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Original Article

Improving technetium-99m methylene diphosphonate bone scan images using histogram specification technique

ABSTRACT

In this study, we have proposed and validated that histogram of a good-quality bone scan image can enhance a poor-quality bone scan image. The histograms of two good-quality technetium-99m methyl diphosphonate bone scan images I_A and I_B recommended by nuclear medicine physicians (NMPs) were used to enhance 87 poor-quality bone scan images. Processed images and their corresponding input images were compared visually by two NMPs with scoring and also quantitatively using entropy, Structural similarity index measure, edge-based contrast measure, and absolute brightness mean error. Barnard's unconditional test was applied with a null hypothesis that the histogram of both I_A and I_B produces similar output image at α =0.05. The mean values of quantitative metrices of the processed images obtained using I_A and I_B were compared using Kolmogorov–Smirnov test. Histogram of a good-quality bone scan image can enhance a poor-quality bone scan image. Visually, histogram of I_B improved statistically significantly higher proportion ($P < 0.0001$) of images (86/87) as compared to histogram of I_A (51/87). Quantitatively, I_B performed better than I_A, and the Chi-square distance of input and I_B was smaller than that of I_A. In addition, a statistically significant ($P < 0.05$) difference in all the quantitative metrics among the outputs obtained using I_A and I_B was observed. In our study, reference histogram of good-quality bone scan images transformed the majority of poor-quality bone scan images (98.85%) into visually good-quality images acceptable by NMPs.

Keywords: Histogram specification, image enhancement, technetium 99m methyl diphosphonate bone scan

INTRODUCTION

Technetium-99m methyl diphosphonate (Tc-99m MDP) bone scan plays an important role in the diagnosis and staging of benign and malignant bone diseases. Most of the referrals for Tc-99m MDP bone scans come for the diagnosis of metastatic diseases such as primary (e.g., Ewing's sarcoma and osteosarcoma) and secondary tumors for staging; evaluation of response to therapy and follow-up; and metabolic disorders such as Paget disease, osteoporosis, skeletal trauma, iatrogenic trauma, stress fractures, shin splints, osteomyelitis, bone infarction, osteonecrosis, and prosthesis evaluation (loose or infected joint prosthesis). The scan is performed 3–4 h after the administration of Tc-99m MDP.[1] The acquired images are then displayed on monitors for visualization purpose.[2] Clinical utility of the scans may be limited by the quality of the acquired image, and often the only enhancement option available, i.e., nuclear medicine physicians (NMPs), may be a window-level adjustment tool to interactively modify contrast and brightness.

The window-level adjustment tool scales the displayed intensity values of the image (brightness) and absolute versus

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relative intensities (contrast) linearly with respect to the display attributes of the device (monitor). The slider provided lets the user adjust to the "optimal" or preferred rendering of the image, where one may be best satisfied about the displayed attributes of the image.

A tool as above has undoubtedly changed the original intensities of pixels, to produce another temporary version of the image that is opted by the user. However, such change has been linear, that is, the amount of change per pixel is uniformly distributed over all pixels as follows:[2]

$$r = \begin{cases} \beta I, t \le I \le t + w \\ 0, I < t \\ Q, I > t + w \end{cases} \quad (1)$$

with $\beta = Q/W$.

Where "*r*" is gray-scale value, "*I*" is pixel intensity, "*t*" is intensity threshold level, "*w*" is window width, and "*Q*" is available gray-scale range of the display monitor which is normally in the range of 0–255.

The linearity of the above system limits the enhancement that may be possible in an image. However, a nonlinear change, that is, the one that adjusts the pixel intensities nonuniformly over the set of all pixels may eventually produce a better enhancement, without creating in any artifacts. In such a case, finding which pixels should be changed in what way may be a difficult question to answer.

A pragmatic way to answer the above question is to consider a similar image (of same radiopharmaceutical and organ), which has all the "good-" quality attributes, and use it as a model to emulate. The description of the global distribution of intensities in such model image can be used as a guide in the enhancement process of another image. In other words, the histogram from an image selected by NMPs as a "good-quality image" could be used to guide the enhancement.[3,4]

Several studies have found encouraging enhancement in images using such a method, but the question of how to identify an appropriate histogram to lead the process has not been sufficiently explored or documented. In this study, we have focused on selecting an appropriate histogram for the purpose and compared the results produced by two such different selected histograms on the same dataset.

MATERIALS AND METHODS

All bone scan images included in the study were acquired using a dual-head SPECT gamma camera (Symbia E, Siemens Medical Solutions Inc., IL USA) equipped with low-energy, high-resolution collimator. Before the administration of Tc-99m MDP, patients were instructed to drink at least 1 to 2 L of water and void their bladder frequently in order to reduce the radiation burden in the body. 7–11 MBq Tc-99m MDP per kg body weight was administered intravenously. After a waiting period of 3–4 h, the whole-body bone scan was acquired with both anterior and posterior views with a table speed of approximately 1.66×10^3 m/s, zoom of 1.0, and resolution of 256×1024 pixels.

Selection of images to be used as model images

Bone scan images acquired during January to June 2017 in our facility were exported in DICOM format. An in-house personal computer-based application program was used to convert the images in *PNG* format, which were then visually inspected on a personal computer (having Windows 7 Home Basic [copyright© 2009 Microsoft Corporation], 64-bit operating system, 2 GB RAM, and Intel® Core™ i3, 2120 CPU at 3.30 GHz processor). As in our facility about twenty bone scans are done per day, and data were collected for 6 months, approximately 2400 bone scan images were inspected. We visually assessed the quality of these unprocessed bone scan images and sorted these images in descending order based on their image quality. In this way, we selected a set of fifty best bone scan images. These fifty images were finally reviewed by two NMPs, out of which two best-quality bone scan images, "image A and image B," were selected [Figure 1].

Image data set selection for enhancement as per our proposition

Among the thousands of images available, about a hundred were selected on the basis of poor image quality. The images having the following characteristics were considered as poor-quality images:

1. Images having poor counts, may be due to less dose injected
2. Images appearing dark due to dose extravasation or bladder activity and
3. Images in which parts of skeleton were not properly visible.

Eighty-seven poor-quality bone scan images were shortlisted for this experiment as per the advice of NMPs, within the constraints of their review time.

Enhancement of the images using histogram of images A and B

The output image for each of the 87 input images was obtained as below:

1. Histogram of input image (*I*) was equalized using cumulative density function (CDF) CDF_I
2. CDF of reference image () was calculated for both images A and B

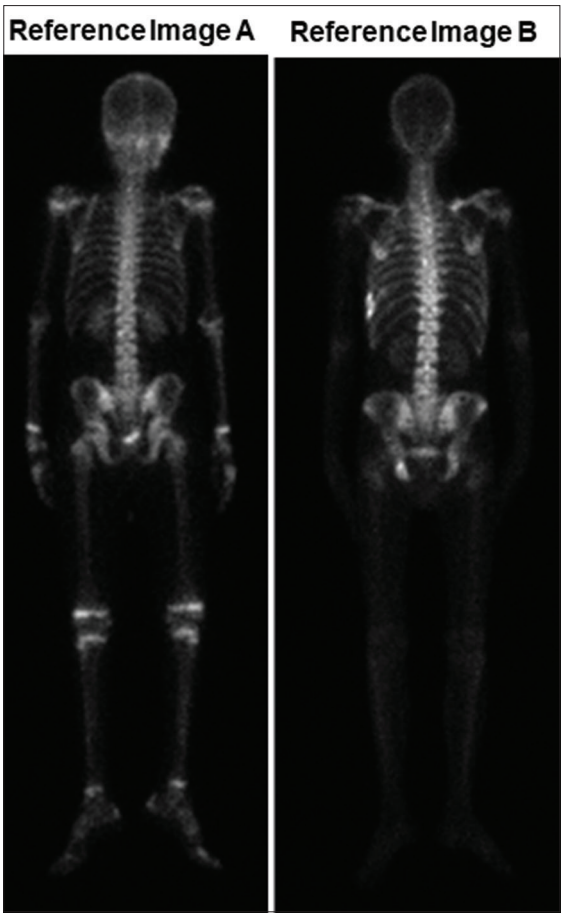

Figure 1: Reference image A and reference image B

3. Finally, the output image I' having the histogram that matches the histogram of reference image (images A and B) I_{ref} was calculated using Eq. (1) as given below:[5]

$$I'(x,y) = CDF_{I_{ref}}^{-1}\left\{CDF_{I}\left(F(x,y)\right)\right\} \quad (2)$$

The input bone scan images were processed twice, once using image A and second time using image B as reference image. This resulted in a total of 184 processed images. A Matlab script was written for this task.

Output image quality assessment – qualitative and quantitative

Qualitative assessment

The inputs and their corresponding processed images as obtained above were displayed side by side on a personal computer and two NMPs independently reviewed them under normal ambient lighting condition. The NMPs visually compared the input images with their corresponding output images and marked the output image with labels IMPROVED (Score 1) and NOT-IMPROVED (Score 0). The label IMPROVED was assigned when output image quality was better than the input image, i.e., in output image, the long bones, ribs, spines, and metastatic sites visually appeared better in comparison to the input image. The label NOT-IMPROVED was assigned when output image was either visually similar to the input image or had become inferior to the input image. Their responses were recorded for analysis.

In cases where there was a difference in the scores of both NMPs, the images were again reviewed collectively by the NMPs, to assign a score by consensus.

Quantitative assessment

Entropy, Structural SIMilarity index measure (SSIM), edge-based contrast measure (EBCM), and absolute brightness mean error (ABME) were used to calculate the enhancement produced in output images.[6-8]

Statistical analysis

Inter-rater agreements between two observers were performed using kappa statistics. Barnard's unconditional test was applied with a null hypothesis that the number of images improved using reference images A and image B which are same at $\alpha = 0.05$ using the package "Barnard," installed with free software R version 3.4.1 (R foundation for statistical computing, Vienna, Austria).[9]

The image enhancement was quantified using the metrics mentioned above. The mean values of all the metrics were compared among the output images processed with the reference images A and B using Kolmogorov–Smirnov test. $P < 0.05$ was considered statistically significant.

RESULTS

Images A and B and their intensity histograms that were used in this study are depicted in Figures 1 and 2, respectively. Image quality assessment of output images was done both qualitatively and quantitatively. The respective proportions of the images improved by reference images A and B were also compared.

Results of qualitative assessments

There was an excellent agreement between the scores of both observers with kappa equals to 0.718 for scores of output images generated using reference image A and 1.00 for reference image B [Table 1]. The discordance was found in only 12 images processed with the reference image A. These 12 images were again reviewed by the NMPs jointly and with the consensus of both, out of the 12 images, 7 were kept in "improved" category and 5 were kept in "not improved" category. The number of images labeled with improved or not improved (by consensus of both the NMPs) for both the reference images is summarized in Table 2.

The number of images improved by reference image B was statistically significantly higher (86/87) than that using reference image A (51/87), at $\alpha = 0.05$ with $P < 0.0001$.

Table 1: The concordance in the scores given by both observers with the values of corresponding Kappa values

Scores by observer 1	Scores by observer 2			κ
	Not improved (0)	Improved (1)	Total images	
Concordance in scores by both observers for reference image A				
Not improved (0)	31	8	39	0.718
Improved (1)	4	44	48	
Total Images	35	52	87	
Concordance in scores by both observers for reference image B				
Not improved (0)	1	0	1	1.000
Improved (1)	0	86	86	
Total images	1	86	87	

Table 2: Total number of images labeled as improved or not improved for both reference images A and B

	Frequency (%)	
	Reference image A	Reference image B
Not improved	36 (41.37)	1 (1.15)
Improved	51 (58.62)	86 (98.85)
Total	87 (100)	87 (100)

Figure 3 depicts the representative input images with the corresponding output images, which were enhanced by reference image B.

There were 35 images which were not improved by reference image A but improved by reference image B [representative image is given in Figure 4: Image 1]. The quality of one image was not improved by either of the reference images [Figure 4: Image 2]. In this image, the application of the method increased the brightness, but still the quality of image was not considered sufficient for reporting by the NMPs. Hence, it was considered in the "Not Improved" category for both reference images. Out of 87 images, 51 images were improved by both the reference images [Figure 5 shows such an image].

Results of quantitative assessment

Entropy, EBCM, SSIM, and ABME were computed for the input and output images to have an insight into how the images changed after the enhancement process.

Entropy

The discrete entropy of gray-level images is a statistical measure of randomness that is used to characterize an

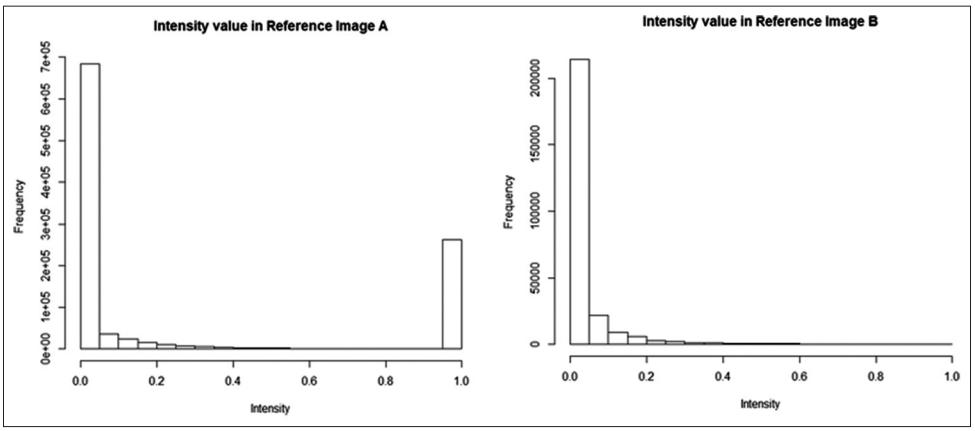

Figure 2: Intensity histograms of reference images A and B

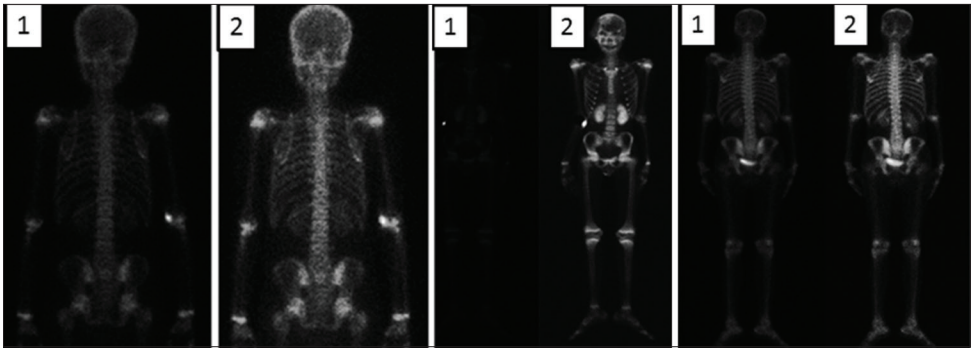

Figure 3: Images marked as "1" are the input images and images marked as "2" are the corresponding output images generated using the intensity histogram of reference image B

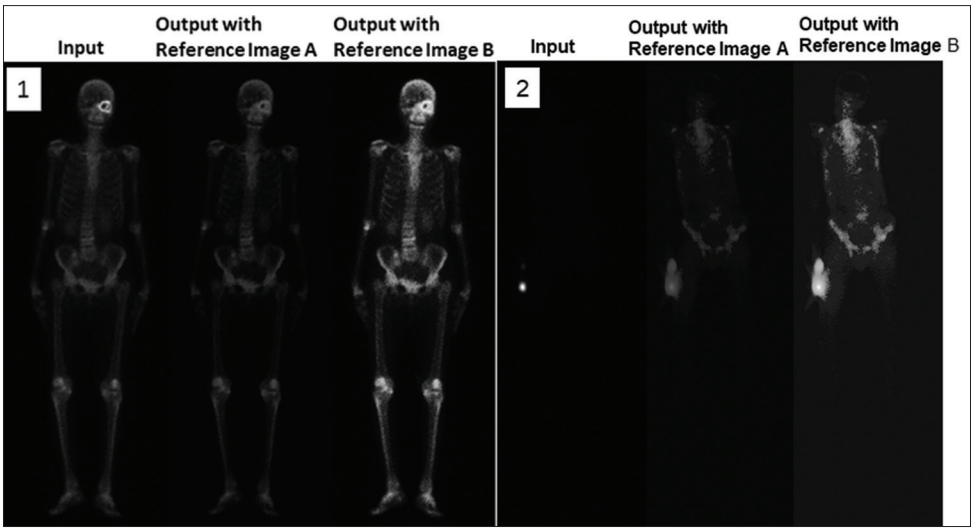

Figure 4: Input and corresponding output images along with their intensity histograms. Image 1 shows the input image and its two output images. The input image is not improved by intensity histogram of reference image A but is improved by the intensity histogram of reference image B. Image 2 shows that there was no improvement in the quality of input image by either of the intensity histograms

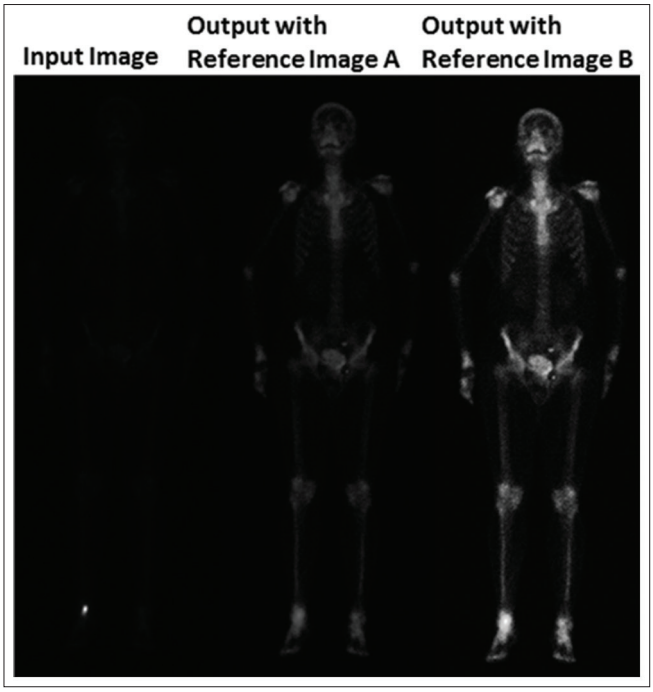

Figure 5: Input image and the corresponding output images obtained using reference images A and B. The input image is improved by both

average amount of information conveyed from the image. The computation of entropy shows that the entropy of the output images decreased in both cases of reference images A and B. The mean difference in entropy between the input and output images was found to be significantly higher for images processed using reference image A [Table 3].

Entropy of an enhanced image normally remains lower than that of the original image, as no extra information is ever added to the image in a true sense. Nevertheless, targeting for entropy to remain as close as possible to the original entropy, is always preferred because the information content is further preserved by doing so. This means that the lower the difference in entropy between the input and output images, better is the image enhancement process. The image modified by reference image B shows a significant preservation of entropy without introduction of any new distortion as compared to the image modified by histogram of image A.

Edge-based contrast measure

Entropy does not measure or convey local enhancement of the image. EBCM is used to measure local detail enhancement. Image with higher contrast is expected to have larger EBCM value. The obtained EBCM values for reference images A and B are compared and are summarized in Table 3. The mean value of EBCM is significantly higher for images processed using reference image B as compared those processed using reference image A [Table 3].

Structural similarity index measure

SSIM is a perception-based measure which models image degradation as perceived change in structural information incorporating important perceptual phenomena such as both luminance-masking and contrast-masking terms. Structural information is based on the idea that the pixels have strong inter-dependencies, especially when they are spatially close. These dependencies carry important information about the structure of the objects in the visual scene. Luminance masking is a phenomenon whereby image distortions tend to be less visible in bright regions, whereas contrast masking is a phenomenon whereby distortions become less visible where there is significant activity or "texture" in the

Table 3: Description of the four matrices for the output images using reference images A and B along with the results of Kolmogorov-Smirnov test on 87 input images

Parameter (n=87)	Mean±SD		*P*	*D*
	Reference image A	Reference image B		
Difference in entropy from input image	0.4258±0.32	0.1890±0.20	2.061e-08	0.45977
EBCM	−0.14444±0.13	2.607±0.45	6.661e-16	1
SSIM	0.75168±0.24	0.65214±0.32	0.04801	0.2069
AMBE	2.65888±2.64	7.76460±6.58	2.776e-15	0.6092

SD: Standard deviation; EBCM: Edge-based contrast measure; SSIM: Structural similarity index measure; AMBE: Absolute mean brightness error

image. The mean values of SSIM were found to be higher for images processed using reference image A as compared those processed using image B. This shows that the structural details of input images were more preserved in case of reference image B as compared to A [Table 3]. The same was observed visually, that is, when SSIM value was higher, the input and output images looked visually different, and when SSIM value was lower, the input and output images were structurally similar.

Absolute mean brightness error

Absolute mean brightness error (AMBE) indicates the deviation of the mean intensity of the enhanced image from the mean intensity of the original image. We calculated it by finding the absolute difference between the mean intensity of output and input images.[6] The mean intensity was calculated as the sum of all pixel values divided by a number of pixels in the image. Lower AMBE indicates that the brightness is better preserved. We found that the mean value of AMBE is significantly higher in the images processed with reference image B as compared to reference image A. Thus, images processed with the histogram of reference image B were brighter as compared to those processed using image A [Table 3].

Kolmogorov-Smirnov test was used to find out whether the difference in parameters (SSIM, Difference in entropy from input image, AMBE and EBCM) between input image and images processed with reference image A and B is significant. The result of the test is summarized in Table 3.

Figure 6 shows two input images and their corresponding output images obtained using reference images A and B, along with the value of the above four quantitative measures. It can be observed from Figure 6 that the images processed using reference image B are structurally more or less similar to the input image (the distortion is present but has not hampered the clinical details required by the NMPs. This was true for all input images). However, the output images are brighter and have better local contrast than input images. Similar observations were recorded by NMPs in 86 processed images out of 87 images using reference image B, and the 86 images were labeled as "improved" by both NMPs.

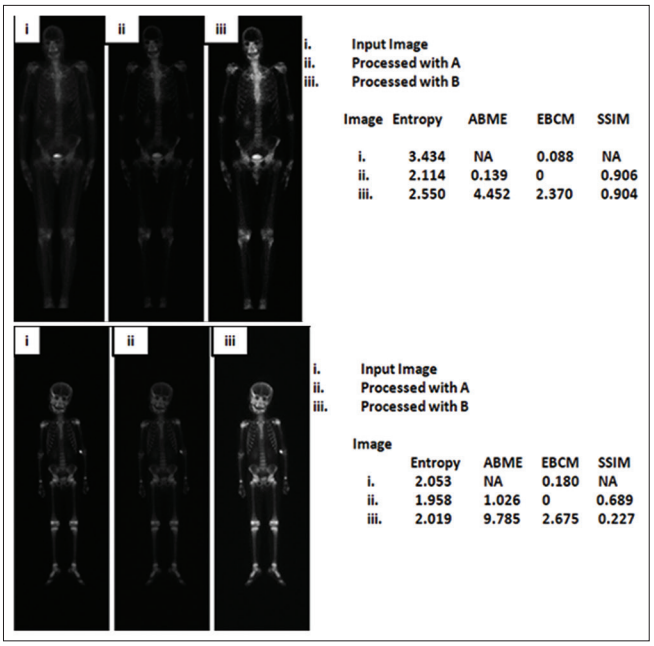

Figure 6: Two input and their corresponding output images obtained using reference images A and B, along with the value of quantitative measures: entropy, absolute brightness mean error, edge-based contrast measure, and Structural SIMilarity index measure

The results of our study showed that the reference image B performed better than reference image A. In order to investigate the reason behind this, the Chi-square distance between input and reference images A and B was evaluated. The smaller is the Chi-square distance, the more similar are the histograms of the images.[10] Figure 7 depicts Chi-square distance between the histograms of the input image and the histogram of reference images A and B. It can be seen from Figure 7 that the histogram of all input images had better similarity to that of the reference image B (Chi-square distance <0.2), as compared to that of reference image A (Chi-square distance ≥ 0.4). Interestingly, this indicates that there may be a clue to selecting the reference image itself – if the Chi-square distance between the histogram of input and reference image is smaller, the histogram of output image will be closer to the histogram of the reference image and there may be good enhancement. The histogram (numerical details) of the reference image B is depicted in Table 4 as a suggestion.

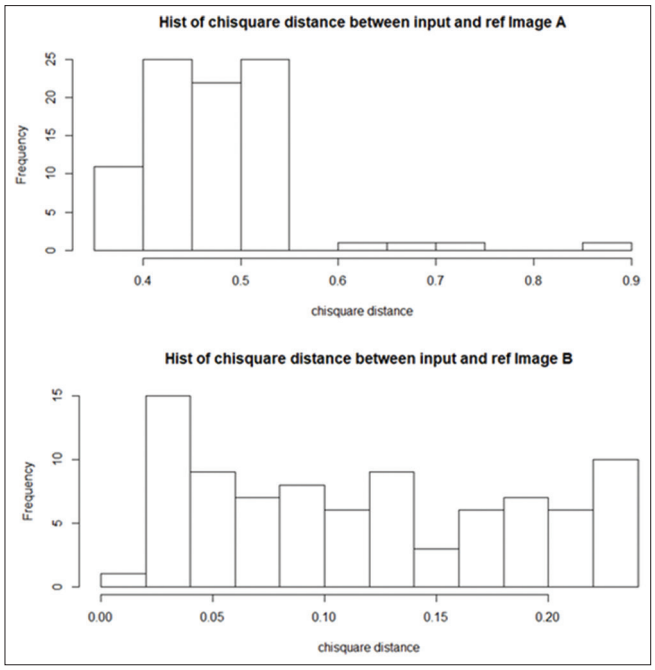

Figure 7: Histograms of Chi-square distance between input images and reference images - image A: Chi-square distance between the histogram of input images and the reference image A was ≥0.4. Image B: Chi-square distance between histogram of input images and the reference image B was <0.2

Table 4: The histogram data of reference image B

X (mids)	Frequency (h1.counts)	*P* (*x*) nh1
0.01	219,149	0.835987
0.03	15,628	0.059616
0.05	8942	0.034111
0.07	5778	0.022041
0.09	3017	0.011509
0.11	2847	0.01086
0.13	1873	0.007145
0.15	1595	0.006084
0.17	892	0.003403
0.19	1061	0.004047
0.21	558	0.002129
0.23	443	0.00169
0.25	166	0.000633
0.27	80	0.000305
0.29	47	0.000179
0.31	31	0.000118
0.33	16	6.10E-05
0.35	11	4.20E-05
0.37	9	3.43E-05
0.39	1	3.81E-06

DISCUSSION

In this study, we have processed 87 poor-quality Tc-99m MDP bone scan images using histogram specification. The histograms of two good-quality bone scan images (reference images A and B) recommended by NMPs were used. The histogram of reference image B improved the quality of 98.85% (86 out of 87) of images included in this study, whereas the histogram of reference image A could only improve the quality of 58.62% (51 out of the 87) of images. The experiment with this technique resulted an image of diagnostic quality that does not need further processing. The processed images retained good similarity to the original input image. Further, post this enhancement process, no artifacts were noticed qualitatively. In addition, quantitative measures support the enhancement by the technique.

The visual image quality of reference image A is better than that of reference image B. In image A, spines and long bones are clearly visible in comparison to image B. In image B, upper half of the whole-body image is very bright and details are very clear, however the long bones are not clearly visible. Hence, initially looking at both the reference images visually, we speculated that the histogram of reference image A might improve the image quality better than image B and might also improve significantly larger proportions of images out of the 87 images. But interestingly, the results of our study showed that the histogram of reference image B worked better (improved 86 out of the 87 images) than the histogram of reference image A (51 out of the 87).

In the study done by Gonzalez *et al*.,[3] they observed that "There are no rules for specifying histograms, and one must resort to analysis on a case-by-case basis for any given enhancement task. Selection of the shape of histogram is a challenging task which involves trial-and-error process." In yet another study, Coltuc *et al*.[11] had studied the exact histogram specification method for improving the contrast of the image and concluded that "Exact histogram specification guarantees that the histogram of the image obtained after enhancement is almost exactly the desired one. However, there does not exist any obvious choice for the desired histogram."

A re-examination of the attributes of our reference images and input data revealed that there appears a relationship between the histograms of input and reference images. It was found that the Chi-square distance between the histograms of input images and that of reference images A and B was, respectively, ≥0.4 and <0.20, that is, the Chi-square distance for reference image B was smaller. Chi-square distance is a measure of the similarity between histograms. It is established that the smaller is the Chi-square distance, more similar are the histograms.[10] Correspondingly, the images processed with the histogram of reference image B were visually more acceptable to physicians. This suggests that when the Chi-square distance between input images and the

reference images is small, the probability of images getting improved may be high.

In the past, studies have been done to improve the quality of bone scintigraphic images.[12-18] Various other authors[3,19] have also worked on the digital image processing and tried to improve the quality of these images by using histogram specification.

Gonzalez *et al*.[20] have developed the mathematical framework for histogram specification and included the experimental results, which establishes the superiority of the histogram specification over histogram equalization. For specifying the histogram, they have used the following four parameters: mean (m), height (h) at m, left spread (SL) about m, and right spread (SR) about m. These parameters can be controlled by a joystick with four degrees of freedom and used to establish a piece-wise linear approximation to the desired density. Thus, hardware control is used for specifying the histogram interactively. Coltuc *et al*.[11] have addressed the problem of finding a transformation for a discrete image so that its histogram *exactly* matches the specified histogram. Jeong *et al*.[13] have used the exact histogram specification method developed by Coltuc *et al*. and, on comparison among six different histogram equalization methods, have found exact histogram matching as the best method of image enhancement based on histograms for diagnosing successive whole-body bone scans. Frei[21] had explored the use of histogram specification procedures that produced enhanced images possessing exponential or hyperbolic-shaped histograms. Ketcham[22] and Hummel[23] have demonstrated improved results by an adaptive histogram specification procedure. Pavithra *et al*.[4] have addressed the issues of the shape and characteristics of the histogram that play a major role in the image enhancement using histogram specification. They have proposed to use histogram of the target image which is obtained by the fusion of multiple high-resolution and noise-free images having a wide range of gray values. Their results showed that histogram specification with target images of same category provides better result.

In our study, we have used histogram of the target image which is obtained by visual selection of a good-quality bone scan image to enhance the bone scan image. Moreover, we have demonstrated that a single-target histogram (whose Chi-square distance was ≤0.20) enhances the image quality of the majority of input images. Our approach is similar to the study conducted by Pavithra *et al*.[4] because both have used histogram of a single-target image, however the method used to obtain the target image is different.

It can be speculated that if Chi-square distance between the reference image and the histograms of input images is ≤0.20, poor-quality bone scan images transformed using such reference image may always be of good quality and acceptable to NMPs. Another study to verify this would be our future plan. Besides, we would like to apply the same technique for the scintigraphic images acquired with various other radiopharmaceuticals and collimators, for a wider evaluation and verification.

CONCLUSION

In our study, reference histogram of good-quality bone scan images transformed the majority of poor-quality bone scan images (98.85%) into visually good-quality images acceptable by NMPs. Further, Chi-square distance between input and reference images may be a mechanism for selecting appropriate reference image.

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Conflicts of interest
There are no conflicts of interest.

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