HIROSAKI UNIVERSITY

Radiation Environment and Medicine 2021 Vol.10, No.2 82–86

REM
Radiat Environ Med

Note

The Clinical Usefulness of Water/Iodine Material Density Measured by DE-CT

Kazuki Hasegawa[1], Ryo Saga[1*], Yuta Sato[2], Mitsuki Tanaka[3], Ryo Katagishi[4], Masahiko Aoki[3] and Yoichiro Hosokawa[1]

[1]*Department of Radiation Sciences, Hirosaki University Graduate School of Health Sciences, Hirosaki, Aomori 036-8564, Japan*
[2]*Department of Medical Radiation Technology, Teine-Keijinkai Hospital, Sapporo, Hokkaido 006-8555, Japan*
[3]*Department of Radiation Oncology, Hirosaki University Graduate School of Medicine, 5 Zaifu-cho, Hirosaki, Aomori 036-8562, Japan*
[4]*Department of Radiology, Hirosaki University School of Medicine and Hospital, 53 Hon-cho, Hirosaki, Aomori 036-8563, Japan*

Received 17 August 2020; revised 30 November 2020; accepted 22 December 2020

Dual energy-computed tomography (DE-CT) can discriminate between materials using the material density obtained by two types of X-ray energies. This study investigated the characteristics of the water density value (WDV) used as a prognostic indicator. WDV with any contrast medium concentration was measured using a bottled diluted contrast medium. In addition, we studied retrospective reviews of 117 patients who underwent DE-CT between 2013 and 2018 and compared them with WDVs before and after contrast enhancement (CE). The WDVs were obtained from the abdominal aorta and superior vena cava. In the ex-vivo study, the WDV decreased slightly by of 0-10% contrast medium concentration, however, it increased gradually above 10%. The number of patients whose WDV of the CT image increased after CE-CT were 28 in the arteries and 50 in the veins. The results suggested that the concentration of the contrast medium was over 10% in arteries and veins. The differences between WDVs in arteries and veins obtained from CT images were very small, with or without CE. Therefore, it was revealed that WDV was less affected by the difference in arteries and veins, or by using contrast medium.

Key words: DE-CT, material density, water density value

1. Introduction

Dual energy-computed tomography (DE-CT) acquires two X-ray energy datasets from the same anatomic location with different tube voltage by a combination of two pairs of X-ray tubes and detectors, and rapid switching of low or high tube voltage. Gemstone spectral imaging (GSI) is the application of DE-CT that has been made available for materials discrimination in recent years[1-3]. The material density image is expressed using the different X-ray attenuation data obtained from two different materials. The most common material pair is iodine and water[4, 5]. A previous study showed that the iodine density value (IDV) correlated with the blood flow in a tumor, and the reduction of the IDV was associated with an increase in cancer cell population in the hypoxic microenvironment, which shows radioresistance[6-8]. In contrast, the water density value (WDV) in the tumor is presumed to reflect cell density and cell necrosis, and our previous study suggested that the reduction of WDV has a positive effect on overall

*Ryo Saga: Department of Radiation Science Hirosaki University Graduate School of Health Sciences, 66-1 Hon-cho, Hirosaki, Aomori 036-8564, Japan
E-mail: sagar@hirosaki-u.ac.jp

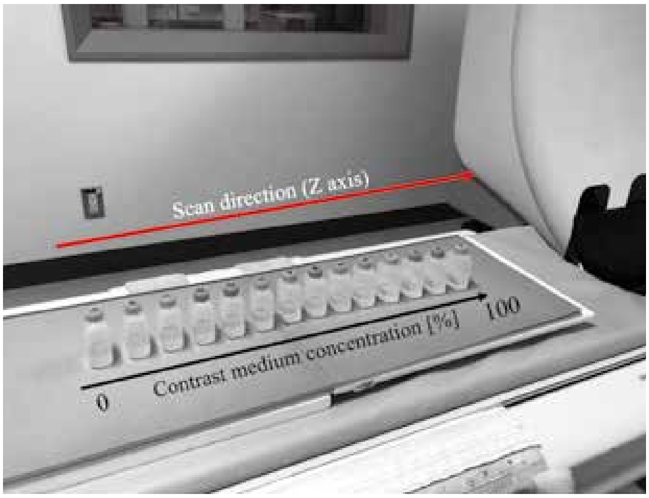

Fig. 1. The bottled diluted contrast medium. A total of 50 ml polyethylene container was used. A nonionic, low-osmolar contrast medium 300 (mg I/ml) was mixed with distilled water, and 30 ml each was enclosed in the container. The bottled diluted contrast medium was placed at 2 cm intervals to prevent artifact and scanned continuously.

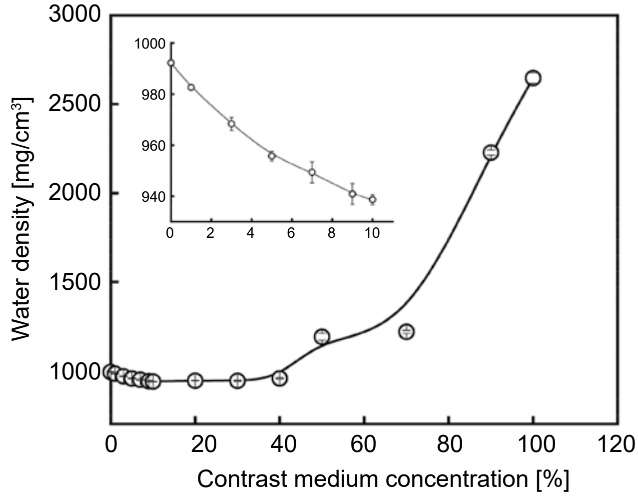

Fig. 2. Evaluation of WDV for contrast medium concentrations of 0-100%. Data are shown as mean ± standard deviation.

survival after radiotherapy[9]. Therefore, the IDV and the WDV obtained from dual energy of X-rays enable us to estimate the quantitative assessment of tumor invasion and the prediction analysis of patient prognosis[9, 10]. However, some issues need to be resolved to use the WDV as a prognostic indicator. For instance, in contrast enhanced (CE)-CT, WDV of tissue may be affected by iodine contained in the contrast medium. In addition, there were few clinical applications using WDV, most recently, only reported that WDV can be used to detect bone marrow edema[11].

In this study, to identify the characteristics of the WDV as a prognostic indicator, we investigated whether the contrast medium or, the difference between arterial blood and vein blood, affects WDV.

2. Materials and Methods

Scanning procedure

Discovery CT750 HD (GE Healthcare, USA) was used for DE-CT. A fast kV switching method was used for CT imaging. Omnipaque 350 (GE Healthcare, USA) and Iopamiron 300 (Bayer Yakuhin, Ltd., Japan) were used as a nonionic, low-osmolar contrast medium, and the concentration 600 mg I per kg body weight, with an iodine content of 300 or 350 mg I/ml. The contrast medium with an iodine content of 300 mg I/ml was used in the ex-vivo study, and 300 and 350 mg I/ml were used in the clinical study.

Evaluation of water density value for contrast medium concentration change

Low-osmolar contrast medium 300 (mg I/ml) was diluted with distilled water to concentration 0, 1, 3, 5, 7, 9, 10, 20, 30, 40, 50, 70, 90 and 100%. Mixtures with adjusted concentrations were enclosed in a polyethylene container with a capacity of 50 ml (Fig. 1), and scanning was performed under conditions of a tube voltage of 80 and 140 kVp and a tube current of 360 mA in air. The bottled diluted contrast medium was placed at 2 cm interval and scanned continuously. The scanned CT images were transferred to a workstation (GSI Viewer, GE Healthcare, USA) for data analysis. Data analysis was performed using Advantage Workstation (AW) volume share 5 software (GE Healthcare, USA) with a slice thickness of 5.0 mm. The region of interest (ROI) was set in the center of the mixture, and the mean WDV in the ROI was acquired. The relationship between the mean WDV and contrast medium concentration was shown by 4-parametric logistic curve.

Patients' characteristics

From 2013 to 2018, 117 patients with medically inoperable lung cancers who underwent DE-CT were retrospectively reviewed. CE-CT scanning was performed with nonionic, low-osmolar contrast medium, and the dose of the contrast medium was 600 mg I per kg body weight. The total amount of contrast medium was intravenously injected within 30 s. The scan was started 25 s after initiating the injection of contrast medium. The CT images of plain CT and CE-CT imaging were transferred

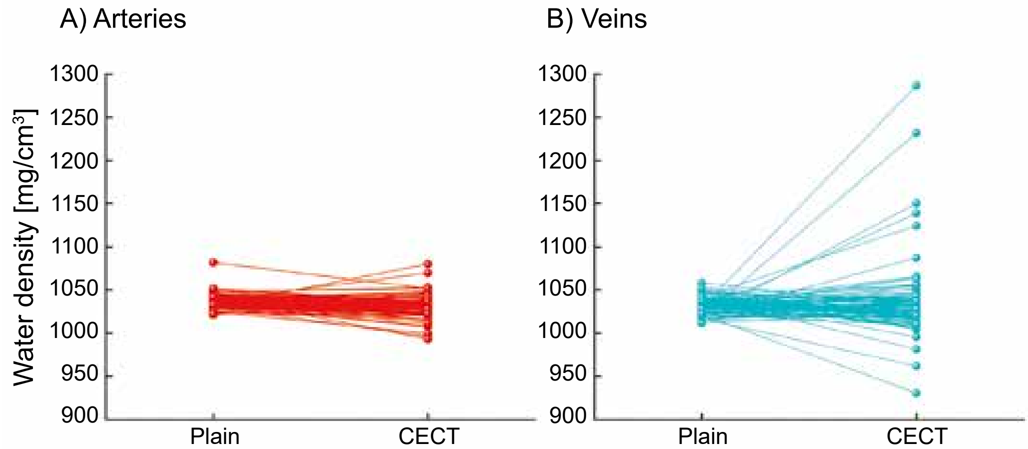

Fig. 3. The comparison of WDVs between plain and CE-CT, A) in arteries, B) in veins.

to a workstation and were subjected to data analyses with AW volume share 5 software. The slices used for data analysis had a thickness of 0.625 mm. After setting the ROI of the abdominal aorta and superior vena cava CT image including no vessel wall using a pulmonary window (window width: 1,000 HU; window level: −700 HU), the WDVs were obtained for each scan. The WDV of the abdominal aorta and superior vena cava in the same patient were compared using plain and CE imaging in the same scan range, respectively.

Statistics

All statistical analyses were performed using Microsoft Excel 2016 (Microsoft Corporation) with the add-on software Statcel v4 (OMS Publishing, Saitama, Japan) for all patients as a group. The difference between the mean WDV in patients' arteries and veins was assessed using Student's t-test and Mann-Whitney test. Differences were regarded as statistically significant at a P-value of < 0.05. The effect size of statistical significance was calculated using Cohen's d[12]. In this study, the effect size was considered as small at $d \leq 0.2$, medium at $0.2 < d \leq 0.5$, and large at $d \geq 0.8$, respectively.

3. Results

Evaluation of water density value for changes in contrast medium concentration.

To investigate the concentration of contrast medium affecting the WDV, we measured the WDV with continuously changing contrast medium concentration. From 0-10% contrast medium concentration, the WDV tended to slightly decrease with increasing concentration (Fig. 2). In contrast, in over 10%, the WDV gradually increased in a concentration-dependent manner.

Evaluation of water density for arteries and veins.

A total of 117 patients who underwent DE-CT between 2013 and 2018 were reviewed for comparison of WDVs before and after contrast enhancement. The number of the patients whose WDV after contrast enhancement increased was 78 (28 in artery, 50 in vein) (Fig. 3A, B). As further investigation, we evaluated whether arteries and veins were distinguishable by measuring the WDV. The WDVs obtained from the artery and the vein in plain CT images were significantly different, 1,037 ± 12 and 1,032 ± 12 ($P < 0.01$), respectively (Fig. 4A). In contrast, the WDVs obtained from the artery and the vein by CE-CT imaging were 1,030 ± 15 and 1,035 ± 62 ($P = 0.50$), respectively (Fig. 4B). In addition, the WDV obtained from the artery on CE-CT showed a statistically significant decrease compared with plain CT ($P<0.01$). The effect sizes were calculated for the WDV of arteries and veins obtained from plain CT imaging and the WDV before and after CE in the arteries. The effect sizes were $d = 0.36$ between the artery and vein and 0.61 between before and after CE in the arteries. These values were medium effect size, respectively[13, 14].

4. Discussion

This study investigated the characteristics of WDV as a prognostic indicator. When the concentration of contrast medium was less than 10%, the WDV slightly decreased in a concentration-dependent manner. However, the WDV was increased when the contrast medium concentration exceeded 10% (Fig. 2). Among the 117 patients, the number of patients who increased the WDVs after contrast enhancement was 28 in arteries and 50 in veins (Fig. 3). As further investigation, we evaluated whether the WDV obtained from DE-CT could identify arteries

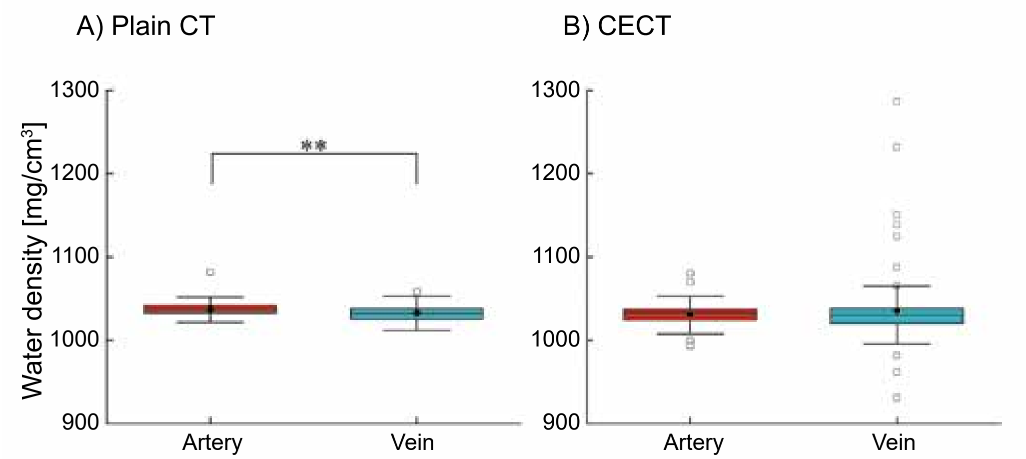

Fig. 4. Comparison of WDV of arteries and veins. A) Plain imaging, B) contrast imaging. Values are shown as mean ± standard deviation. **P < 0.01. Black circle and blank square show mean value and outlier, respectively.

and veins with few differences in tissue components. The WDVs in arteries and veins obtained from plain CT imaging showed a statistically significant difference, but not CE-CT (Fig. 4).

Our previous study revealed that the WDV in a tumor was negatively correlated with overall survival after radiotherapy and positively correlated with average CT values (CTV)[8, 9]. The WDV is also simply expressed by the subtraction between CTV and IDV, thereby decreasing the WDV in a contrast medium concentration-dependent manner. In contrast, our results showed that WDV was increased in the contrast medium concentration exceeding 10%. It has been reported that a material containing higher iodine causes beam-hardening artifacts[15-17], and water (iodine) image accentuates beam-hardening artifacts that have less intense or unchanged CT attenuation at low versus high kVp[17]. In fact, the artifact pattern was observed in the contrast medium concentration exceeding 10% in phantom imaging, and also observed in the patient data in which the WDV increased after CE (data not shown). Therefore, it was suggested that the WDV might be affected by beam-hardening artifacts at over 10% contrast medium. The concentration of contrast medium to patients in this study was 600 mg I per kg body weight, with an iodine content of 300 or 350 mg I/ml. This concentration is commonly used clinically[19, 20], which is less than 5% of the whole-body blood volume. Theoretical whole-body contrast medium concentration which calculated by blood volume from Ogawa formula and the dose of contrast medium, is less 4% for both men and women. However, in the patient data, the patients who showed increasing WDV obtained from arteries and veins after CE-CT were 28 and 50 patients, respectively. This means that the concentration of contrast medium in the ROI exceeded 10%.

In DE-CT, the tissue attenuation coefficient is calculated from two different X-ray energies, and discriminates materials by representing each image with water and iodine[21, 22]. In plain CT images, there was a statistically significant difference in the WDV of the arteries and the veins, and the effect size was medium. However, the difference in WDV between arteries and veins was extremely small, and it seems difficult to distinguish by using the value. In CE-CT images, there was a statistically significant decrease in the WDV of the arteries compared with plain CT, while the difference in WDV was extremely small. These results indicate that the WDV was less affected by subtle differences in components such as arteries, veins, and contrast medium. In addition, our previous study revealed that no effect on CT value and WDV by tumor contrast enhancement[8]. Therefore, it was suggested that the patient prognosis can be determined by the WDV of any ROI in the tumor, and the WDV could be used as a prognostic indicator. However, the number of patients with outliers on CE-CT is higher in veins than in other imaging methods, this could be including several factors such as patient characteristics, contrast medium injection rate, and scan delay. Moreover, it is difficult to handle WDV in low IDV such as veins, and WDV may less reliable in diagnosis because the WDV variability is large when the tumor has a low IDV. Thus, there is still a limitation to use WDV as a prognostic indicator.

5. Conclusions

The results of this study revealed that WDV was less affected by subtle differences in component and contrast medium, suggesting that WDV can be used as a clinical indicator. Further studies are required to establish the WDV as a prognostic indicator because there are still factors that influence WDV.

Conflict of Interest

The authors declare that there are no conflicts of interest regarding the article.

References

1. Matsumoto K, Jinzaki M, Tanami Y, Ueno A, Yamada M and Kuribayashi S. Virtual monochromatic spectral imaging with fast kilovoltage switching: improved image quality as compared with that obtained with conventional 120-kVp CT. Radiology. 2011;259(1):257–62.
2. Zhang D, Li X and Liu B. Objective characterization of GE Discovery CT750 HD scanner: gemstone spectral imaging mode. Med Phys. 2011;38(3):1178–88.
3. Pinho DF, Kulkarni NM, Krishnaraj A, Kalva SP and Sahani DV. Initial experience with single-source dual-energy CT abdominal angiography and comparison with single-energy CT angiography: image quality, enhancement, diagnosis and radiation dose. Eur Radiol. 2013;23(2):351–9.
4. Johnson TR, Krauss B, Sedlmair M, Grasruck M, Bruder H, Morhard D, *et al*. Material differentiation by dual energy CT: initial experience. Eur Radiol. 2007;17(6):1510–7.
5. Kaza RK, Caoili EM, Cohan RH and Platt JF. Distinguishing Enhancing From Nonenhancing Renal Lesions With Fast Kilovoltage-Switching Dual-Energy CT. AJR Am J Roentgenol. 2011;197(6):1375–81.
6. Lee SH, Hur J, Kim YJ, Lee HJ Hong YJ and Choi BW. Additional value of dual-energy CT to difference between benign and malignant mediastinal tumors: an initial experience. Eur J Radiol. 2013;82(11):2043–9.
7. Moding EJ, Clark DP, Qi Y, Li Y, Ma Y, Ghaghada K, *et al*. Dual-energy micro-computed tomography imaging of radiation-induced vascular changes in primary mouse sarcomas. Int J Radiat Oncol Biol Phys. 2013;85(5):1353–9.
8. Aoki M, Takai Y, Narita Y, Hirose K, Sato M, Akimoto H, *et al*. Correlation between tumor size and blood volume in lung tumors: a prospective study on dual energy gemstone spectral CT imaging. J Radiat Res. 2014;55(5):917–23.
9. Aoki M, Hatayama Y, Kawaguchi H, Sato M, Tanaka M, Fujioka I, *et al*. Measurements of Substance Densities of Non-Small Cell Lung Cancer Using Dual Energy Computed Tomography Are Useful for Prediction of Local Control and Overall Survival after Stereotactic Body Radiation Therapy. Int J Radiat Oncol Biol Phys. 2018;102:671.
10. Aoki M, Hirose K, Sato M, Akimoto H, Kawaguchi H, Hatayama Y, *et al*. Prognostic impact of average iodine density assessed by dual-energy spectral imaging for predicting lung tumor recurrence after stereotactic body radiotherapy. J Radiat Res. 2016;57(4):381–6.
11. Son W, Park C, Jeong HS, Song YS and Lee IS. Bone marrow edema in non-traumatic hip: high accuracy of dual-enery CT with water-hydroxyapatite decomposition imaging. Eur Radiol. 2020;30(4):2191–8.
12. UNESCO 2012. International standard classification of education ISCED 2011. Montreal: UNESCO Institute for Statistics. 2012:1–84.
13. Jung-Hui Li, Yeh-Ming Du and Hsuan-Ming Huang. Accuracy of dual-energy computed tomography for the quantification of iodine in a soft tissue-mimicking phantom. J Appl Clin Med Phys. 2015;16(5):418–26.
14. Toepker M, Moritz T, Krauss B, Weber M, Euller G, Mang T, *et al*. Virtual non-contrast in second-generation, dual-energy computed tomography: reliability of attenuation values. Eur J Radiol. 2012;81(3):e398–e405.
15. McCollough CH, Leng S, Yu L and Fletcher JG. Dual- and multi-energy CT: principles, technical approaches, and clinical applications. Radiology. 2015;276(3):637–53.
16. Johnson T. R. C. Dual-energy CT: general principles. AJM Am J Roentgenol. 2012;199(5 Suppl):S3–S8.
17. Cohen J. Statistical power analysis for the behavioral sciences (2nd ed). Hillsdale, NF: Lawrence Erlbaum. 1988.
18. Winklhofer S, Lambert JW, Sun Y, Wang ZJ, Sun DS and Yeh BM. Pelvic Beam-Hardening Artifacts in Dual-Energy CT Image Reconstructions: Occurrence and Impact on Image Quality. AJR Am J Roentgenol. 2017;208(1):114–23.
19. Coursey CA, Nelson RC, Boll DT, Paulson EK, Ho LM, Neville AM, *et al*. Dual-energy multidetector CT: how does it work, what can it tell us, and when can we use it in abdominopelvic imaging? Radiographics. 2010;30(4):1037–55.
20. Forghani R, Srinivasan A and Forghani B. Advanced tissue characterization and texture analysis using dual-energy computed tomography. Neuroimaging Clin N Am. 2017;27(3):533–46.
21. Cohen J. A power primer. Psychol Bull. 1992;112(1):155–9.
22. Fleischmann D and Kamaya A. Optimal vascular and parenchymal contrast enhancement: the current state of the art. Radiol Clin North Am. 2009;47(1):13–26.