Improvement of the Visibility of Hepatocellular Carcinoma Lesions in Early Phase Abdominal Contrast Enhanced Computed Tomography Images: Utilization of Optimal Pseudo-Colorization

赤嶺, 寛地

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医用画像表示用 liquid-crystal display における
グレイスケール画像と疑似カラー画像の
視認性に関する研究

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九州大学大学院 医学系学府保健学専攻

Department of Health Sciences,

Graduate School of Medical Sciences,

Kyushu University

赤嶺 寛地

Hiroshi Akamine

Original Article

Improvement of the Visibility of Hepatocellular Carcinoma Lesions in Early Phase Abdominal Contrast Enhanced Computed Tomography Images : Utilization of Optimal Pseudo-Colorization

Hiroshi Akamine[1,2], Junji Morishita[3], Taku Kuramoto[4], Hiroshi Hamasaki[1], Shinya Takarabe[1], Noriaki Wada[5], Keisuke Ishimatsu[5], Yasuhiro Ushijima[5], Toyoyuki Kato[1], Kousei Ishigami[5] and Masayuki Sasaki[3]

[1]*Division of Radiology, Department of Medical Technology, Kyushu University Hospital*
[2]*Department of Health Sciences, Graduate School of Medical Sciences, Kyushu University*
[3]*Department of Health Sciences, Faculty of Medical Sciences, Kyushu University*
[4]*Department of Radiological Technology, Faculty of Health Sciences, Kobe Tokiwa University*
[5]*Department of Clinical Radiology, Graduate School of Medical Sciences, Kyushu University*

Abstract

Purpose : The specific objectives of our study were to examine whether the visibility of hepatocellular carcinoma (HCC) lesions on early phase abdominal contrast-enhanced computed tomography (CT) images can be improved by optimal pseudo-colorization with a rainbow color map.

Methods : The chromaticity of grayscale and rainbow color maps displayed on a medical liquid-crystal display was measured using a colorimeter. The differences in the chromaticity, ΔE_{00}, between the HCC lesion and liver parenchyma in 22 cases were evaluated. The rainbow color map was revised by changing only the window level (WL) to match the HCC lesion with a peak of ΔE_{00}. Visual evaluation of the 22 cases was performed using Scheffe's paired comparison by ten observers. The average psychological measurement ($\overline{\alpha}$) was calculated using the grayscale, rainbow color map, and revised rainbow color map to examine the effectiveness of the proposed method.

Results : In all cases, the $\overline{\alpha}$ measure was highest in the order of revised rainbow, grayscale, and rainbow. These results indicate that the visibility of HCC lesions in early phase abdominal contrast-enhanced CT images could be improved by modifying the pseudo-color map with optimal colorization based on ΔE_{00}.

Conclusions : The visibility of HCC lesions in early phase abdominal contrast-enhanced CT images was improved by shifting only the WL setting so that the HCC contrast would match the pixel range with higher ΔE_{00} on the rainbow color map. This method can be applied to various cases and color maps, and the visibility of the target lesion can be easily improved.

Key words : pseudo-color image, discrimination ability, hepatocellular carcinoma, computed tomography, contrast enhancement

Introduction

A pseudo-color image is a colored image in which the image data are artificially colored by converting the RGB value to each pixel. Pseudo-color images have been used in computed tomography (CT) imaging, magnetic resonance imaging, and other digital imaging techniques

Corresponding author : Hiroshi Akamine
Department of Health Sciences, Faculty of Medical Sciences, 3-1-1, Maidashi, Higashi-ku, Fukuoka, 812-8582, Japan
Tel & Fax : + 81-92-642-5791
E-mail : akamine.hiroshi.070@m.kyushu-u.ac.jp

Fig. 1 Grayscale and rainbow color map used in this study. The left and right sides of each image correspond 0 and 255 in the pixel value, respectively.

including nuclear medicine, to improve the visibility of the lesion[1~4]. Most of these are used for displaying functional images, but some applications to morphological images have also been reported[5,6]. Ogura *et al.* reported that the detectability of acute cerebral infarction might be better on brain CT scans with a yellow color map compared to grayscale[5]. Saba *et al.* suggested that the use of a color scale instead of a conventional grayscale improves the diagnostic confidence of internal carotid artery dissection on CT images[6]. The interpretation of the CT image is performed with window level (WL) and window width (WW) settings to increase the contrast of the target organ. CT values indicate relative values when water is 0 Hounsfield unit (HU) and air is −1,000 HU, but not all CT values can be expressed on a medical image display with one window setting. To make it easier to interpret the target organ, we select only the range of the target CT value and display the width with 256 gradations in the grayscale image. For example, WL/WW was set to 50/300 when observing abdominal organs, and −600/1,500 when observing lung fields. When interpreting grayscale CT images, the window setting is automatically changed to the default setting in the hospital for various scanning procedures. If pseudo-color display can be easily performed as an additional method of window setting, radiologists and physicians may easily find lesions with low contrast in grayscale images.

Abdominal contrast-enhanced CT imaging is performed to identify hepatocellular carcinoma (HCC) lesions and plays a major role in the diagnosis[7]. Although the contrast between the HCC lesion and liver parenchyma on the CT images is important for diagnosing HCC, the HCC lesions appear as low-contrast lesions on the CT images. In some cases, such as low-dose CT imaging, heavier weight of the patient, and CT with less contrast medium, the contrast required for diagnosis may not be maintained, making it difficult for radiologists to recognize the HCC lesion[8,9]. Although there have been some reports on improving the visibility of HCC[7,10~12], there have been no reports on the improvement in visibility using pseudo-color images.

The rainbow color map is typical color maps[13,14] (Fig. 1) and is often used as a standard for visualization software. However, users of rainbow color maps must understand that the map may not improve the visibility of the lesion[15]. Developing a method that appropriately uses a rainbow color map might improve the visibility of a target lesions on images that the observer finds difficult to see due to the less contrast in grayscale images. In addition, in the interpretation of CT images, it is possible to easily use the pseudo-color image display according to the target lesion to switch the window setting. This study aimed to develop a method for improving the visibility of HCC lesions on CT images with optimal pseudo-colorization using a rainbow color map.

Materials and Methods

Clinical images

In this study, early phase abdominal contrast-enhanced CT images 124 patients (age, 36–94 years ; mean age, 76.2 years) diagnosed with HCC between April 2017 and December 2019 were used. In all cases, multiphase contrast-enhanced dynamic CT and MRI, and biochemical examination were performed, and HCC was comprehensively diagnosed. A radiologist who did not participate in the visual evaluation randomly selected 22 cases with HCC lesions from the image data that met the following conditions : one HCC lesion on one slice (15 men and 7 women, age, 65–78 years ; mean age, 73.3 years, size of HCC, 7.1–26.5 mm ; mean, 12.4 mm). This study received institutional review board approval and the requirement for informed consent was waived.

CT scan and contrast material infusion protocols

All CT examinations were performed using a multidetector CT scanner (Aquilion ONE Vision Edition : CANON Medical Systems, Otawara, Japan). The scanning parameters were as follows : 120 kV ; tube current, automatic exposure control (noise level, standard deviation 10 ; reconstructed slice thickness, 0.5 mm) ; section thickness and intersection gap, 5.0 mm ; and reconstructed field of view, 320 or 400 mm. In this study, the amount of contrast medium and the injection rate were fixed based on some published literature[16)~18)]. Each patient received 100 ml of intravenous nonionic contrast material containing 370 mg I/ml iopamidol (Iopamiron ; Bayer, Osaka, Japan) at a rate of 3.0 ml/s using a power injector (Dual Shot GX 7 ; Nemoto-Kyorindo, Tokyo). The administration of contrast material was followed by the injection of 30 ml of saline at the same rate as that used for contrast material injection. The early phase scan began 43 s after the injection of the contrast agent.

Imaging devices and color maps

Two-color medical liquid-crystal displays (LCDs) of the same model were used (RX340 ; 1,536 × 2,048, 3 megapixels, 400 cd/m^2, EIZO, Ishikawa, Japan). The color space and color temperature were calibrated to sRGB and 7,500 Kelvin (K), respectively. Grayscale and rainbow color map were used in this study (Fig. 1).

Measurement of chromaticity and calculation of the differences in chromaticity

To achieve optimal pseudo-colorization, the quantitative color values of grayscale and rainbow color maps were investigated. The chromaticity for the grayscale and rainbow color maps in the CIE L*a*b* color space, (L^*, a^*, b^*)[19)] corresponding to the 0-255-pixel value was measured in a dark room using a telescope-type colorimeter (CS-200 ; KONICA MINOLTA, Tokyo).

To examine the differences in chromaticity for each case, the CIE 2,000 color-difference formula (CIEDE 2,000 or ΔE_{00}) was calculated from the measured chromaticity (L^*, a^*, b^*) by using the Eq. (1).

$$\Delta E_{00}=\sqrt{\left(\frac{\Delta L'}{K_L S_L}\right)^2+\left(\frac{\Delta C'}{K_C S_C}\right)^2+\left(\frac{\Delta H'}{K_H S_H}\right)^2+R_T\left(\frac{\Delta C'}{K_C S_C}\right)\left(\frac{\Delta H'}{K_H S_H}\right)} \quad (1)$$

where $\Delta L'$, $\Delta C'$, and $\Delta H'$are the CIELAB metric, lightness, chroma, and hue differences for one pair of samples ; K_L, K_C, and K_H are parametric factors, and S_L, S_C, and S_H are the weighting functions for lightness, chroma, and hue, respectively, and R_T is the interaction term between differences in chroma and hue in the blue region[20)].

Determination of optimal pseudo-colorization based on the differences in chromaticity

Optimal pseudo-colorization was achieved using a three-step procedure. First, the contrast between the HCC lesion and the liver parenchyma was examined, that is, the difference in PV between the HCC lesions and the liver parenchyma was observed using general-purpose image analysis software (ImageJ, NIH, Bethesda, MD, USA) for each case. A radiologist who did not participate in the visual evaluation specified the areas of the HCC and healthy parenchyma. The measured CT values were converted into pixel values (PVs) with an abdominal window setting (WL of 50 HU and WW of 300 HU) of 8 bits. We calculated the difference in PV between the HCC lesions and the liver parenchyma for each case (hereafter referred to as the HCC contrast).

Second, we examined the PV region in which the difference in chromaticity, ΔE_{00}, of the HCC contrast was the highest on the rainbow color map for each case. Differences in the chromaticity of the HCC contrast were obtained for the grayscale and rainbow scales according to PVs ranging from 0 to 255.

Finally, the grayscale CT image was optimally colorized using a rainbow color map. Based on the difference in chromaticity of HCC contrast, the revised PVs of the HCC lesions and the liver parenchyma were calculated so that the PVs of the HCC lesions and the liver parenchyma would match the PV region with the highest ΔE_{00} in the rainbow color map. In conformity to the revised PVs of the HCC lesions and the liver parenchyma, the WL setting of a rainbow color map was revised (hereafter referred to as the revised rainbow). To visually evaluate the improvement in visibility by appropriate colorization, three types of images for each case were prepared grayscale, rainbow, and revised rainbow images.

Visual evaluation using Scheffe's paired comparison

A qualitative visual evaluation of visibility of the CT image, including the HCC, was performed using Scheffe's paired comparison method[21]. Scheffe's paired comparison method is a visual evaluation method in which two arbitrary objects are extracted and compared simultaneously. Two out of the three images (grayscale, rainbow, and revised rainbow) were displayed on a color LCD side by side, and all combinations for 22 cases in a total of 66 pairs were evaluated for "the visibility of HCC lesions" in five categories (−2, A is much better than B ; −1, A is better than B ; 0, A is equivalent to B ; 1, B is better than A ; 2, B is much better than A).

The observers were two radiologists (12 and 15 years of clinical experience) and eight radiological technologists (4–20 years of clinical experience). All observers were trained before visual evaluation. The observer was informed in advance that the case had been diagnosed with HCC and of the location of HCC on the CT image. Therefore, the observer did not need to diagnose HCC or identify the location. The observer compared the HCCs of the two images and evaluated only the visibility. The ambient light condition for the visual evaluation was approximately 30 lux, which was the same as that of the diagnostic reading room for radiologists at Kyushu University Hospital. The observation date and order of observation were changed to avoid bias in the observation results, such as inter-observer variation and order effects.

The significance of Scheffe's paired comparison method was evaluated using the average psychological measure ($\bar{\alpha}$) and 95% confidence interval for each case. Greater $\bar{\alpha}$ indicates a better image for easily detecting subtle lesions.

Results

Difference in the chromaticity in grayscale and rainbow color maps

Table 1 shows the CT values of the HCC lesions and liver parenchyma and the HCC contrast for 22 cases. The differences in chromaticity, ΔE_{00}, of the HCC contrast in each PV of the grayscale and rainbow color maps for a case are shown in Fig. 2 (a) and (b). Horizontal axis is the HCC contrast in each PV. Vertical axis is ΔE_{00}. We found that the ΔE_{00} of the rainbow color map varied greatly depending on PV. The ΔE_{00} value of the rainbow color map had two large peaks of ΔE_{00}. The areas ΔE_{00} of the rainbow color map were higher or lower than those in grayscale.

Table 1 Computed tomography (CT) value of hepatocellular carcinoma lesions and liver parenchyma and hepatocellular carcinoma (HCC) contrast for 22 cases.

		Max － Min	Mean ± SD*
CT value [HU]	HCC	149.3 － 71.6	108.4 ± 20.5
	Liver parenchyma	110.7 － 52.2	76.8 ± 12.7
Difference of CT values		60.1 － 11.4	12.4 ± 4.7
HCC contrast (difference of PV)		51.1 － 9.7	27.0 ± 11.4

*SD : standard deviation

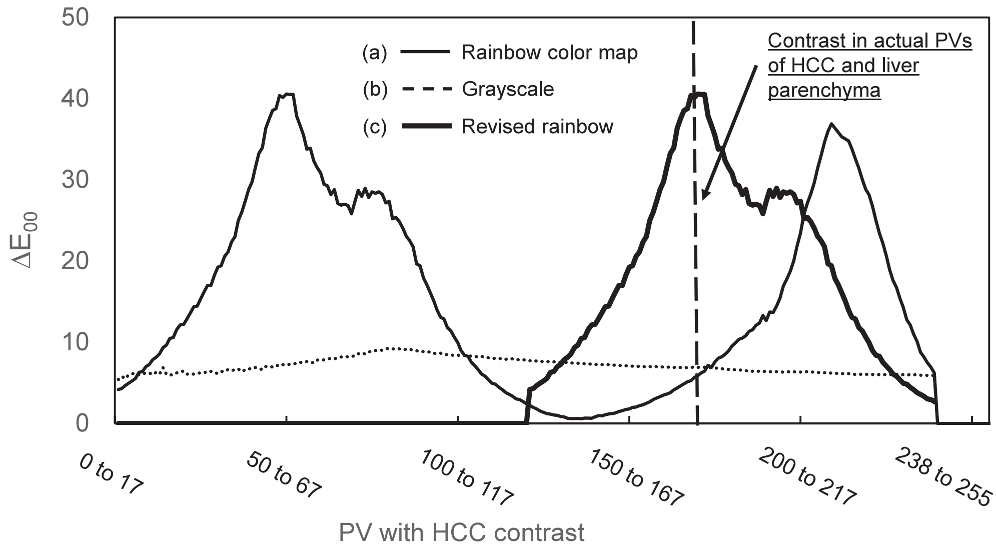

Fig. 2 An example of the difference in chromaticity, ΔE_{00}, of HCC contrast in each PV for grayscale, rainbow color map, and revised rainbow for a case (Example case : PV of HCC is 187, PV of liver parenchyma is 170, HCC contrast is 17). The horizontal axis is PV with HCC contrast, and represents changes in HCC contrast in each case. The vertical axis is the ΔE_{00} of HCC contrast in each PV. In this example, the value on the vertical axis is the ΔE_{00} when the PV differs by 17 for each pixel value. The dotted line indicates ΔE_{00} in the grayscale (a). The solid line on the graph indicates ΔE_{00} in the rainbow color map (b). The thick line on the graph indicates ΔE_{00} in the revised rainbow (c). The vertical dashed line on graph indicates the actual PVs of HCC and liver parenchyma.

Differences in the chromaticity of HCC contrast

An example of the difference in chromaticity, ΔE_{00}, of HCC contrast in each PV for grayscale, rainbow color map, and revised rainbow for a case are shown in Fig. 2 (Example case : PV of HCC is 187, PV of liver parenchyma is 170, HCC contrast is 17). By revising the WL setting, the PVs of the HCC lesions and the liver parenchyma matched the PV region with the highest ΔE_{00} in the rainbow color map. Fig. 3 shows the average ΔE_{00} of the HCC contrast for 22 cases. The ΔE_{00} showed higher values in the order of revised rainbow, grayscale, and rainbow color maps. Error bars indicate the standard deviation.

Visual evaluation using Scheffe's paired comparison

Fig. 4 shows the results of the visual evaluation using Scheffe's paired comparison for all cases. The horizontal axis represents the average psychological measurement ($\overline{\alpha}$), and a higher value indicates better visibility of the HCC lesion. The vertical axis indicates the number of cases. Error bars indicate the standard deviation. In all cases, $\overline{\alpha}$ was highest in the order of revised

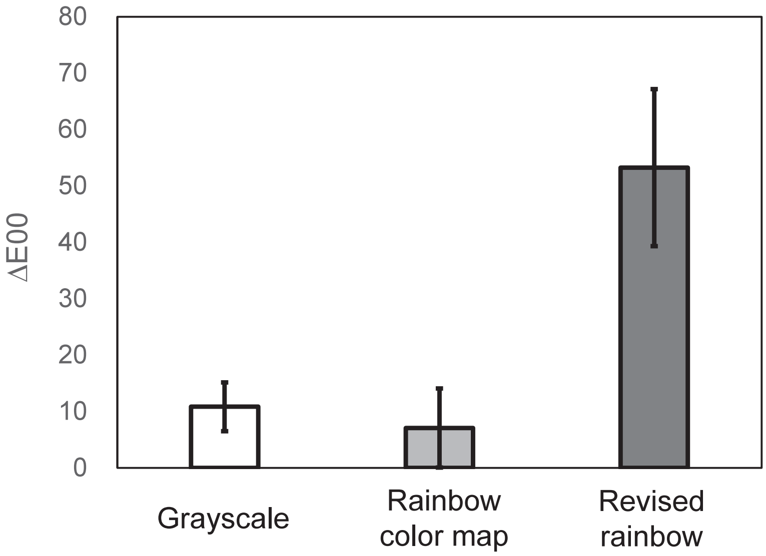

Fig. 3 The average of ΔE_{00} for 22 cases of the hepatocellular carcinoma contrast in grayscale, rainbow color map, and revised rainbow. Error bars indicate the standard deviation.

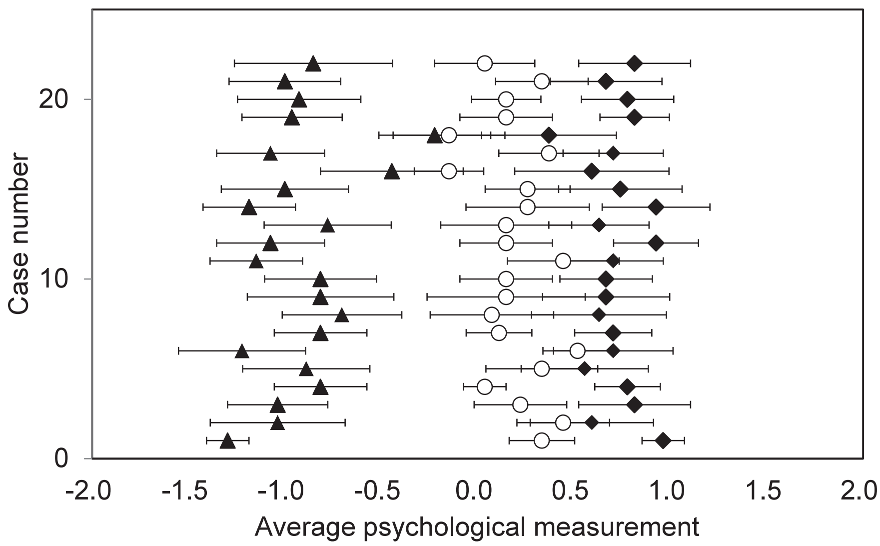

Fig. 4 The results of visual evaluation using Scheffe's paired comparison. The horizontal axis is the average psychological measurement ($\bar{\alpha}$). The greater value means the better visibility of hepatocellular carcinoma lesion. The rhombus (◆), circle (○), and triangle (▲) indicate the ($\bar{\alpha}$) of the revised rainbow, grayscale, and rainbow color map, respectively. Error bars indicate the standard deviation.

rainbow, grayscale, and rainbow. In 15 of the 22 cases, the revised rainbow showed significantly better visibility than the grayscale ($p < 0.05$). No significant differences were found between radiologists and radiological technologists.

The results of ΔE_{00} (Fig. 3) and the visual evaluation (Fig. 4) were consistent. In the cases used in this study, this result showed the same tendency regardless of the HCC size, HCC concentration (CT value), and HCC contrast (difference in CT value between the HCC lesion and liver parenchyma).

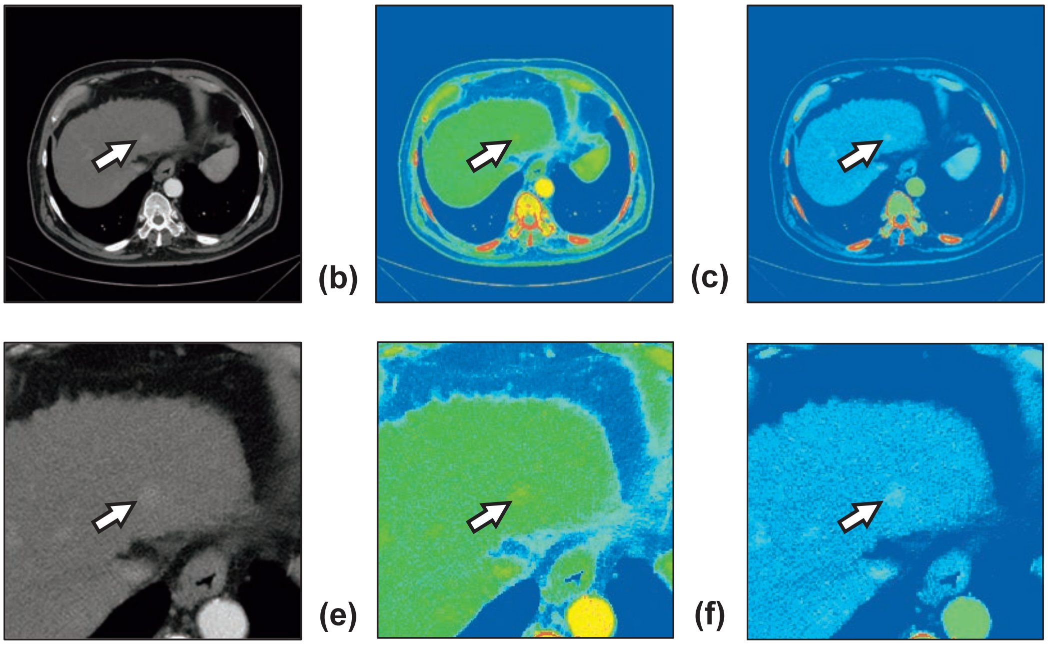

Fig. 5 One of the cases where visibility is significantly improved over the grayscale (a, d). The visibility of hepatocellular carcinoma is significantly reduced in the rainbow (b, e) compared to the grayscale. Meanwhile, the visibility was improved in the revised rainbow (e, f). In all cases, $\overline{\alpha}$ was highest in the order of revised rainbow, grayscale, and rainbow. In 15 of the 22 cases, the revised rainbow showed significantly better visibility than the grayscale ($p < 0.05$).

Discussions

In this study, improvement in the visibility of HCC lesions on CT images by optimal pseudo-colorization based on differences in chromaticity was examined. Rainbow was chosen as a typical color map used in clinical areas in various modalities[15]. ΔE_{00}, as a psychological measure of the rainbow color map, changes significantly compared to grayscale, as shown in Fig. 2. Moreover, some areas were superior or inferior to that of grayscale images. It should be noted that if no revision in the WL setting was performed to display clinical images on the color map, the visibility of the pseudo-color image was consistently lower than that of the grayscale image (Fig. 4) in our observer study. The distribution of ΔE_{00} changed depending on the selected color map and the PV for the target lesion. Our results clearly indicated that insufficient consideration of the characteristics of the color scale may have a risk of inferior visibility compared to grayscale images. Meanwhile, the proposed method is believed to be effective in improving the visibility of lesions with low contrast in grayscale images (Figs. 4 and 5). Therefore, the proposed method is considered one of the methods that aids in image interpretation.

The optimized pseudo-color map is also expandable to other color maps. If a radiologist and/or physician knows which part of the PV corresponds to a questionable lesion, as well as the characteristics of ΔE_{00} for specific color scales, the color scale can be used efficiently to detect lesions. Furthermore, it should be adaptive to any type of lesion with low contrast, such as low-dose CT imaging and CT with less contrast medium, to improve the detection of subtle lesions. In future work, it will be necessary to investigate the reduction in dose and the amount of contrast medium using optimal pseudo-colorization.

When a pseudo-color display is performed based on the target lesion, the appearance of the surrounding tissues may differ significantly from that of the grayscale image. The contrast of adipose tissue was lost, even in the revised rainbow image used in this experiment. This point should be noted, but the same can be said for the interpretation of CT images in conventional grayscale images by adjusting WL/WW. Furthermore, this technique may be useful for screening of lesion. Moreover, optimality colorized pseudo images will also be useful when doctors explain patients' conditions using images to patients and their families who are unfamiliar with medical images.

In a clinical practice, the HCCs are detected and confirmed by contrast-enhanced dynamic CT and MRI. The contrast enhancement differs depending on histological grading. In this study, the target lesions were only early phase contrast-enhanced CT images, and the number of cases was limited. Based on this study, it is necessary to select each histological grading and consider its effectiveness for the improvement of visibility in HCC.

In this study, visual evaluation was performed using the Scheffe's paired comparison method[18]. In the paired comparison method, two samples are selected from the entire set, compared, and the results of all the sample pair combinations are combined to evaluate the entire sample. It is possible to compare images created from two or more systems and rank them according to certain criteria by using paired comparisons. This visual evaluation was performed for the purpose of evaluating the improvement in visibility of cases that are faint and easily overlooked. It is a fact that visibility was improved by using this method, which is useful for interpretation including screening. Conversely, unlike receiver operating characteristic (ROC) analysis and free-response ROC (FROC) analysis[22][23], it is not possible to directly evaluate the accuracy of diagnosis such as lesion detection and differentiation. Further studies are needed on the detectability of pseudo-color images.

In this study, the grayscale image was colorized using general-purpose image analysis software. In addition, a rainbow color map was used. The target lesions were only early phase abdominal contrast-enhanced CT images, and the number of cases was limited. This study has some limitations. Therefore, further investigation is required to establish a new technique for detecting subtle lesions. Additionally, it is necessary to develop an automated method to revise the color map to investigate the reduction in dose and amount of contrast medium using optimal pseudo-colorization.

Conclusions

A promising result was observed in improving the visibility of HCC lesions in early phase abdominal contrast-enhanced CT images by changing the WL based on the difference in the chromaticity pseudo-color map. The proposed method would be useful to help the physician's interpret and explain to the patient by performing optimal pseudo-colorization in addition to of grayscale images.

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（和文抄録）

腹部造影 CT 動脈相における肝細胞癌病変の視認性の向上：最適な疑似カラー画像化の利用

[1)]九州大学病院　医療技術部　放射線部門
[2)]九州大学大学院　医学系学府　保健学専攻　博士後期課程
[3)]九州大学大学院　医学研究院　保健学部門　医用量子線科学分野
[4)]神戸常盤大学　保健科学部　診療放射線学科
[5)]九州大学大学院　医学研究院　臨床放射線科学分野

赤嶺寛地[1)2)]，杜下淳次[3)]，倉本　卓[4)]，濱崎洋志[1)]，寳部真也[1)]，
和田憲明[5)]，石松慶祐[5)]，牛島泰宏[5)]，加藤豊幸[1)]，
石神康生[5)]，佐々木雅之[3)]

【目的】本研究は，腹部造影コンピュータ断層撮影（CT）動脈相における肝細胞癌（HCC）病変の視認性が，rainbow カラーマップを使用した適切な疑似カラー画像化によって改善することを目的とした．

【方法】医用画像表示用液晶ディスプレイに表示される grayscale および rainbow カラーマップの色度を，色彩輝度計を使用して測定した．2017 年 4 月から 2019 年 12 月までに腹部造影 CT 動脈相を撮影された 22 症例の HCC 病変を対象とした．22 症例において，HCC 病変と肝実質の間の色度の違い（ΔE_{00}）を評価した．適切なカラー画像化として，ウィンドウレベル（WL）のみを変更して，HCC 病変のコントラストが Rainbow カラーマップのΔE_{00}の最も高いピクセル範囲に一致するように Rainbow カラーマップを修正した（revised rainbow）．10 名の観察者により Scheffe の一対比較法を用いて 22 症例の HCC 病変の視認性を評価した．提案した手法の有用性を調査するため，grayscale，rainbow，revised rainbow それぞれにおいて，平均嗜好度（$\overline{\alpha}$）を求めた．

【結果】すべての症例において（$\overline{\alpha}$）は，revised rainbow，grayscale，rainbow の順に高かった．これらの結果は，提案手法であるΔE_{00}に基づいた適切な疑似カラー画像化によって，腹部造影 CT 動脈相における HCC 病変の視認性を改善できることを示している．

【結論】腹部造影 CT 動脈相における HCC 病変の視認性は，HCC 病変のコントラストが rainbow カラーマップ上のより高いΔE_{00}のピクセル範囲と一致するように WL 設定のみをシフトすることによって改善された．本提案手法は，さまざまな症例やカラーマップに適用でき，標的病変の視認性を簡単に向上させることができる．

キーワード：疑似カラー画像，視認性，肝細胞癌，CT，造影

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