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Variation of degree of stenosis quantification using different energy level with dual energy CT scanner

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Abstract

Purpose To investigate the variation in the quantification of the carotid degree of stenosis (DoS) with a dual energy computed tomography (CT), using different energy levels during the image reconstruction.

Methods In this retrospective study, 53 subjects (37 males; mean age 67 ± 11 years; age range 47–83 years) studied with a multi-energy CT scanner were included. Datasets were reconstructed on a dedicated workstation and from the CT raw data multiple datasets were generated at the following monochromatic energy levels: 66, 70, 77, and 86 kilo-electronvolt (keV). Two radiologists independently performed all measurements for quantification of the degree of stenosis. Wilcoxon test was used to test the differences between the Hounsifield unit (HU) values in the plaques at different keV.

Results The Wilcoxon analysis showed a statistically significant difference ($p = 0.001$) in the DoS assessment among the different keVs selected. The Bland-Altman analysis showed that the DoS difference had a linear relation with the keV difference (the bigger is the difference in keV, the bigger is the variation in DoS) and that for different keVs, the difference in DoS is reduced with its increase.

Conclusion A standardization in the use of the energy level during the image reconstruction should be considered.

Keywords CT · Dual energy CT · Carotid artery

Introduction

The quantification of the degree of stenosis (DoS) of carotid artery is considered up to now the leading parameter for the choice of the therapeutic option in symptomatic subject [1]. Currently, the North American Symptomatic Carotid Endarterectomy Trial (NASCET) method, originally used in the angiographic analysis of the carotid arteries, is the reference modality for the quantification of DoS in the CT exams [2, 3].

With the introduction of dual energy CT (DECT) scanners, it is possible to generate multiple datasets with different level of kilo-electronvolt (keV) [4]. The advantage of this technology is the possibility to observe the variation of attenuations in terms of Hounsfield units (HU) of a tissue according to the level of energy selected increasing the number of information [5–9].

In particular, iodinated contrast material shows a great variation depending on the energy level; in fact, as the keV gets closer to the k-shell binding energy of the atom of iodine, there is an increase of photoelectric effect with consequent higher HU [10]. In the study of carotid arteries, the exams are performed with an arterial phase with a high iodine concentration in the arterial vessel; therefore, this target is significantly reactive to the keV selected [11]. The attenuation of the opacified blood according to the variation of the keV could determine variation in perception and measurements of the vessels size with subsequent variation in the DoS.

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Therefore, the purpose of this study is to assess if variation of keV with DECT scanner significantly affects the DoS.

Material and methods

Study design and patient population

This is a retrospective study. The institutional review board approval for this study was obtained and patients' consent was waived. All the DECT of carotid arteries performed from March 2014 to June 2015 were included for a total of 53 subjects (37 males; mean age 67 ± 11 years; age range 47–83 years). CT of carotid arteries is performed in case of pathological findings in US exams or for subjects with occurrence of acute cerebrovascular events.

CT technique

All patients were studied with a multi-energy CT scanner (Discovery HD 750, Gemstone Spectral Imaging, GE Healthcare, Milwaukee, Wis USA). Angiographic phase imaging was performed by injecting 60 mL of contrast medium (Ultravist 370; Bayer Schering Pharma AG, Berlin, Germany) through an antecubital vein using a power injector at a flow rate of 5 mL/s and an 18-gauge intravenous catheter. A smart prep technique was used to calculate the correct timing of the CT acquisition, and each patient received a 15-mL timing bolus of contrast medium to synchronize the data acquisition with the arrival of contrast material in the carotid arteries. The angiographic acquisition was performed breath-hold in caudo-cranial direction and included the carotid siphon. The convolution kernel used was intermediate.

Image reconstruction and plaque analysis

Images were reconstructed on a dedicated workstation (Advantage Windows Workstation version 4.4, GE Healthcare) and from the CT raw data multiple datasets were generated at the following monochromatic energy levels: 66, 70, 77, and 86 keV (Fig. 1). Two radiologists (blinded for peer review) independently performed all measurements for quantification of the degree of stenosis and the analysis was performed according to the NASCET technique. Because of the measurement of the degree of stenosis is affected by the window-level and window-width settings, a fixed parameter was used according to Saba et al [2] (window width at 850 HU, level of 300 HU).

Statistical analysis

Statistical analysis was performed with the SPSS 13.0 statistical package (SPSS Inc., Chicago, IL). The normality of each continuous variable group was tested using the Kolmogorov-Smirnov *Z* test. Continuous data were described as the mean value ± SD or as median [Q_1−Q_3] if not normally distributed. Wilcoxon test was used to test the differences between the HU values in the plaques at different keV; it was also used to check whether a statistically significant difference was present in degree of stenosis according the selected keV. Concordance among the different keV as well as the inter-reader variability was assessed with the Bland-Altman analysis. Graphics were plotted with MedCalc 15.0 software (MedCalc, Mariakerke, Belgium). A p value < 0.05 was considered significant and all values were calculated using a two-tailed significance level.

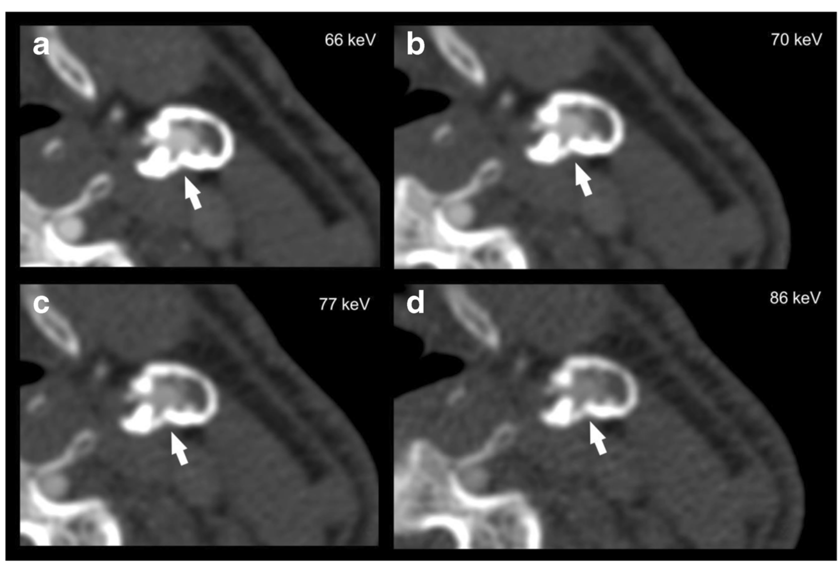

Fig. 1 Example of plaque at different keV energy levels. In case the left ICA plaque of a 75-year-old subject is visualized at different energy levels: panel **a** shows 66 keV; panel **b** shows 70 keV; panel **c** shows 77 keV; panel **d** shows 86 keV

Table 1 Patients characteristics

Patient (n)	56
Age (years)	67 ± 11
Sex (male)	37 (86%)
Smoker (never)	19 (34%)
Smoker (ex)	9 (16%)
Smoker (current)	2 (4%)
Hypertension	28 (50%)
CAD	23 (46%)
Diabetes	9 (16%)
Dyslipidemia	24 (42%)
Statins and other drugs*	29 (52%)

Results

General results

Patient characteristics are summarized in the Table 1. Of the 53 patients, 36 were referred to radiology to perform CT in case of pathological findings in US exams and 17 were referred due to the occurrence of acute cerebrovascular events. None of the patients were excluded from this study for sub-optimal image quality; therefore, a total of 106 carotid arteries were analyzed. An overall view of the results is given in Table 2. The Wilcoxon analysis showed a statistically significant difference in the DoS assessment among the different keVs selected (Table 3). The Bland-Altman for the different keV analyses showed two findings: the DoS difference had a linear relation with the keV difference (the bigger is the difference in keV, the bigger is the variation in DoS). The second finding was that for different keVs, the difference in DoS is reduced with its increase: therefore, for mild grades of stenosis there was a maximum variability whereas for severe grades of stenosis the variation due to the difference in keV was minimal (Fig. 2). We also tested the inter-observer agreement at the different energy level using and the Bland-Altman plots (Fig. 3) and it observed an optimal agreement between the two readers.

Discussion

Currently, the quantification of the degree of stenosis is considered a key parameter for the choice of the therapeutic option and one of the most frequently used techniques to quantify DoS of carotid artery is the CT [1].

With the introduction of DECT scanner, it is possible to reconstruct the acquired dataset with different mono-energetic keV level. Nowadays, different dual energy CT technologies are currently available but all these approaches offer the potentiality to have monochromatic images. This approach allows the visualization of the images with different tissue attenuation values according to the specific diagnostic requirement.

DECT implies the acquisition of two datasets utilizing two different X-ray energy spectra [5, 10] with the potential to characterize different materials on the basis of their elemental compositions (atomic number) [10]. DECT material decomposition is based on the photoelectric effect that is highly dependent on the atomic number of the absorber and to the binding energy of the innermost electron shell (the k-shell). The probability of photoelectric absorption increases substantially as the energy of the incident photon approaches the K-shell binding energy, the "K-edge." Therefore, the simultaneous CT acquisition of two X-ray spectra at different peak tube voltages allows for the detection of specific attenuation characteristics based on differing energy levels for material with high atomic number such as iodine ($Z = 53$) [6, 7].

In the previous years, some papers have been published covering the application of DECT in definition of carotid artery pathology [6, 7, 12, 13], in particular exploring the variation of the HU attenuation [8, 14], or the change in size of the plaques [7] according to the variation of the energy level used but, to the best of our knowledge this is the first research study covering the relationship between the use of the different keV levels and the degree of stenosis.

Because of different iodine attenuation values depending on the keV selected, we aimed to assess if variation of keVs used during the reconstruction process significantly affects the carotid DoS quantification. Recently published studies [15–18] demonstrated that in the supra-aortic carotid artery, the image quality is better using low keV. In particular, Leithner et al [17] found that the use of protocols with very low keV (40 keV) showed similar and, in some cases, better image quality when compared with protocols with higher values. However, the effect of variation of keV to DoS remains to be disclosed.

Table 2 Overall view of the findings (in percentage)

	Mean	95% CI	Median	Minimum	Maximum	2.5–97.5 P	2.5–97.5 P
NASCET 66 keV	37,811	32.508–43.115	43	−46	93	−24.550–89.000	0,0243
NASCET 70 keV	43,047	37.690–48.404	49	−42	93	−22.250–91.700	0,0025
NASCET 77 keV	48,528	43.075–53.982	53	−41	94	−20.950–93.850	0,0002
NASCET 86 keV	53,632	48.107–59.157	60	−37	95	−19.650–95.000	< 0.0001

Table 3 Wilcoxon analysis

	66 keV vs 70 keV	66 keV vs 77 keV	66 keV vs 86 keV	70 keV vs 77 keV	70 keV vs 86 keV	77 keV vs 86 keV
Number of positive differences	104	106	106	106	106	103
Number of negative differences	0	0	0	0	0	0
Large sample test statistic Z	−8,852,864	−8,937,183	−8,937,183	−8,937,183	−8,937,183	−8,810,402
Two-tailed probability	$P < 0.0001$	$P < 0.0001$	$P < 0.0001$	$P < 0.0001$	$P < 0.0001$	$P < 0.0001$

In our study, Wilcoxon analysis showed significant differences in the DoS quantification among the different keVs selected (Table 1). This finding suggests that the different attenuations, due the keV, significantly affect the DoS values.

Moreover, it is important to remember that two of the most recurrent artifacts linked to CT arterial vessel analysis are the edge blur and the halo artifact [19, 20]. The edge blur artifact consists in the presence of a blurred edge at the level of the outer luminal margin of the vessel. The halo artifact refers to peri-luminal increased attenuation; both these artifacts are assessed on a scale as a percentage relative to the luminal diameter. These two conditions are affected by the entity of attenuation of the opacified blood in the vessel lumen and may be the cause differences in the carotid DoS quantified through different keV levels.

However, the effect due to the different attenuation values dependent on the keV selected and the consequent different entity edge blur and the halo artifacts could in part explain the variation in the DoS. The second effect could be due to the tissue composition of the plaque. In this study, we did not analyze the impact of the different types of plaque (calcified, mixed, fatty) to the DoS variation because this type of analysis would require significant bigger cohort size due to the need to compare three different groups. However, it is important to underline that the

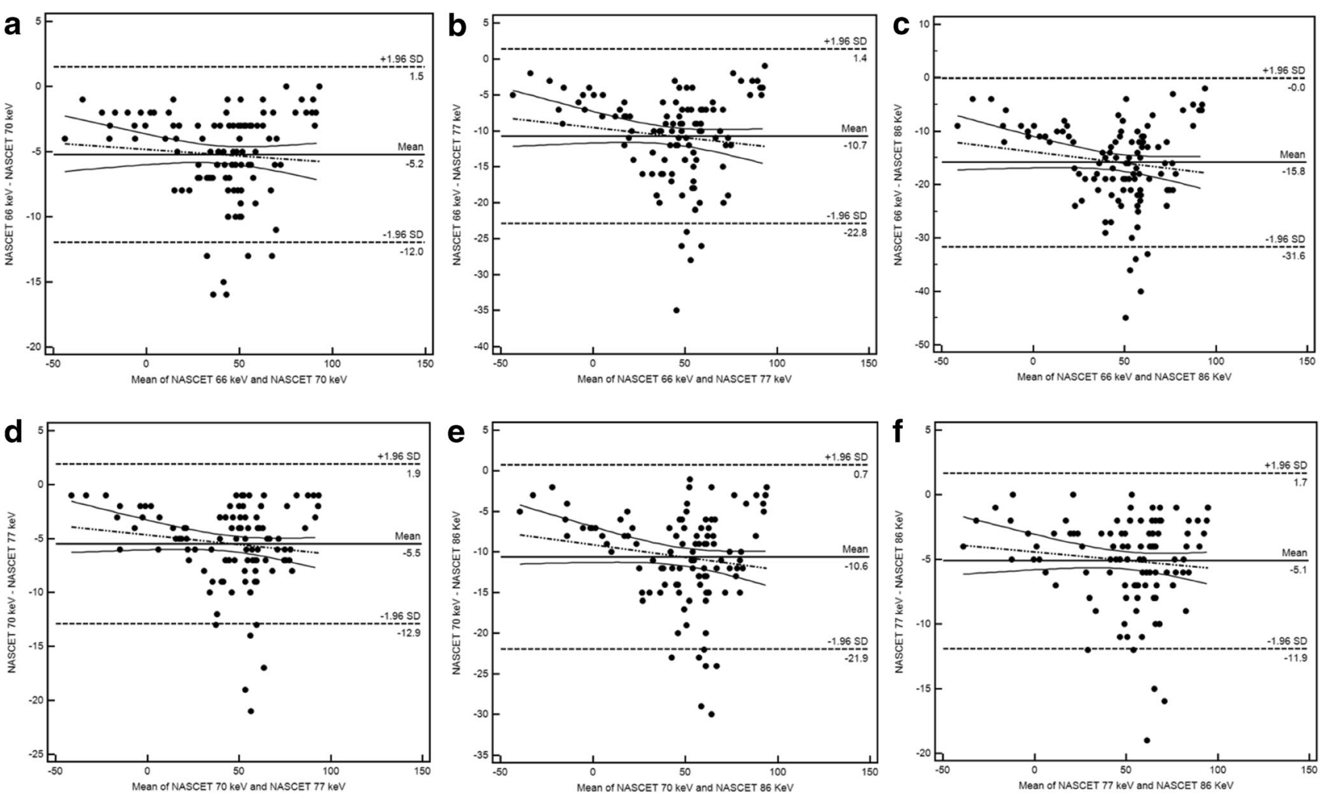

Fig. 2 Bland-Altman plots analysis of the DoS according to the keV difference. Panel **a** shows the DoS difference between 66 and 70 keV. Panel **b** shows the DoS difference between 66 and 77 keV. Panel **c** shows the DoS difference between 66 and 86 keV. Panel **d** shows the DoS difference between 70 and 77 keV. Panel **e** shows the DoS difference between 70 and 86 keV. Panel **f** shows the DoS difference between 77 and 86 keV

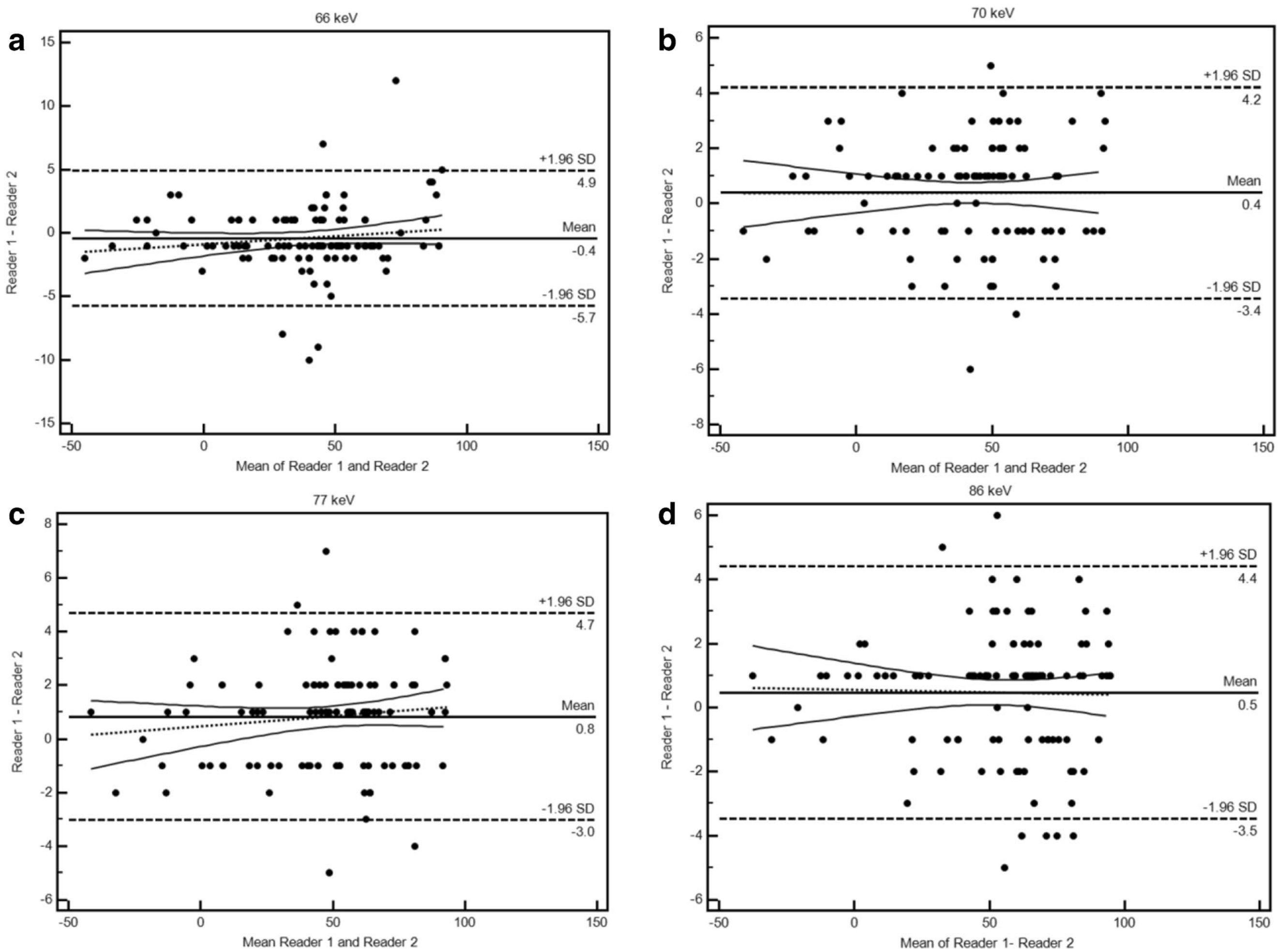

Fig. 3 Inter-observer agreement analysis for the DoS quantification. Panel **a** shows the DoS difference between at 66 keV between reader 1 and reader 2. Panel **b** shows the DoS difference between at 70 keV between reader 1 and reader 2. Panel **c** shows the DoS difference between at 77 keV between reader 1 and reader 2. Panel **d** shows the DoS difference between at 86 keV between reader 1 and reader 2

different plaque composition could play a significant role as demonstrated in previously published papers: Mannelli et al [14] found that there is an overestimation of calcified stenosis using low keV values for image reconstruction and similar findings were found in other body regions such as the coronary arteries and lower extremity [21, 22].

Other findings were also detected with the Bland-Altman analysis. First, the magnitude of the difference in terms of DoS increases with the keV difference (the bigger is the difference in keV between the two reconstructions, the bigger is the variation in DoS). The second effect showed by the Bland-Altman analysis is that the difference is reduced with the increase of the DoS: therefore, for a moderate level of stenosis, the variability is the highest whereas for severe grades of stenosis the variation due to the difference in keV is minimal. The increased variability for moderate level of stenosis could represent an important clinical point. This is because this category of patients (moderate level of stenosis) could be treated with different approaches (revascularization, best medical treatment) and the correct quantification of the degree of stenosis currently represents the key parameter of this choice. Moreover, this finding implies, as simple physical consequence, that also with the use of a conventional CT scanner could be present in the same subjects a variability depending on the level of energy applied. This is because the higher or lower use of kV (non-monocromatic) determines an increased or reduced photoelectric effect.

In this study, there are some limitations. The first one is related to the small cohort of subjects we analyzed ($n = 53$) and the heterogeneity in the validation process with ultrasound; dual-modality validation could be a solution to this weakness. The second one is related to the fact that we focused our attention as the direct consequence of the keV to the opacified level, but also the type of the plaque could play a role: based on CT imaging physics, this is a well-known phenomenon; the degree of *calcium blooming* is increased on the lower keV monochromatic images. Therefore, the degree of stenosis of a heavily calcified carotid plaque can be overestimated on low keV images, and by the same token, underestimated on the high keV images. We did not categorize the effect of the keV according to the type of plaque (fatty, mixed, calcified) because of the small number of subjects that do not allow to perform the statistical analysis regarding this further interaction.

Conclusion

In conclusion, we found that keV value significantly affects the quantification of the DoS of the carotid artery; therefore, a standardization in the energy levels used for the image reconstruction could potentially be considered.

Compliance with ethical standards

Funding No funding was received for this study.

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in the studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

References

1. Saba L, Yuan C, Hatsukami TS, Balu N, Qiao Y, DeMarco JK, Saam T, Moody AR, Li D, Matouk CC, Johnson MH, Jäger HR, Mossa-Basha M, Kooi ME, Fan Z, Saloner D, Wintermark M, Mikulis DJ, Wasserman BA (2018) Vessel Wall Imaging Study Group of the American Society of Neuroradiology. Carotid artery wall imaging: perspective and guidelines from the ASNR Vessel Wall Imaging Study Group and Expert Consensus Recommendations of the American Society of Neuroradiology. AJNR Am J Neuroradiol. https://doi.org/10.3174/ajnr.A5488
2. Saba L, Mallarini G (2008) MDCTA of carotid plaque degree of stenosis: evaluation of interobserver agreement. AJR Am J Roentgenol 190(1):W41–W46
3. Saba L, Mallarini G (2010) A comparison between NASCET and ECST methods in the study of carotids: evaluation using multi-detector-row CT angiography. Eur J Radiol 76(1):42–47. https://doi.org/10.1016/j.ejrad.2009.04.064
4. Tawfik AM, Kerl JM, Razek AA, Bauer RW, Nour-Eldin NE, Vogl TJ, Mack MG (2011) Image quality and radiation dose of dual-energy CT of the head and neck compared with a standard 120-kVp acquisition. AJNR Am J Neuroradiol 32(11):1994–1999. https://doi.org/10.3174/ajnr.A2654 Epub 2011 Sep 8
5. Machida H, Tanaka I, Fukui R, Shen Y, Ishikawa T, Tate E, Ueno E (2016) Dual-energy spectral CT: various clinical vascular applications. Radiographics 36(4):1215–1232. https://doi.org/10.1148/rg.2016150185 Review
6. Shinohara Y, Sakamoto M, Kuya K, Kishimoto J, Iwata N, Ohta Y, Fujii S, Watanabe T, Ogawa T (2015) Assessment of carotid plaque composition using fast-kV switching dual-energy CT with gemstone detector: comparison with extracorporeal and virtual histology-intravascular ultrasound. Neuroradiology 57(9):889–895
7. Mannelli L, Mitsumori LM, Ferguson M, Xu D, Chu B, Branch KR, Shuman WP, Yuan C (2013) Changes in measured size of atherosclerotic plaque calcifications in dual-energy CT of ex vivo carotid endarterectomy specimens: effect of monochromatic keV image reconstructions. Eur Radiol 23(2):367–374
8. Saba L, Argiolas GM, Siotto P, Piga M (2013) Carotid artery plaque characterization using CT multienergy imaging. AJNR Am J Neuroradiol 34(4):855–859
9. Agostini A, Mahmood U, Erdi Y, Borgheresi A, Ragucci M, Sawan P, Ryan D, Laino ME, Corrias G, Mannelli L (2018) Quantification of iodine concentration using single-source dual-energy computed tomography in a calf liver. J Comput Assist Tomogr 42(2):222–229
10. Marin D, Boll DT, Mileto A, Nelson RC (2014) State of the art: dual-energy CT of the abdomen. Radiology 271(2):327–342. https://doi.org/10.1148/radiol.14131480 Review
11. Riffel P, Haubenreisser H, Meyer M, Sudarski S, Morelli JN, Schmidt B, Schoenberg SO, Henzler T (2016) Carotid dual-energy CT angiography: evaluation of low keV calculated monoenergetic datasets by means of a frequency-split approach for noise reduction at low keV levels. Eur J Radiol 85(4):720–725. https://doi.org/10.1016/j.ejrad.2016.01.015
12. Korn A, Fenchel M, Bender B, Danz S, Thomas C, Ketelsen D, Claussen CD, Moonis G, Krauss B, Heuschmid M, Ernemann U, Brodoefel H (2013) High-pitch dual-source CT angiography of supra-aortic arteries: assessment of image quality and radiation dose. Neuroradiology 55(4):423–430
13. Mahmood U, Horvat N, Horvat JV, Ryan D, Gao Y, Carollo G, DeOcampo R, Do RK, Katz S, Gerst S, Schmidtlein CR, Dauer L, Erdi Y, Mannelli L (2018) Rapid switching kVp dual energy CT: value of reconstructed dual energy CT images and organ dose assessment in multiphasic liver CT exams. Eur J Radiol 102:102–108. https://doi.org/10.1016/j.ejrad.2018.02.022
14. Mannelli L, MacDonald L, Mancini M, Ferguson M, Shuman WP, Ragucci M, Monti S, Xu D, Yuan C, Mitsumori LM (2015) Dual energy computed tomography quantification of carotid plaques calcification: comparison between monochromatic and polychromatic energies with pathology correlation. Eur Radiol 25(5):1238–1246. https://doi.org/10.1007/s00330-014-3523-0
15. Zopfs D, Lennartz S, Laukamp K, Große Hokamp N, Mpotsaris A, Maintz D, Borggrefe J, Neuhaus V (2018) Improved depiction of atherosclerotic carotid artery stenosis in virtual monoenergetic reconstructions of venous phase dual-layer computed tomography in comparison to polyenergetic reconstructions. Eur J Radiol 100:36–42. https://doi.org/10.1016/j.ejrad.2018.01.008
16. Neuhaus V, Große Hokamp N, Abdullayev N, Maus V, Kabbasch C, Mpotsaris A, Maintz D, Borggrefe J (2017) Comparison of virtual monoenergetic and polyenergetic images reconstructed from dual-layer detector CT angiography of the head and neck. Eur Radiol 28(3):1102–1110. https://doi.org/10.1007/s00330-017-5081-8
17. Leithner D, Mahmoudi S, Wichmann JL, Martin SS, Lenga L, Albrecht MH, Booz C, Arendt CT, Beeres M, D'Angelo T, Bodelle B, Vogl TJ, Scholtz JE (2018) Evaluation of virtual monoenergetic imaging algorithms for dual-energy carotid and intracerebral CT angiography: effects on image quality, artefacts and diagnostic performance for the detection of stenosis. Eur J Radiol 99:111–117. https://doi.org/10.1016/j.ejrad.2017.12.024
18. Leithner D, Wichmann JL, Mahmoudi S, Martin SS, Albrecht MH, Vogl TJ, Scholtz JE (2018) Diagnostic yield of 90-kVp low-tube-voltage carotid and intracerebral CT-angiography: effects on radiation dose, image quality and diagnostic performance for the detection of carotid stenosis. Br J Radiol 91:20170927. https://doi.org/10.1259/bjr.20170927

19. Saba L, Mallarin G (2009) Window settings for the study of calcified carotid plaques with multidetector CT angiography. AJNR Am J Neuroradiol 30:1445–1450
20. Claves JL, Wise SW, Hopper KD (1997) Evaluation of contrast densities in the diagnosis of carotid stenosis by CT angiography. AJR Am J Roentgenol 169:569–573
21. Stehli J, Clerc OF, Fuchs TA, Possner M, Gräni C, Benz DC, Buechel RR, Kaufmann PA (2016) Impact of monochromatic coronary computed tomography angiography from single-source dual-energy CT on coronary stenosis quantification. J Cardiovasc Comput Tomogr 10(2):135–140. https://doi.org/10.1016/j.jcct.2015.12.008
22. Kau T, Eicher W, Reiterer C, Niedermayer M, Rabitsch E, Senft B, Hausegger KA (2011) Dual-energy CT angiography in peripheral arterial occlusive disease-accuracy of maximum intensity projections in clinical routine and subgroup analysis. Eur Radiol 21(8): 1677–1686. https://doi.org/10.1007/s00330-011-2099-1