Temporal subtraction system on torso FDG-PET scans based on statistical image analysis

Yusuke Shimizu*[a], Takeshi Hara[a], Daisuke Fukuoka[b], Xiangrong Zhou[a], Chisako Muramatsu[a], Satoshi Ito[c], Kenta Hakozaki[d], Shin-ichiro Kumita[d], Kei-ichi Ishihara[d], Tetsuro Katafuchi[e], Hiroshi Fujita[a]

[a] Department of Intelligent Image Information, Graduate School of Medicine, Gifu University, 1-1 Yanagido, Gifu 501-1194, Japan;

[b] Faculty of Education, Gifu University, 1-1 Yanagido, Gifu 501-1193, Japan;

[c] Department of Radiology, Daiyukai General Hospital, 1-9-9 Sakura, Ichinomiya, Aichi 491-8551, Japan;

[d] Department of Radiology, Nippon Medical School, 1-1-5 Sendagi, Bunkyo, Tokyo 113-8602, Japan;

[e] School of Health Science, Gifu University of Medical Science, 795-1 Ichihiraga, Nagamine, Seki, Gifu 501-3892, Japan;

ABSTRACT

Diagnostic imaging on FDG-PET scans was often used to evaluate chemotherapy results of cancer patients. Radiologists compare the changes of lesions' activities between previous and current examinations for the evaluation. The purpose of this study was to develop a new computer-aided detection (CAD) system with temporal subtraction technique for FDG-PET scans and to show the fundamental usefulness based on an observer performance study. Z-score mapping based on statistical image analysis was newly applied to the temporal subtraction technique. The subtraction images can be obtained based on the anatomical standardization results because all of the patients' scans were deformed into standard body shape. An observer study was performed without and with computer outputs to evaluate the usefulness of the scheme by ROC (receiver operating characteristics) analysis. Readers responded as confidence levels on a continuous scale from absolutely no change to definitely change between two examinations. The recognition performance of the computer outputs for the 43 pairs was 96% sensitivity with 31.1 false-positive marks per scan. The average of area-under-the-ROC-curve (AUC) from 4 readers in the observer performance study was increased from 0.85 without computer outputs to 0.90 with computer outputs (p=0.0389, DBM-MRMC). The average of interpretation time was slightly decreased from 42.11 to 40.04 seconds per case (p=0.625, Wilcoxon test). We concluded that the CAD system for torso FDG-PET scans with temporal subtraction technique might improve the diagnostic accuracy of radiologist in cancer therapy evaluation.

Keywords: CAD, torso FDG-PET, temporal subtraction, statistical image analysis

1. INTRODUCTION

Diagnostic imaging on FDG-PET scans was often used to evaluate chemotherapy results of cancer patients. Radiologists compare the changes of lesions' activities between previous and current examinations for the evaluation. Temporal subtraction technique between two examinations has been proposed for bone scintigraphy and chest radiography, and its usefulness has been reported in many papers [1-4]. Nie et al. also reported the initial approach of CAD scheme of FDG-PET scan images for lung nodule diagnosis [5]. The purpose of this study was to develop a new computer-aided detection system (CAD) with a temporal subtraction technique for torso FDG-PET scans and to show the fundamental usefulness of the system based on an observer performance study.

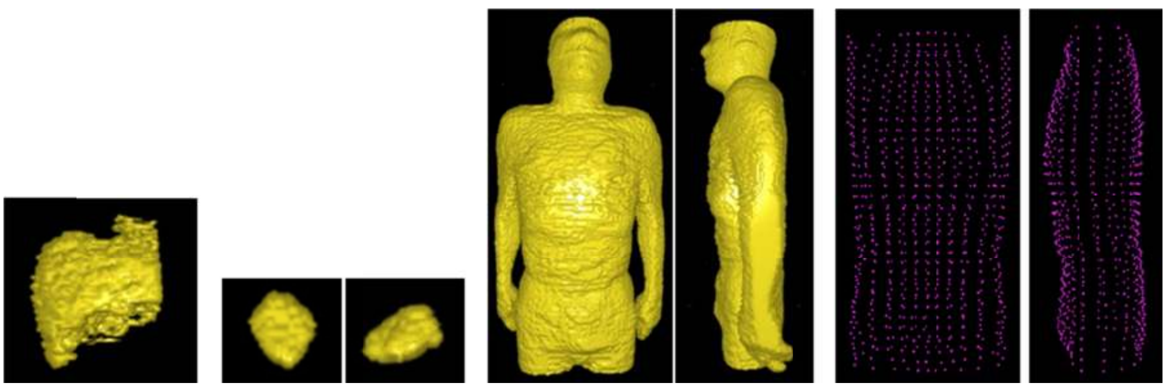
Medical Imaging 2013: Computer-Aided Diagnosis, edited by Carol L. Novak, Stephen Aylward, Proc. of SPIE Vol. 8670, 86703F · © 2013 SPIE · CCC code: 1605-7422/13/$18 · doi: 10.1117/12.2007886

2. METHODS AND MATERIALS

The developed CAD system consists of the following 6 steps: (1) anatomical standardization of normal FDG-PET scans, (2) normal model construction from the normal FDG-PET scans, (3) Z-score mapping based on statistical image analysis, (4) automated detection of abnormal region, (5) comparison of detected regions between previous and current scans, and (6) image subtraction of previous and current scans.

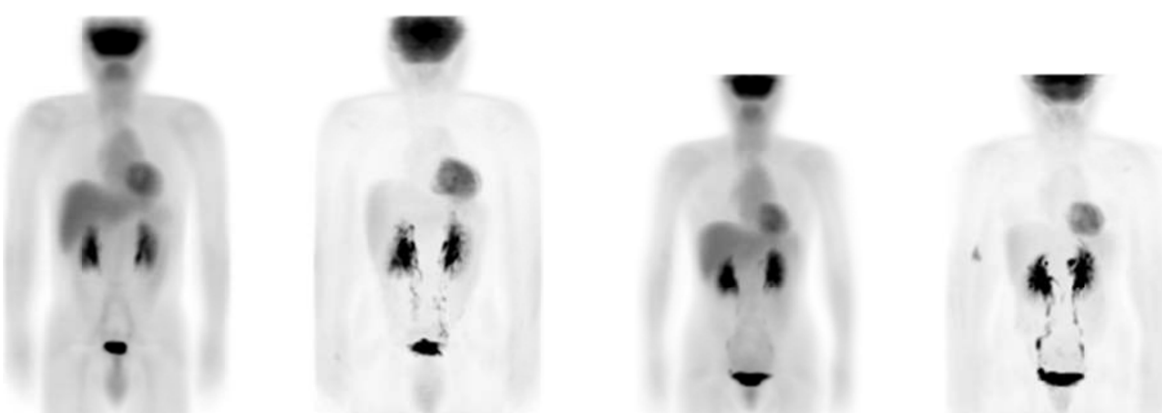
The first step of the anatomical standardization requires a data collection of normal cases. The normal cases were collected from a medical checkup institution for cancer screening by using FDG-PET scans in Japan. All of the normal cases were deformed into a standard body surface after the organs locations of liver, bladder, shoulder, and body surface were recognized based on the image recognition methods at the second step. Fig. 1 shows an example of recognized regions of the surfaces of liver (a) and bladder (b). All of the body shape as shown Fig. 1 (c) was divided into points on the body surface (Fig. 1 (d)) used as landmarks of image deformation by using thin-plate spline (TPS) technique.

The image deformation of many normal cases into one body structure can create two data of mean (*M*) and standard deviation (*SD*) of pixel values in each pixel. The pixel value in the original scan images represents the standard uptake value (SUV) as a quantified index of glucose accumulation. The original SUVs can be converted into statistical values by the *M* and *SD*. Fig. 2 shows the MIP (Maximum Intensity Projection) image of the distribution of *M* and *SD* for male and female.



(a) (b) (c) (d)

Fig. 1 Example of organ and body shape recognition. (a) Liver surface on FDG-PET scan, (b) Two examples of bladder surface, (c) Standard body surface to be deformed, (d) Landmark distribution set on the body surface to deformed by TPS



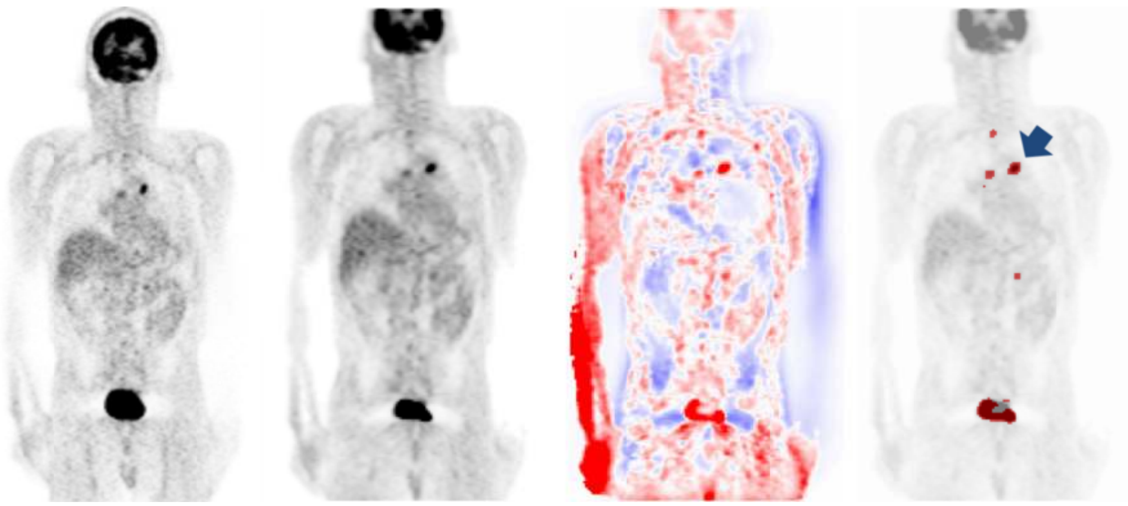
(a) (b) (c) (d)

Fig. 2 MIP images of mean (*M*) and standard deviation (*SD*)

Male: (a) mean and (b) *SD*. Female: (c) mean and (d) *SD*

Patient's scan was also deformed into a standard body shape. An example of an original FDG-PET image and the deformed one are shown in Fig. 3 (a) and (b), respectively. The *M* and *SD* can show the confidence interval of the *SUV* in each pixel, and the Z-score of *SUV* in patients' scans can be obtained as Z-score map on image at the third step. An example of the Z-score image with color map of the same patient is shown in Fig. 3 (c). The Z-score was given by the simple equation (1):

$$\text{Z-score} = \frac{Patient's\ SUV - M}{SD} \tag{1}$$



(a) (b) (c) (d)

Fig. 3 Example of automated detection for abnormal regions

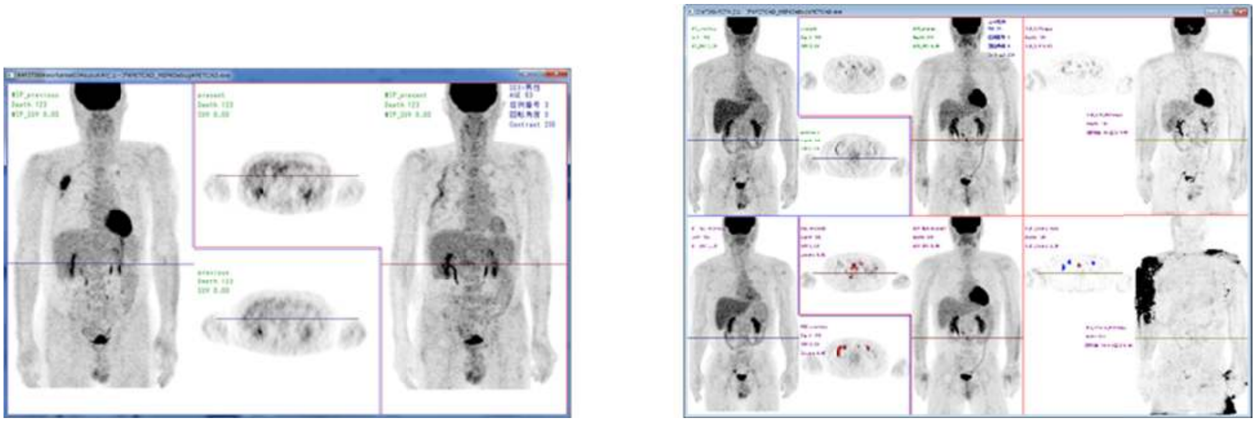
(a) Original image (b) Anatomical standardization image (c) Z-score image (d) Detection results of abnormal regions

An automated detection technique has also been applied to each scan of previous and current examinations independently at the fourth step. The detection technique is based on SUV and Z-score thresholding. An example of a detection result of abnormal region is shown in Fig. 3 (d).

The detected regions were compared between two scans to show the changes of activities. In chemotherapy, the changes of activities were categorized into five of disappearance, decrease, no-change, increase, and appearance. The process at step five gives the category of the change to every detected region. These results were displayed on the subtraction images at the final step. The subtraction image can be obtained based on the anatomical standardization results because all of the patients' scans were deformed into one body shape. The subtraction results show the temporal changes of activities and the automated detection results provide a color map to indicate the category of activity changes on the subtracted image.

Observer performance study based on ROC (receiver operating characteristics) was performed without and with the computer results to investigate the usefulness of the CAD scheme. Readers responded a confidence of activity changes between two scans from absolutely no change to definitely change on a continuous scale. An example of viewer without computer outputs is shown in Fig. 4 (a). The viewer without computer outputs provided two examinations of the previous scans on the left and the current ones on the right. An example of viewer with computer outputs is also shown in Fig. 4 (b). The viewer with computer outputs provided the detection results of abnormal region and the subtraction images based on SUV and Z-score in addition to the viewer without CAD. Observer asked to interpret the cases with the MIP and axial images with patient’s informations of gender and age. SUVs and Z-scores were also displayed by pointing the location on image by the mouse device during the interpretations.

To measure the interpretation time, an independent method for ROC study was employed.



(a) (b)

Fig. 4 Example of viewer (a) without computer outputs and (b) with computer outputs

In this study, FDG-PET images scanned by Discovery LS (GE Healthcare) were employed. The number of image matrix and slices were 128 x 128 pixels (4.3 mm spatial resolution) and 195 - 259 slices (4.25 mm slice thickness), respectively.

We employed 43 pairs of torso FDG-PET scans using computer performance evaluation. All of the cases were verified by a board-certificated radiologist on nuclear imaging. The numbers of normal cases for the normal model composition were 143 (male) and 100 (female). The normal cases were also verified by the radiologists.

Four radiology residents took part in the observer performance study. The scan images of 43 patients who underwent the cancer treatments of surgical or chemotherapeutic procedures were collected to evaluate the automated detection system of abnormal regions. Additional 60 pairs (32 regional changes and 28 regional no changes) were collected for the observer performance study.

3. RESULT

The recognition performance for the 43 pairs was 96% in sensitivity with 31.1 false-positive (FP) marks per scan. Fig. 5 shows an example that the system correctly detects abnormal regions in the mediastinum and the clavicle.

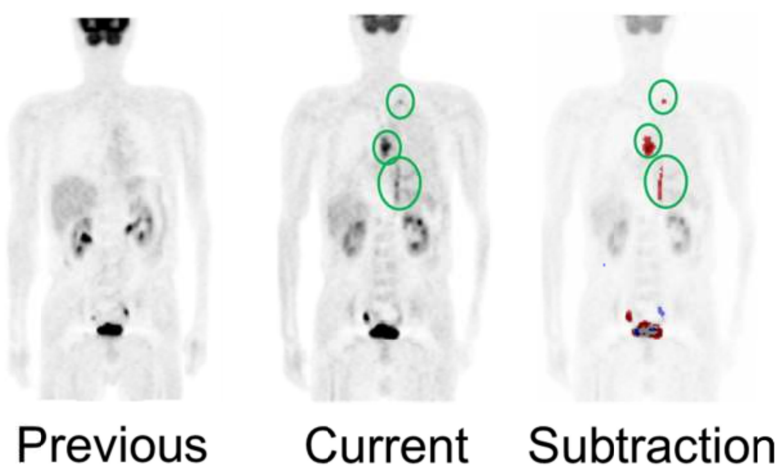


Fig. 5 Automated detection results on current and subtraction image

The average of area-under-the-ROC-curves (AUCs) from 4 readers was increased from 0.85 without computer outputs to 0.90 with computer outputs (p=0.0389, DBM-MRMC). The average of interpretation time was slightly decreased from 42.11 to 40.04 seconds per case (p=0.625, Wilcoxon test). Fig. 6 shows the ROC curves (a) without and (b) with computer outputs for 4 readers. Fig. 7 indicates a case of nasopharyngeal carcinoma, which was treated to the patient in one year. The confidence level of Reader 2 was increased from 0% to 100% in this case.

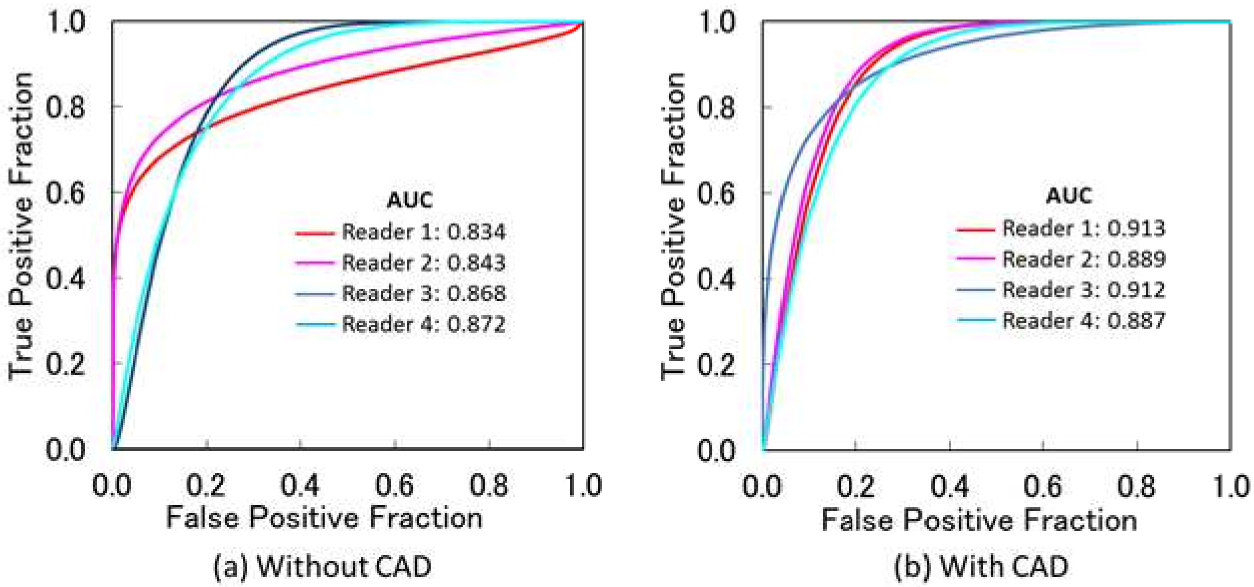


Fig. 6 ROC curves and AUCs for four readers without (a) and with (b) computer outputs

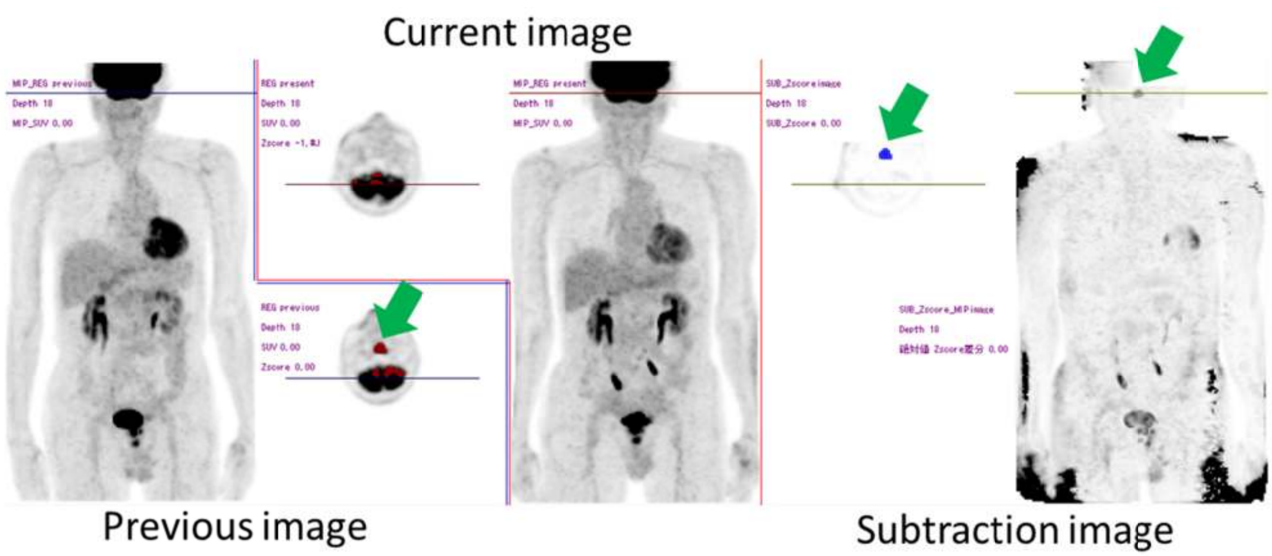


Fig. 7 An example of CAD beneficial case

4. DISCUSSIONS AND CONCLUSIONS

As shown on the example case in Fig. 7, readers missed the change of abnormal region and disappearance. The high activities of FDG in brain might conceal the abnormal regions, but the temporal subtraction image of Z-score revealed the activities difference between previous and current scans. The change was not confirmed on the temporal subtraction image of SUV. The recognition help of precise activities changes will be required for some kind of cancer therapy such as malignant lymphoma, because the amelioration of the diseases was obtained by the disappearance of all abnormal regions.

We supposed that the reading time would increase because readers had to compare their opinions with computer outputs, but the actual reading time measured by the independent observer study method was slightly decreased when readers used the computer outputs. Statistical significance was not confirmed between without and with computer outputs. These results implied that the computer outputs would not disturb the interpretation procedures during the comparison of abnormal regions.

In conclusion, our CAD scheme developed for torso FDG-PET scans with temporal subtraction technique may improve the diagnostic accuracy of radiologists in cancer therapy evaluation.

ACKNOWLEDGMENTS

The authors thank members of the Fujita Laboratory for their valuable discussions, and grateful to Daiyukai General Hospital staffs. This research was supported in part by Grants-in-Aid for Scientific Research on Innovative Areas(Computational Anatomy for Computer-aided Diagnosis and Therapy: 21103004) and Grants-in-Aid for Scientific Research (C: 23591802, 24500543), Ministry of Education, Culture, Sports, Science and Technology, Japan, Technology Regional Innovation Cluster Program (City Area Type) in Southern Gifu Area "Development of Advanced Medical Equipment Using Manufacturing Technologies and Information Technologies," and research grants from Gifu University.

REFERENCES

[1] Kano A, Doi K, MacMahon H, et al., "Digital image subtraction of temporally sequential chest images for detection of interval change," Med Phys, 21(3), 453-61(1994).
[2] Ishida T, Ashizawa K, Engelmanm R, et al., "Application of temporal subtraction for detection of interval changes on chest radiographs: improvement of subtraction images using automated initial image matchings," Journal of Digital Imaging, 12(2), 77-86(1999).
[3] Kawamura S, Fukushima S, Yoshinaga Y, et al., "An Attempt of Temporal Image Subtraction Technique on Bone Scintigraphy," Japanese Journal of Radiological Technology, 60(2), 299-302(2004).
[4] Shiraishi J, Li Q, Appelbaum D, et al., "Development of a computer-aided diagnostic scheme for detection of interval changes in successive whole-body bone scans," Med Phys 34(1), 25-36(2007).
[5] Y. Nie, Q. Li, F. Li et al., "Integrating PET and CT information to improve diagnostic accuracy for lung nodules: A semiautomatic computer-aided method," J Nucl Med, 47(7), 1075-80 (2006).