Classification of Regional Radiographic Emphysematous Patterns Using Low-Attenuation Gap Length Matrix

Kok Liang Tan *, Toshiyuki Tanaka *, Hidetoshi Nakamura **, Toru Shirahata ***, and Hiroaki Sugiuira **

Abstract: The standard computer-tomography-based method for measuring emphysema uses percentage of area of low attenuation which is called the pixel index (PI). However, the PI method is susceptible to the problem of averaging effect and this causes the discrepancy between what the PI method describes and what radiologists observe. Knowing that visual recognition of the different types of regional radiographic emphysematous tissues in a CT image can be fuzzy, this paper proposes a low-attenuation gap length matrix (LAGLM) based algorithm for classifying the regional radiographic lung tissues into four emphysema types distinguishing, in particular, radiographic patterns that imply obvious or subtle bullous emphysema from those that imply diffuse emphysema or minor destruction of airway walls. Neural network is used for discrimination. The proposed LAGLM method is inspired by, but different from, former texture-based methods like gray level run length matrix (GLRLM) and gray level gap length matrix (GLGLM). The proposed algorithm is successfully validated by classifying 105 lung regions that are randomly selected from 270 images. The lung regions are hand-annotated by radiologists beforehand. The average four-class classification accuracies in the form of the proposed algorithm/PI/GLRLM/GLGLM methods are: 89.00%/82.97%/52.90%/51.36%, respectively. The p-values from the correlation analyses between the classification results of 270 images and pulmonary function test results are generally less than 0.01. The classification results are useful for a followup study especially for monitoring morphological changes with progression of pulmonary disease.

Key Words: CT image, low-attenuation gap length matrix, regional features, regional emphysema type, neural network.

1. Introduction

The primary risk factor for Chronic Obstructive Pulmonary Disease (COPD) is chronic tobacco smoking. The pathophysiology of COPD includes emphysema. Emphysema is defined histologically as the enlargement of the air spaces distal to the terminal bronchioles, with destruction of their walls [1]. Radiologists diagnose emphysema based on visual recognition of the radiographic pattern of emphysema alongside reference to pulmonary function tests (PFTs) results. However, radiographic patterns observed from computer tomographic (CT) image are often varied and subtle and that human observers do not usually see early abnormal lung pathology on CT images [2].

Many papers have proposed objective methods of quantification of emphysema by focusing on the overall lung density histogram (number of pixels falling below a threshold) [3] in the image. The classical computer-based methods used for assessing the severity of emphysema are those employing pixel the image. The classical computer-based methods used for assessing the severity of emphysema are those employing pixel values lower than a certain limit value [4]. Pixels below the limit are thought to be air-filled lung regions. PI describes the amount of air presented in the CT and thus detects the extent of emphysematous lesions [5]. MLD [6] represents the fifth or tenth percentile of the CT histogram data [7]. Although PI and MLD methods are still widely used for quantifying emphysema severity, they are not expressive for differentiating regional radiographic emphysematous patterns due to averaging effect. On the other hand, the texture-based approach using image classification with machine learning [2],[8],[9] has been showing good potential for quantifying emphysema severity. Texture feature subset selection is always required as a pre-processing step to machine learning for reducing dimensionality, eliminating irrelevant data and improving classifier performance [10]. However, the generic usefulness of the selected texture feature subset is often dependent on the CT data set in use. For instance, a selected texture feature subset which is useful for the CT data set A might not be useful for the CT data set B. CT images are often varying and subtle. Consequently, it is very hard to find a generic texture feature subset for the quantification of emphysema [2],[10],[11].

Gray level gap length matrix (GLGLM) and gray level run length matrix (GLRLM) are texture-based methods. The GLGLM method defines a gap as a peak or a valley between two pixels having the same gray value [12]. On the other hand, the GLRLM method defines a run length as some collinearly adjacent pixels having the same gray value [12],[13]. In this paper, we propose a method called low-attenuation gap length matrix (LAGLM). The LAGLM method defines a gap as some collinearly adjacent low-attenuation pixels where low-attenuation pixels refer to pixels below a certain threshold. As compared to the GLGLM and GLRLM methods, features gen-
erated from the LAGLM method are more closely related and easily comparable to the descriptions of emphysema. Therefore, it is much easier for users to interpret the features and thus select the useful feature subset based on the rationale of the quantification of regional emphysema severity. Further explanations bearing on this point are written in Section 2.3.3.

Mura et al.[14] compared 29 patients (Group I), with bullous emphysema and diffuse emphysema with a group of patients without bullous emphysema matched, among other criteria, for radiographic extent of diffuse emphysema (Group II). They concluded that bullous emphysema contributes to the functional impairment of patients with concomitant diffuse emphysema and the confounding functional effect of bullae depends on bullous emphysema extent: relatively milder obstruction can be observed with severe bullous emphysema, whereas moderate bullous emphysema causes modest deterioration of diffusing capacity [14]. Hence, the authors believe that assessing emphysema severity without taking into account the distribution of the different types of emphysematous lesions is premature. For this reason, this paper focuses on classifying regional radiographic lung tissues into four emphysema types to realize the distribution of the different emphysema types of tissues throughout the entire lung.

2. Methodology

2.1 Material

In this paper, the original CT images captured from the transverse plane of human thorax were provided by the Division of Pulmonary Medicine, Department of Medicine, Keio University, Japan. The images were stored in digital image and communications in medicine (DICOM) format and made anonymous beforehand. All images are of 16 bits in depth. The size of the images used was 512 × 512 pixels. A total of 27 COPD-verified patients were assessed. For each patient, 10 images which were captured from the upper to the lower lung were retrieved for processing. The calculation used for the selection of the 10 images is illustrated in Eq. (1):

\[
\text{index}(\beta) = \left( \frac{\beta}{10} \right) \times S
\]  

(1)

where \( S \) is the sum of CT images in the patient’s CT data set and \( \text{index}(\beta) \) represents the index of the \( \beta \)-th selected image for integer \( 1 \leq \beta \leq 10 \). \( \text{index}(\beta) \) is rounded toward infinity.

2.2 Visual Impression of the Regional Radiographic Pattern of Emphysema

When analyzing an image, radiologists visually divide the radiographic lung tissues presented in the image into a few emphysema types before concluding the overall emphysema severity of the lung. In this paper, the characteristics of the four regional emphysema types, N, DE, BEDE and BE, are defined as follows:

1. N — visually smooth lung tissues without apparent bullae,

2. DE — visually smooth lung tissues but with diffuse small-sized bullae,

3. BEDE — visually rough lung tissues that imply moderate destruction of airway walls or with medium-sized bullae (with or without concomitant small-sized bullae), and

4. BE — visually rough lung tissues that imply severe destruction of airway walls or with big-sized bullae.

Figure 1 shows a typical thoracic CT image with regions being labeled as N, DE, BEDE and BE. If we look at Fig. 2, the bullae in the left lung is visually easier to detect compared to the right lung that has less obvious emphysematous patterns. Having said that, compared to images that have apparent emphysema pattern like the left lung in Fig. 2, most of the images used in this paper have rather varied and subtle emphysematous radiographic patterns which are visually harder to recognize like the image in Fig. 1.

The classical CT-based method, \( PI \), is not effective for discriminating emphysema type. Explanation bearing on this point is illustrated through Fig. 3. Region A in Fig. 3(a) is characterized by diffuse emphysema (homogenously distributed small-sized continuous low attenuated areas) while region B in Fig. 3(b) is characterized by mildly bullous emphysema. Both regions were thresholded at \(-940\) Hounsfield Unit (HU) as shown in Figs. 3(c) and 3(d) where the pixels/areas marked white represent the pixels below the threshold. Thresholds from \(-930\) HU to \(-960\) HU are usually used for detecting emphysema lesions in CT image. If we look at Figs. 3(e) and 3(f), \( PI_{-940HU} \) for region A and B are approximately the same but in fact these regions’ radiographic pattern are significantly different. Therefore, one can not objectively discriminate the emphysema type of a region simply based on \( PI \). On the other hand, although region A’s and region B’s \( PI_{-940HU} \) are approximately the same, the regions’ \( PI_{-950HU} \), \( PI_{-960HU} \) and \( PI_{-970HU} \) are quite different. This knowledge is applied in the implementation of our proposed algorithm.

2.3 The Proposed Algorithm

In this paper, we evaluated 27 COPD-verified subjects and for each subject, 10 images were retrieved for processing. We chose 10 images as a result of trade-off between time of pro-
The calculations implemented in this paper were based on the original data. As a result, we chose a value between 10% and 60% for the size of region under examination. For each image, the following steps are implemented.

1. Starting from the top left corner of the image, overlap an empty 60-by-60-pixel mask region on the image.

2. If more than 70% of the overlapped region comprises lung region, calculate regional features for the region, classify the emphysema type of the region using the trained neural network, paint the region with the color that corresponds to its emphysema type, then slide the mask region by 10 pixels horizontally to the right. Otherwise, slide the mask region to the right by one pixel.

3. If the mask region spans beyond the horizontal limit of the image, slide it horizontally back to the leftmost position and then slide it vertically by 10 pixels down towards the bottom. If the mask region spans beyond the vertical limit of the image, then proceed to step 4. Otherwise, repeat steps 2 and 3.

4. Calculate the area of green, blue, magenta and red regions in the image, respectively. After gathering the area of green, blue, magenta and red regions for all 10 images, we compute the percentage of area of each color across the 10 images. The detailed algorithm of the region-by-region processing is described in Appendix A where "(*)" denotes side notes, p represents subject number, s represents image number, c represents color number from one to four corresponding to N- (green), DE- (blue), BEDE- (magenta) and BE-oriented (red) regions, respectively. T A represents the area of each color on each classified image for 27 subjects and MPA represents the percentage of total area of each color across 10 images for the 27 subjects.
2.3.3 Regional feature calculation

From the algorithm of region-by-region processing, regional feature calculation is implemented in step 24 (see Appendix A). In order to calculate the regional features, the algorithm scans a region from the first to the last row of pixels from the top to the bottom of the region and for each row of pixels, it scans from left to right pixel-by-pixel. The algorithm uses multiple thresholds between and including –1000 HU to –930 HU where pixels with less than a particular threshold are considered as the low-attenuation pixels. Figures 4(a) and 4(b) show a highlighted horizontal line in sample region A and B, respectively. The highlighted horizontal line represents the row of pixels being scanned in the region. Figures 4(c) and 4(d) show the pixel profile for the highlighted row of pixels in region A and B, respectively. In this paper, a gap is defined as some collinearly adjacent low-attenuation pixels where the gap length of a single low-attenuation pixel that has no collinearly adjacent low-attenuation pixels is one. For instance, the parts of the pixel profile in Fig. 4(d) that are below the lower horizontal line are the thresholded gaps for the case of threshold \( \theta = -960 \) HU. There are a total of six thresholded gaps in this case where the gap length of the first gap is six pixels.

The detailed explanation bearing on the proposed regional feature calculations are described in the following. For illustration, Table 1(b) shows an example of the element of LAGLM, \( r_{LAGLM}(t, g|\theta) \), based on a simple image [see Table 1(a)]. \( r_{LAGLM}(t, g|\theta) \) specifies the estimated number of times a region contains a thresholded gap length \( g \), for threshold \( t \), in the direction of angle \( \theta \).

Emphysema in CT image is represented by low-attenuation areas. Therefore, to quantify regional emphysematous patterns, two key factors are considered: gray level distribution and low-attenuation (\( \leq -930 \) gap lengths. Basically, the lower the gray level and the longer the low-attenuation gap length, the more extensive the severity of emphysema becomes. Standard texture methods like GLGLM and GLRLM are not adequately relatable to the descriptions of emphysema owing to their definitions. Therefore, we proposed to use LAGLM for quantifying regional emphysema pattern because LAGLM collectively takes into account both gray level distribution (multiple gray level thresholds) and low-attenuation gap lengths. Features derived from LAGLM are expected to be able to reflect the degree of regional severity of emphysema.

For comparison purposes, two categories of features were derived from LAGLM. The first category of features were texture-based features which consisted of thresholded short gap emphasis (TSGE), thresholded long gap emphasis (TLGE), threshold distribution (TD), thresholded gap length distribution (TGLD), thresholded gap percentage (TGP), low threshold gap emphasis (LTGE) and high threshold gap emphasis (HTGE). The calculations of these features are shown in the following:

\[
TSGE = \frac{1}{T} \sum_{t=-1000}^{-930} IS \sum_{g=1}^{IS} \frac{r_{LAGLM}(t, g|\theta)}{g^2} \tag{3}
\]

\[
TLGE = \frac{1}{T} \sum_{t=-1000}^{-930} g^2 r_{LAGLM}(t, g|\theta) \tag{4}
\]

\[
TD = \frac{1}{T} \sum_{t=-1000}^{-930} \left( \sum_{g=1}^{IS} r_{LAGLM}(t, g|\theta) \right)^2 \tag{5}
\]

\[
TGLD = \frac{1}{T} \sum_{t=-1000}^{-930} r_{LAGLM}(t, g|\theta)^2 \tag{6}
\]

\[
TGP = \frac{1}{T} \sum_{t=-1000}^{-930} IS \sum_{g=1}^{IS} r_{LAGLM}(t, g|\theta) \tag{7}
\]

\[
LTGE = \frac{1}{T} \sum_{t=-1000}^{-930} r_{LAGLM}(t, g|\theta)^2 \tag{8}
\]

\[
HTGE = \frac{1}{T} \sum_{t=-1000}^{-930} \sum_{g=1}^{IS} r_{LAGLM}(t, g|\theta)^2 \tag{9}
\]

where \( IS \) is the maximum possible gap length in the region and

\[
T_p = \sum_{t=-1000}^{-930} \sum_{g=1}^{IS} r_{LAGLM}(t, g|\theta) \tag{10}
\]

where \( t = -1000, -995, -990, ..., -930 \), and \( T_p \) is the number of points in the image. In this paper, \( T_p = 360 \) because the size of region under examination is 60-by-60 pixels.

As compared to texture features generated from GLGLM and GLRLM, LAGLM-based texture features are more direct, more relevant and easier to interpret when it comes to describing radiographic emphysematous patterns. Thus, this makes the selection of optimal feature subset easier. For instance, \( TSGE \) and \( TLGE \) indicate the distribution of short and long low-attenuation gap lengths in the region, respectively. Higher
Table 2  Gap length classes for the case of threshold equals –940 HU and –960 HU.

<table>
<thead>
<tr>
<th>gap length class, c</th>
<th>range of gap length, L, for threshold = –940 HU</th>
<th>range of gap length, L, for threshold = –960 HU</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2≤L≤4</td>
<td>1≤L≤3</td>
</tr>
<tr>
<td>2</td>
<td>5≤L≤7</td>
<td>4≤L≤6</td>
</tr>
<tr>
<td>3</td>
<td>8≤L≤11</td>
<td>7≤L≤9</td>
</tr>
<tr>
<td>4</td>
<td>L&gt;11</td>
<td>L&gt;9</td>
</tr>
</tbody>
</table>

TSGE indicates less severe type of emphysema, usually diffuse and smaller-sized emphysema while higher TLGE indicates more severe type of emphysema, usually bullous emphysema. LTGE and HTGE indicate how extensive the low-attenuation gap lengths are toward the lower end and upper end, respectively, of the range of gray-level threshold. Higher LTGE indicates more severe emphysema owing to the more extensive low-attenuation areas toward the lower end of the range of gray-level threshold while higher HTGE indicates milder emphysema owing to the low-attenuation areas toward the upper end of the range of gray-level threshold. From the seven texture features derived from LAGLM, we selected TLGE, LTGE and HTGE as the features for the first category because we hypothesized that these features are more relevant to the descriptions of emphysema. We shall hereafter refer these features as the LAGLM-based texture features.

The second category of features were directly derived from \( r_{LAGLM}(t, g | \theta) \). The features consisted of the average frequency of gap lengths based on two thresholds and four gap length classes. For each row of pixels in a region, the algorithm identifies the low-attenuation gap lengths and divides the gap lengths into four gap length classes as shown in Table 2. After that, the algorithm calculates the average frequency of gap lengths across all rows of pixels within the region based on the gap length classes. For each region, the same calculation was executed from four principle directions: \( \theta = 0^\circ, 45^\circ, 90^\circ \) and \( 135^\circ \), and the average values across the four directions became the features for the region. Consequently, let \( f(n, c | t, \theta) \) be the frequency of gap lengths that belong to gap length class \( c \) along the \( n \)-th row of pixels in an image which has been rotated by an angle \( = \theta \) given threshold = \( t \), we defined \( M(c|t, \theta) \) as the average frequency of gap lengths across all rows of pixels that belong to gap length class \( c \) in an image which has been rotated by an angle \( = \theta \) given threshold = \( t \), for integers \( 1 \leq n \leq N \), \( 1 \leq c \leq 4 \), \( t = -960 \) and \( -940 \), and \( \theta = 0^\circ, 45^\circ, 90^\circ \) and \( 135^\circ \) where \( N \) is the sum of row of pixels in the rotated image. Pixels on the border of the rotated image that were not part of the image were ignored in the calculation. The calculation of \( M(c|t, \theta) \) is shown in Eq. (11).

\[
M(c|t, \theta) = \frac{1}{N} \sum_{n=1}^{N} f(n, c | t, \theta) \tag{11}
\]

feature1 and feature2 are row vectors containing the first and the second four regional features, respectively, as shown in Eqs. (12) and (13).

\[
feature1(c) = \frac{\sum_{n=0}^{135} M(c|\theta = -940, \theta)}{4} \tag{12}
\]

\[
feature2(c) = \frac{\sum_{n=0}^{135} M(c|\theta = -960, \theta)}{4} \tag{13}
\]

Hence, a total of eight regional features were produced. These features were then directly fed into the neural network for classification. We shall hereafter refer these features as the LAGLM-based two-threshold features.

The reason why we separate gap lengths into multiple classes instead of just calculating the overall average gap length is to avoid the problem of averaging effect that originates from the difference between small gap lengths and large gap lengths. The range of threshold that reflects the existence of emphysema is from and including –1000 HU to –930 HU. We defined the gap length classes based on the reasoning that generally, the lower the threshold, the smaller the low-attenuation gap length becomes. Therefore, the gap length classes defined for –960 HU is just slightly smaller than that of the case of –940 HU. Despite the small difference, the effects are significant. For instance, see the significant difference between the gap length distribution for threshold –960 HU and –940 HU in Table 1(b).

The purpose of calculating the frequency of gap length in a row-by-row manner within a region from four different angles is to gather the small detail bearing on the radiographic emphysematous patterns along each row of pixels within the 60-by-60-pixel region meticulously. We proposed to use a two-threshold algorithm because we learnt that for two different regions, let’s say region no. 1 and region no. 2, it is probable that region no. 1’s \( PL_{-960HU} \) > region no. 2’s \( PL_{-940HU} \) but region no. 1’s \( PL_{-940HU} \) < region no. 2’s \( PL_{-960HU} \), or region no. 1’s \( PL_{-940HU} \approx \) region no. 2’s \( PL_{-960HU} \) but region no. 1’s \( PL_{-940HU} \ll \) region no. 2’s \( PL_{-960HU} \) (see Fig. 3). In order to take into account of these differences, we employed two thresholds, –940 HU and –960 HU, for generating the second category of features.

2.3.4 Classification of region using neural network

From the algorithm of region-by-region processing, classification of region using neural network is implemented in step 25 (see Appendix A). We adopted a multilayer perceptron neural network as the classifier for classifying the 60-by-60-pixel regions of lung into four emphysema types. The neural network consisted of eight input nodes in the input layer to receive the eight regional features, and four output nodes in the output layer that corresponded to the four regional emphysema types: N, DE, BEDE and BE, respectively. There were 30 and 15 neurons in the first and second hidden layer of the neural network, respectively.

We adopted back-propagation learning algorithm [17] for neural network training. In this study, a total of 55 60-by-60-pixel regions, which had been consensus-classified into N, DE, BEDE, and BE by radiologists, were used as the training regions for the neural network. Figure 5 shows the training regions. We employed automated stopping criteria inspired by the Steady-State Identification algorithm (SSID) [18] for stopping the neural network training. After each epoch, about 25% of the data is randomly selected as the validation set for that epoch [18]. Therefore this method enables the use of 100% of the data for training. The trained neural network was used for classifying the regions. The output node of the neural network that had the largest output value corresponded to the emphysema type of the region in which output node one to four corresponded to N, DE, BEDE and DE, respectively.

3. Results

In order to evaluate our algorithm, we first validated the 55 training regions of the lung using cross validation method.
Based texture features such as long gap emphasis, low gray level run emphasis as the regional features. For GLGLM-based features, we used short run emphasis, long run emphasis, gray level distribution, run length distribution, run percentages, low gray level run emphasis and high gray level emphasis as the regional features. For GLRLM-based features, we used the features that are comparable to LAGLM-based texture features such as long gap emphasis, low gray level gap emphasis and high gray level gap emphasis, as the regional features.

The four-class cross-validation accuracies in the form of LAGLM-based two-threshold features/LAGLM-based texture features/GLRLM/GLGLM were: N: 93.75%/87.50%/100%/62.50%/75.00%; DE: 92.31%/84.62%/84.62%/30.77%/23.08%; BEDE: 88.89%/88.89%/66.67%/55.56%/44.44%; and BE: 100%/100%/94.12%/76.47%/82.35%. The average four-class cross-validation accuracies in the form of LAGLM-based two-threshold features/LAGLM-based texture features/GLRLM/GLGLM were: 93.74%/90.25%/86.35%/56.32%/56.22%. These results show that the proposed features, LAGLM-based two-threshold features and LAGLM-based texture features, are more expressive than the conventional methods in classifying regional radiographic emphysematous patterns into four classes especially in discriminating BEDE from DE and BE.

### 3.2 Classification of Regions

#### 3.2.1 Classified images

We trained the neural network using 55 training regions then by using the trained neural network, we classified a total of 270 images from 27 COPD-verified subjects. Figure 6 shows four examples of classified images produced by using LAGLM-based two-threshold features. Green, blue, magenta and red regions correspond to N-, DE-, BEDE- and BE-oriented regions, respectively. The comments about the different radiographic emphysematous patterns in the original images in Fig. 6 were hand-annotated by radiologists. Figure 7 shows the comparison between original CT image with diseased areas annotated by radiologist and classified image produced by LAGLM-based two-threshold features and LAGLM-based texture features, respectively. By visual comparison, we can see that the labeled diseased areas in the original images correspond fairly to the classified regions in the classified images. Besides, we can also see that there is a slight difference in classified regions between the classified images produced by LAGLM-based two-threshold features and the classified images produced by LAGLM-based texture features.

We plotted the classification results, $MPA$, of five sample subjects which have significantly different emphysema severities in Fig. 8. From the figure, we can relate the distribution of the percentage of different emphysematous lung tissues to the extent of the subject’s emphysema severity. If we look at Fig. 8, there is an obvious increase in $MPA$ (.4) from the case of severe to very severe emphysema and there is a general increase in $MPA$ (.3) from normal to severe emphysema.

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### Table 3

<table>
<thead>
<tr>
<th>Predicted regional emphysema type</th>
<th>Actual regional emphysema type</th>
</tr>
</thead>
<tbody>
<tr>
<td>N (%) (case)</td>
<td>N (%) (case)</td>
</tr>
<tr>
<td>93.75 (15)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>DE (%) (case)</td>
<td>62.5 (1)</td>
</tr>
<tr>
<td>92.31 (12)</td>
<td>11.11 (1)</td>
</tr>
<tr>
<td>BEDE (%) (case)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>76.67 (8)</td>
<td>88.89 (8)</td>
</tr>
<tr>
<td>BE (%) (case)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>100.00 (17)</td>
<td></td>
</tr>
</tbody>
</table>

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### Table 4

<table>
<thead>
<tr>
<th>Actual regional emphysema type</th>
<th>N (%) (case)</th>
<th>DE (%) (case)</th>
<th>BEDE (%) (case)</th>
<th>BE (%) (case)</th>
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</thead>
<tbody>
<tr>
<td>N (%) (case)</td>
<td>87.50 (14)</td>
<td>13.38 (2)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>DE (%) (case)</td>
<td>12.50 (2)</td>
<td>84.62 (11)</td>
<td>11.11 (1)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>BEDE (%) (case)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>88.89 (8)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>BE (%) (case)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>100.00 (17)</td>
<td></td>
</tr>
</tbody>
</table>

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Fig. 5 The four emphysema types: (a) N-oriented training regions, (b) DE-oriented training regions, (c) BEDE-oriented training regions, and (d) BE-oriented training regions. All regions are 60-by-60 pixels in size.
This implies that $MPA(:,3)$ (BEDE-oriented lung tissues) and $MPA(:,4)$ (BE-oriented lung tissues) are significant indicators for the extent of the subjects’ emphysema severity. Note that in Fig. 8, there are cases where the sum of $MPA$ does not equal to 100% because some of the small edges of the lung in the images were not classified.

Fig. 6 Four examples of original and classified images: (a) original image no. 1 — little mildly bulloss emphysema along with substantial normal lung tissue, (b) classified image no. 1, (c) original image no. 2 — the radiographic patterns suggest a severe destruction of airway walls, (d) classified image no. 2, (e) original image no. 3 — both severe and mild destruction of airway walls can be visually recognized, (f) classified image no. 3, (g) original image no. 4 — severe destruction of airway walls in the right lung and diffuse emphysema in the left lung and (h) classified image no. 4.

Fig. 7 A comparison between original image with diseased areas annotated by radiologist using colored arrows and the corresponding classified images produced by LAGLM-based two-threshold features and LAGLM-based texture features, respectively: (a) original image A — the radiographic patterns suggest moderate to severe destruction of airway walls along with diffuse emphysema where more destruction is observed in the left lung, (b) classified image A produced by LAGLM-based two-threshold features, (c) classified image A produced by LAGLM-based texture features, (d) original image B — obvious emphysematous bulla in the left lung and considerable concomitant diffuse emphysema in both the right and left lung, (e) classified image B produced by LAGLM-based two-threshold features and (f) classified image B produced by LAGLM-based texture features. The color green, blue, magenta and red correspond to N, DE, BEDE and BE, respectively.

This implies that $MPA(:, 3)$ (BEDE-oriented lung tissues) and $MPA(:, 4)$ (BE-oriented lung tissues) are significant indicators for the extent of the subjects’ emphysema severity. Note that in Fig. 8, there are cases where the sum of $MPA$ does not equal to 100% because some of the small edges of the lung in the images were not classified.

Fig. 8 The classification results of five sample subjects with significantly different emphysema severity.

Table 5 The contingency table of the classification of 105 randomly selected regions from 270 images using LAGLM-based two-threshold features.

<table>
<thead>
<tr>
<th>Predicted emphysema type</th>
<th>Actual regional emphysema type</th>
<th>N (%) (case)</th>
<th>DE (%) (case)</th>
<th>BEDE (%) (case)</th>
<th>BE (%) (case)</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>(case)</td>
<td>92.31</td>
<td>5.26</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>DE</td>
<td>(case)</td>
<td>7.69</td>
<td>84.21</td>
<td>14.29</td>
<td>0</td>
</tr>
<tr>
<td>BEDE</td>
<td>(case)</td>
<td>0</td>
<td>10.53</td>
<td>85.71</td>
<td>6.25</td>
</tr>
<tr>
<td>BE</td>
<td>(case)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>93.75</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>99.97</td>
<td>93.71</td>
<td>85.71</td>
<td>93.75</td>
</tr>
</tbody>
</table>

Table 6 The contingency table of the classification of 105 randomly selected regions from 270 images using LAGLM-based texture features.

<table>
<thead>
<tr>
<th>Predicted regional emphysema type</th>
<th>Actual regional emphysema type</th>
<th>N (%) (case)</th>
<th>DE (%) (case)</th>
<th>BEDE (%) (case)</th>
<th>BE (%) (case)</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>(case)</td>
<td>88.46</td>
<td>5.26</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>DE</td>
<td>(case)</td>
<td>11.54</td>
<td>78.95</td>
<td>7.14</td>
<td>0</td>
</tr>
<tr>
<td>BEDE</td>
<td>(case)</td>
<td>0</td>
<td>15.79</td>
<td>89.29</td>
<td>3.12</td>
</tr>
<tr>
<td>BE</td>
<td>(case)</td>
<td>0</td>
<td>0</td>
<td>3.57</td>
<td>96.88</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>99.97</td>
<td>93.71</td>
<td>85.71</td>
<td>93.75</td>
</tr>
</tbody>
</table>

3.2.2 Classification of 105 test regions

In order to assess the accuracy of the classification results, we randomly selected 105 regions from 270 images as the test regions and classified the regions. These regions had been carefully consensus-classified by radiologist in advance. The four-class classification accuracies of the 105 randomly selected regions in the form of LAGLM-based two-threshold features/LAGLM-based texture features/PI/GLRLM/GLGLM were: N: 92.31%/88.46%/96.15%/57.68%/61.54%; DE: 84.21%/78.95%/73.68%/31.58%/15.79%; BEDE: 85.71%/89.29%/71.43%/53.57%/50.00%; and BE: 93.75%/96.88%/90.62%/68.75%/78.12%. The average four-class classification accuracies in the form of LAGLM-based two-threshold features/LAGLM-based texture features/PI/GLRLM/GLGLM were: 89.00%/88.40%/82.97%/52.90%/51.36%. While LAGLM-based features apparently outperformed PI, GLRLM and GLGLM, the evaluation results also showed that LAGLM-based texture features are almost as effective as LAGLM-based two-threshold features for classifying regional emphysema into four classes as illustrated in Tables 5 and 6.
For correlation analyses, we focused on the classification results of 270 images produced by LAGLM-based two-threshold features and performed a series of correlation analyses between the classification results (MPA) and spirometry test results such as FEV1 % predicted [Forced Expiratory Volume in One Second (FEV1) divided by Forced Vital Capacity (FVC)], FEV1 (see Table B.1 in Appendix B) and PFT-based class (see Table C.1 in Appendix C). The correlation analyses were implemented using multiple linear regression. FEV1 % predicted and FEV1 were usually used as the guidelines for determining the PFT-based class (severity) of subject (see Table C.1 [19] in Appendix B). The p-values of correlation of MPA to FEV1 % predicted, FEV1 and PFT-based class, based on three different combinations of the percentage of classified regions: (1) BEDE and BE, (2) DE, BEDE and BE, and (3) N, DE, BEDE and BE, were generally less than 0.01 as shown in Table 7. This implies that the region-by-region classification results correlated fairly well to PFT-based results.

### 3.3 Correlation Analyses

GLGLM defines a gap as a peak or a valley between two pixels having the same gray level [12]. On the other hand, GLRLM defines a run length as some collinearly adjacent pixels having the same gray value [12],[13]. In this paper, the proposed LAGLM defines a gap as some collinearly adjacent low-attenuation pixels where low-attenuation pixels refer to pixels below a certain threshold. Therefore, LAGLM is different from GLRLM and GLGLM. Assume that \( r_{GLGLM}(i, v|\theta) \) is a GLGLM [see Table 8(b)] that specifies the estimated number of times a region contains a gap length \( v \) for gray level \( i \), in the direction of angle \( \theta \), \( r_{GLRLM}(i, j|\theta) \) is a GLRLM [see Table 8(c)] that specifies the estimated number of times a region contains a run length \( j \), for gray level \( i \), in the direction of angle \( \theta \), and \( r_{LAGLM}(i, g|\theta) \) is an LAGLM [see Table 8(d)] that specifies the estimated number of times a region contains a thresholded gap length \( g \) for threshold \( i \), in the direction of angle \( \theta \), we showed the differences among GLGML, GLRLM and LAGLM based on a simple image [see Table 8(a)] in Table 8. The results in Tables 8(c), 8(b) and 8(d) were calculated by assuming the run length of a pixel which has no adjacent pixels of the same gray value as one for GLRLM, the gap length of two neighboring pixels with identical gray level as one for GLGLM, and the gap length of a low-attenuation pixel which has no collinearly adjacent low-attenuation pixels as one for LAGLM.

#### 4. Discussion

The calculations of GLGLM-based and GLRLM-based texture features basically correspond to the calculation of LAGLM-based texture features [see Eqs. (3) to (10)]. The only difference is the use of element, namely \( r_{LAGLM}(i, v|\theta) \), \( r_{GLGLM}(i, v|\theta) \) and \( r_{GLRLM}(i, j|\theta) \) for LAGLM, GLGLM and GLRLM, respectively. For example, the calculation of GLGLM’s short gap emphasis and GLRLM’s short run emphasis correspond to the calculation of LAGLM’s thresholded short gap emphasis, and so on. However, owing to the apparent conceptual difference among GLGML, GLRLM and LAGLM, it results in different values for each corresponding feature.

The underlying rationale of the effectiveness of the proposed algorithm lies in the fact that LAGLM collectively takes into account both of the two key factors for discriminating regional emphysematous severity such as gray level distribution toward the lower end of the range of gray level and the extent of low-attenuation gap lengths in the region. For instance, LTGE derived from LAGLM indicates how extensive the low-attenuation gap lengths are toward the lower end of the range of the gray level threshold and therefore it is able to reflect the extent of regional emphysematous severity. Similarly, LAGLM-based two-threshold features also have approximately the same effect as LAGLM-based texture features in terms of describing the severity of emphysema. It is because LAGLM-based two-threshold features extract the low-attenuation gap length distribution by separating gap lengths into four gap length classes based on two thresholds: a lower threshold and an upper threshold (−940HU and −960HU). Therefore, the four-class classification accuracies of LAGLM-based texture features and LAGLM-based two-threshold features are approximately the same (see Tables 5 and 6).

#### 5. Conclusion

The algorithm in this paper classifies regional radiographic emphysematous patterns into four classes of severity automatically. We proposed a method called low-attenuation gap length matrix (LAGLM). From LAGLM, two categories of features were derived: LAGLM-based two-threshold features and LAGLM-based texture features. The effectiveness of these features were verified through cross validation of 55 training regions and classification of 105 test regions that were randomly selected from 270 images.

The algorithm focuses on the regional radiographic pattern in the image and recognizes whether the region is comprised of BE-, BEDE-, DE- or N-oriented lung tissue. We showed that the proposed algorithm is more expressive in classifying re-
gional radiographic emphysematosus patterns into four classes compared to other similar systems such as P1, GLRLM and GLGLM. The proposed algorithm is in particular found to be significantly more effective in discriminating BEDE-oriented tissues compared to PI. The implementation of the proposed algorithm facilitates the access to the knowledge about the distribution of the different types of emphysematosus tissues across the entire lung. This is particularly interesting for a followup study on improving the monitoring of radiographic morphological changes with progression of pulmonary disease.

Acknowledgment

The authors would like to thank the Department of Medicine, Keio University, Japan, for the anonymous CT image data sets.

References


Appendix A Algorithm for Region-by-Region Processing

1: for $p = 1$ to $27$ do (/*integer $p$ represents subject number*/)
2: for $s = 1$ to $10$ do (/*integer $s$ represents image number*/)
3: $A(s) \Leftarrow$ Area of the lung in image no. $s$ 
4: $S_i = 59$ (/*$S_i$ = height of the region*/)
5: $S_j = 59$ (/*$S_j$ = width of the region*/)
6: $i = 1$ (/*initial x-coordinate for the scan of qualified region*/)
7: $j = 1$ (/*initial y-coordinate for the scan of qualified region*/)
8: $slide_1 = 10$ (/*vertical sliding range of mask region*/)
9: $slide_2 = 10$ (/*horizontal sliding range of mask region*/)
10: $size_1 =$ number of row in the image (/*vertical limit*/)
11: $size_2 =$ number of column in the image (/*horizontal limit*/)
12: $run = 1$
13: while $run = 1$ do
14: if ($S_i + 1 > size_1$) then
15: break (/*if the vertical limit of the image is smaller than ($S_i + 1$) then break*/) 
16: else ($S_i + 1 > size_2$) 
17: break (/*if the horizontal limit of the image is smaller than ($S_i + 1$) then break*/) 
18: else ($i + S_j > size_1$) 
19: break (/*if the mask region spans beyond the vertical limit of the image then break*/) 
20: end if
21: $I \Leftarrow$ image no. $s$ (/*store image no. $s$ in variable I*/)
22: if $I(i + S_j, j) < (j + S_j))$ is covered by lung region by more than 70% then
23: $R = I(i + S_j, j) / (j + S_j))$ (/*store the qualified region in variable R*/
24: Calculate regional features for region $R$
25: Classify region $R$ into four emphysema types using neural network
Paint region $R$ with the color that corresponds to its emphysema type

$$j = j + \text{slide}_2 \{/ \text{slide the mask region to the right by slide}_2 \text{ pixels\}}$$

else

$$j = j + 1 \{/ \text{slide the mask region to the right by one pixel\}$$

end if

if $j + S_j > \text{size}_2$ then

$$j = 1 \{/ \text{slide the mask region back to the left-most position\}$$

$$i = i + \text{slide}_1 \{/ \text{slide the mask region vertically towards the bottom by slide}_1 \text{ pixels\}$$

end if

end while

for $c = 1$ to $4$ do

$$TA(s_i, c, p) = \frac{\sum_{s_i=1}^{10} TA(s_i, c, p)}{\sum_{s_i=1}^{10} A(s_i)} \times 100 \{/ \text{calculate the area of each color on each classified image for the subject\}$$

end for

for $c = 1$ to $4$ do

$$MPA(p, c) = \frac{\sum_{s_i=1}^{10} TA(s_i, c, p)}{\sum_{s_i=1}^{10} A(s_i)} \times 100 \{/ \text{calculate the percentage of area of each color across 10 images for subject no. p\}$$

end for

### Appendix B Spirometry Test Values

Explanation on the common test values in a spirometry test is shown in Table B.1 [19].

### Appendix C Diagnosis of COPD

The severity of COPD can be classified using post-bronchodilator spirometry as shown in Table C.1 [19].

#### Table B.1 
Explanation on the common test values in a spirometry test.

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Name</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>FVC</td>
<td>Forced Vital Capacity</td>
<td>This is the total amount of air that can forcibly be blown out after full inspiration, measured in liters.</td>
</tr>
<tr>
<td>FEV&lt;sub&gt;1&lt;/sub&gt;</td>
<td>Forced Expiratory Volume in 1 Second</td>
<td>This is the amount of air that you can forcibly blow out in one second, measured in liters. Along with FVC, it is considered one of the primary indicators of lung function.</td>
</tr>
<tr>
<td>FEV&lt;sub&gt;1&lt;/sub&gt;/FVC</td>
<td>FEV&lt;sub&gt;1&lt;/sub&gt; as predicted</td>
<td>This is the ratio of FEV&lt;sub&gt;1&lt;/sub&gt; to FVC. In healthy adults this should be approximately 75 – 80%.</td>
</tr>
</tbody>
</table>

#### Table C.1 
Diagnosis of COPD using post-bronchodilator spirometry.

<table>
<thead>
<tr>
<th>PFT-based class (severity)</th>
<th>Post-bronchodilator FEV&lt;sub&gt;1&lt;/sub&gt; (predicted)</th>
<th>FEV&lt;sub&gt;1&lt;/sub&gt;/FVC (%) predicted</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal (1)</td>
<td>≥ 80</td>
<td>≥ 80</td>
</tr>
<tr>
<td>Mild COPD (2)</td>
<td>≥ 60</td>
<td>≥ 80</td>
</tr>
<tr>
<td>Moderate COPD (3)</td>
<td>≥ 50</td>
<td>50-79</td>
</tr>
<tr>
<td>Severe COPD (4)</td>
<td>≥ 32</td>
<td>30-49</td>
</tr>
<tr>
<td>Very severe COPD (5)</td>
<td>&lt; 32</td>
<td>&lt; 50 or 50-79 with Chronic Respiratory Failure symptoms</td>
</tr>
</tbody>
</table>