.69 ± 8.89	62.25 ± 7.61	0.21 ^d	0.83
BMI (kg m ⁻²) ^b	22.45 (19.38–28.96)	22.99 (19.63–28.98)	0.87 ^e	0.39

BMI, Body mass index, calculated as weight height⁻².

^aValues are mean ± standard deviation.

^bValues are median (min-max).

^c χ^2 value.

^d*t* value.

^e*z* value.

Table 2. Quantitative and qualitative image quality and radiation dose comparison between two groups

Parameter	Group A median (min-max)	Group B median (min-max)	<i>z</i> value	<i>p</i> value
Subjective score	4 (3–4)	4 (3–4)	–0.76	0.45
Bone removal effect score	4 (3–4)	3 (2–4)	–4.17	<0.001
CT number difference in cortical bone (HU)	–5.41 (–97.17–18.57)	6.30 (–37.72–46.16)	–2.22	0.03
DLP (mGy*cm)	608.13 (602.88–900.68)	1417.28 (1301.40–1809.52)	–6.88	<0.001
Radiation dose (mSv)	2.53 (2.51–3.75)	5.90 (5.41–7.53)	–6.88	<0.001

DLP, dose length product.

spectral imaging (GSI) protocols were used: GSI-51 for BMI of 28 kg m^{-2} or less, GSI-1 for BMI $\geq 28 \text{ kg m}^{-2}$. The helical pitch, scan slice thickness, and gantry rotation speed were the same as the unenhanced scan. A total of 50 ml contrast agent with iodine concentration of 270 mgI ml^{-1} (Visipaque 270 mgI ml^{-1} , GE Healthcare, WI) was injected via antecubital venous access at flow rate of 4.5 ml s^{-1} with double cylinder power injector. The contrast injection was followed by 40 ml of saline solution at the same injection speed.

Patients in Group B underwent CT scans using the conventional scan method for both the unenhanced scan and contrast-enhanced scan. The scan parameters were 120 kVp tube voltage, automatic tube current modulation (100–600 mA) to achieve a noise index of 12 HU, 0.5 s gantry rotation speed, 0.984:1 helical pitch, and 0.625 mm scan slice thickness. A total of 60 ml contrast agent with iodine concentration of 350 mgI ml^{-1} (Omnipaque, 350 mgI ml^{-1} , GE Healthcare, WI), was injected at a flow rate of 5.0 ml s^{-1} followed by 40 ml of saline solution at the same injection speed.

The contrast-enhanced scans in both groups were triggered using the bolus tracking technique with a region of interest (ROI) placed in the aorta at the aortic arch level as a monitor position and a threshold of 100 HU (Hounsfield unit) for triggering the contrast-enhanced scan.

Data processing and evaluation

Image reconstruction

Images were reconstructed at 0.625 mm slice thickness using the adaptive statistical iterative reconstruction (ASiR) algorithm. The strength of ASiR was 60% in Group A and the standard 40% in Group B. For the contrast-enhanced spectral CT images in the arterial phase in Group A, the energy level of 65 keV was selected and reconstructed. All images were transferred into an advantage workstation (AW4.6; GE Healthcare, Milwaukee, WI) to perform subtraction post-processing: Subtraction images = Images (AP)–Images (non-enhanced). The subtraction images were then analyzed using a 3D software on the AW.

Subjective image quality assessment

The subjective assessment including image quality as well as bone removal effect was performed by two experienced radiologists (HFD and XRZ, with 10 and 5 years of experience in head and neck CT, respectively) independently. All the readers were blinded to the scan method. In terms of image quality, a 4-point system was used. The image quality criteria were: (1) clear image and no obvious artifacts; (2) uniform vascular enhancement; (3) 350–550 HU CT number enhancement in the blood vessels and (4) displaying more than four vascular branches. Add one point for every criterion that was met.

The bone removal effect was also evaluated by using 4-point scoring system: (4) no residual bones, clear vascular walls and distal branches; (3) small amount of residual bones, clear vascular structures with slightly blurred edges, visible distal branches; (2) visible residual bones, sparse distal branches with parts missing and (1) a large amount of residual bones, remote branches not visible, not diagnostic.

Figure 1. Enhanced (a) and plain (b) CT images with dual-energy spectral CT (at 65 keV) and 100 kVp imaging, respectively from a same patient. ROI1 and ROI2 were both 3 mm^2 , and CT values were 344.10 and 372.33 HU for ROI1 and ROI2, respectively. HU, Hounsfield unit; ROI, region of interest.

Objective image quality

One radiologist measured the CT number of the cortical bone in the nonenhanced and contrast-enhanced images in the two groups and calculated the CT number difference: $\text{CT (cortical bone)} = \text{CT}_{\text{cortical bone (enhanced)}} - \text{CT}_{\text{cortical bone (unenhanced)}}$. The ROI for measuring the CT numbers in the cortical bones was about 3 mm^2 and was placed in the same location in both the unenhanced and contrast-enhanced images (Figure 1). The CT numbers and their standard deviations (SDs) in the aortic arch, bilateral common carotid artery, bilateral internal carotid artery, bilateral middle cerebral artery and air in the subtraction images were measured. The size of the ROI was about 100 mm^2 covering for two-thirds of the vascular cross-sectional area (Figure 2). The signal-to-noise

Figure 2. Subtraction CT angiography image. ROI1 and ROI2 were placed in the center of the bilateral common carotid artery to measure CT value and SD; ROI3 and ROI4 were placed around the neck and air to measure the CT value and SD. CT number and SD values were: 339.59 and 6.38 HU, 341.88 and 9.16 HU, 9.73 and 6.44 HU and 6.31 and 6.48 in ROI1, ROI2, ROI3 and ROI4, respectively. HU, Hounsfield unit; ROI, region of interest; SD, standard deviation.

ratio (SNR), contrast-to-noise ratio (CNR) and the average image noise for the arteries in the neck were calculated: SNR (target vessel) = CT (target vessel) / SD (target vessel); CNR (target vessel) = [CT (target vessel) – CT (air)]/SD (air); mean noise (neck) = [SD (common carotid) + SD (internal carotid artery)]/2.

Radiation and contrast dose

The volumetric CT dose index (CTDIvol) and dose-length-product (DLP) for the two groups were recorded to calculate the effective radiation dose (ED): $ED = DLP \times K$, where K is the conversion factor. Since the scan covered head and neck and we estimated the scan coverage was about 40 and 60% in the head and neck, respectively, we adjusted the effective dose calculation to $ED = DLP \times 0.40 \times K_1 + DLP \times 0.60 \times K_2$ where K_1 (for head) was 0.0023 and K_2 (for neck) was 0.0054, according to the European quality standard.¹³ The total contrast volumes in the two group were also recorded and the total iodine load was calculated using the formula: total iodine load (g) = total contrast volume (ml) $\times$ concentration of contrast agent (mgI ml⁻¹)/1000.

Statistical analysis

All statistical analyses were performed using SPSS v. 17.0 software (IBM Corp., New York, NY). In all tests, $p < 0.05$ was considered statistically significant. Measurement data conformed normal distribution were expressed as mean $\pm$ SD; Data conformed skewed distribution were expressed as median (min-max). As we found in experiments, internal carotid artery CT value, carotid artery CNR, internal carotid artery SNR, middle cerebral artery CNR, middle cerebral artery SNR, carotid artery SNR, the mean noise, age and weight conformed normal distribution; therefore, they were compared using the independent samples t test. Aortic CT value, carotid artery CT value, middle cerebral artery CT value, internal carotid artery SNR, subjective score, bone removal effect score, CT number difference in cortical bone, DLP, radiation dose and BMI conformed skewed distribution and they were subjective to Mann-Whitney U test. The patient sex in two groups was compared using the χ^2 test.

The interobserver variability for the subjective scores were estimated using Cohen's κ test. A κ value of less than 0.20 was considered to indicate slight agreement; 0.21–0.40, fair agreement; 0.41–0.60, moderate agreement; 0.61–0.80, substantial agreement and 0.81 or greater, excellent agreement.

RESULTS

The general information for patients in Groups A and B are listed in Table 1 and there was no statistically significant difference between them (all $p > 0.05$).

Objective image quality

Mean attenuations in the aortic, carotid artery, internal carotid artery, middle cerebral artery were 325.1, 359.1, 354.42, 322.94 HU in Group A vs 331.18, 365.58, 359.13, 324.76 HU in Group B. The SNR values of the carotid artery, internal carotid artery, middle cerebral artery were 39.52, 34.70, 48.11 in group A vs 41.07, 33.04, 44.96 in Group B. The CNR values of the carotid artery, internal carotid artery, middle cerebral artery were 52.29,

51.49, 46.81 in group A vs 49.55, 48.65, 43.78 in Group B. The mean noise in Group A and Group B were 9.95 and 10.05, respectively. There was no difference for the CT number, CNR, SNR and image noise between the two groups (all $p > 0.05$) (Figure 3). The CT number difference between the contrast-enhanced scan and unenhanced scan for the cortical bones was more significantly in Group A than that in Group B (Table 2).

Subjective image analysis

There was an excellent agreement between the two radiologists for image quality evaluation ($\kappa > 0.80$). The results obtained from Reader 1 (with 10 years of experience in head and neck CT) were used as the final results. There was no significant difference in the overall image quality subjective score between Group A and group B (3.66 vs 3.56, $p = 0.45$, Table 2). However, Group A with dual-energy spectral CT imaging mode was better in terms of removing bones in the subtraction images (median score of 3.72 in Group A vs 3.06 in Group B, $p < 0.001$, Figure 4 and Table 2).

Radiation and contrast dose

The DLP was significantly lower in Group A ($p < 0.001$, Table 2). The radiation dose in Group A was 2.64 mSv, 57% lower than 6.18 mSv in Group B ($p < 0.001$) (Table 2). The total iodine load in Group A was only 13.5g, 36% lower than 21 g in the conventional Group B.

DISCUSSION

In this study, we investigated the application of using low radiation dose, rapid kV-switching dual-energy spectral imaging mode in the sCTA in the head and neck for better bone removal and contrast dose reduction. We have demonstrated that spectral CT imaging in the subtraction angiography in head and neck provided better bone removal with significantly reduced radiation and contrast dose compared with the conventional subtraction method.

As a noninvasive vascular imaging technology, the head and neck CTA has gained popularity and its applications are generally recognized.^{14,15} But its negative effects brought by the procedure also draws more attention. First is the radiation. Head and neck subtraction CTA has long scan range, and requires two-phase scanning. The scanning range also contains areas sensitive to X-ray such as the lens and thyroid gland organ. Higher radiation doses will cause potential radiation damage to these organs. With the focus on radiological protection, how to reduce the radiation dose has become the focus of the imaging industry and the imaging professionals. Next is the high concentration of contrast agent. Conventional head and neck CTA with subtraction angiography examination often uses non-ionic contrast agent at iodine concentrations of 320 mgI ml⁻¹ 370 mgI ml⁻¹. Due to the different chemical molecules and special chemical compositions of these non-ionic and high concentration contrast agents, they are more prone to cause bad reactions by a person, including contrast induced nephropathy (CIN), systemic allergic reaction, such as vascular extravasation.^{16–18} The happening of the CIN is mainly due to contrast in the kidneys, a large amount of high concentration of contrast medium with renal toxicity, which leads to kidney

Figure 3. CT number, SNR, CNR, subjective score, SD comparison between two groups. CNR, contrast-to-noise ratio; SD, standard deviation; SNR, signal-to-noise ratio.

sudden attenuation, concentrate the metabolites in the blood, and cause the acute renal failure. The greater the concentration and dose of contrast medium, the greater the probability of occurrence of CIN. Therefore, on the premise of meeting the requirements of clinical diagnosis, we should reduce the contrast medium dose as far as possible. According to a 2006 international CIN expert consensus, reducing the dosage of contrast agent (dose, concentration) is one of the main measures for the prevention of CIN.¹⁹ However, with conventional CT scan technique, decreasing the contrast medium may cause a decline of contrast enhancement in blood vessels, leading to image quality degradation, and even affect the clinical diagnosis at the same time.^{20,21} The introduction of dual-energy spectral CT further broadens the scope of CT imaging in clinical applications. The inclusion of virtual monochromatic images of various photon energies, especially the lower photon energies greatly improves the enhancement effect of contrast medium, thus enables the application of low dose and low concentration contrast medium imaging.²²⁻²⁵

In our study, the radiation dose in Group A was 57% lower than that in Group B. It can be recommended for CTA in clinical routine to protect the thyroid gland and ocular lenses from unnecessary high radiation. We selected spectral CT images at 65 keV for the contrast-enhanced CT scans. Our results indicated that with the use of images at lower energy we could still maintain similar attenuation values in the vessels to the conventional

120 kVp scan (with an average energy of about 70 keV) even with the reduced iodine concentration to reduce the total contrast dose by 36% to the patients.

Dual-energy spectral CT using a single X-ray tube with instantaneous voltage switching (0.5 ms) between low and high voltages (80 kVp and 140 kVp) within a scan to generate 101 sets of virtual monochromatic images in the energy ranges of 40–140 keV. Different levels of keV images have different characteristics. Low energy level X-rays have weaker penetration and relatively higher image noise, but produce higher contrast and attenuation in matter; High energy level X-rays have stronger penetrating power and lower image noise, but lower contrast resolution. One of the advantages of dual-energy spectral CT imaging is that one can change the selection of images real time to balance contrast and noise to find the optimal energy level for achieving the best contrast-to-noise ratio for the object of interest. In this study, we selected images at 65 keV to balance image noise and contrast resolution based on previous studies.^{12,26,27} Another reason that the 65 keV was chosen was because at 65 keV, the CT value for bones was similar or slightly lower than that in the non-contrast scan acquired at 100 kVp, resulting in close-to-zero or slightly negative subtraction image for bones. The negative values can be easily truncated using threshold to create cleaner subtraction images for bones.

Figure 4. (a and b): VR and subtraction angiography images with a low dose spectral CT imaging protocol in CTA, respectively, while (c and d) were with the conventional 120 kVp imaging protocol. Image (b) demonstrates less residual bones around the internal carotid artery (white arrow); while more bones are showing (black arrow) around internal carotid artery (white arrow) in figure (d). CTA, CT angiography; VR, volume rendering.

Iterative reconstruction algorithms such as the ASiR technology achieves high quality images through the establishment of model for noise properties of the scanned object, in the original data space model arithmetic, calculation and using the iterative

method to restrain noise.^{22,28} That is, by using ASiR algorithm under the same conditions, we can get a better image quality, or under the condition of the same image quality, scanning dose can be decreased.²⁰ The ability of noise reduction increases as ASiR weight increases. On the basis of the recommendations of the manufacturer, previous study,²⁹ and our practical experience, the ASiR percentage was set at 60 for Group A and 40 for Group B.

In this study, we attempted to reduce radiation dose in two ways: in the unenhanced scan, a lower tube voltage (100 kVp) was used together with a fixed low tube current at 200 mAs; and in the contrast-enhanced scan, BMI-dependent low dose spectral CT imaging protocols were used to reduce the overall radiation dose. A 57% radiation dose reduction was achieved in the study group compared with the conventional subtraction method. Image noise with the lower dose scans were controlled by using a slightly higher strength ASiR. Our study results indicated that by combining the use of low tube voltage and low energy spectral CT images and iterative reconstructions, we could reduce both contrast dose and radiation dose while creating cleaner subtraction images to better separate vessels from bones in head and neck CT imaging.

This study also has some limitations. First, the sample size was still small. Even though we used BMI-dependent dual-energy spectral CT scan protocols, and for patients with BMI >28 kg m⁻², higher radiation dose was used to ensure image quality, most patients in our study population had BMI values less than 28 kg m⁻². More patients with BMI >28 kg m⁻² is needed in the future to more accurately reflect the dose reduction; Second, we selected the photon energy level of 65 keV based on the previous literatures and personal experience in this study. The optimal photon energy maybe patient-dependent, and whether 65 keV is the optimal energy level needs further verification.

In conclusion, low dose dual-energy spectral CT imaging using rapid kV-switching technique in the subtraction CT angiography in head and neck provides better bone removal with significantly reduced radiation and contrast dose compared with conventional subtraction CT method.

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