Adaptive Gaussian Mixture Model-Based Statistical Feature Extraction for Computer-Aided Diagnosis of Micro-Calcification Clusters in Mammograms

Zhang Zhang *, Xiaoyong Zhang **, Kei Ichiji ***, Yumi Takane ****, Satoru Yanagaki ***, Yusuke Kwasumi ***, Tadashi Ishibashi ***, and Noriyasu Homma ****

Abstract: In mammography, detection and categorization of micro-calcification clusters (MCCs) using computer-aided diagnosis (CAD) systems are very important tasks because MCCs are important signs at an early stage of breast cancer. However, the conventional methods of CAD only classify MCCs into benign and malignant types, and no method has been developed for a medical requirement to classify the MCCs into more detailed categories according to the spatial distribution of MCCs. To provide a cogent second opinion, we specifically focus on analyzing MCCs’ spatial distribution and propose an adaptive Gaussian mixture model-based method to extract the statistical features of the spatial distribution in this study. By mimicking the radiologists’ workflow, the proposed method used the main feature of each spatial distributions to classify the MCCs and then provide a cogent second opinion to increase the confidence level of diagnosis decisions. The experiments have been performed on 100 mammographic images with MCCs from a clinical dataset. The experimental results showed that the proposed method was able to detect the MCCs and classify the spatial distribution of the MCCs effectively.

Key Words: mammography, computer-aided diagnosis (CAD), micro-calcification clusters (MCCs), Gaussian mixture model (GMM).

1. Introduction

Mammography has gained wide acceptance as the most effective, low-cost, and highly sensitive technique for detecting breast cancer at an early stage, resulting in at least a 30% reduction of breast cancer deaths [1]. It is a heavy burden on radiologists to provide an accurate and efficient evaluation for the enormous number of mammograms generated in widespread screening. Indeed, there are some limitations of human observation; 10 to 30% of breast lesions are missed during human routine screening [2].

With the advancement of digital image processing, pattern recognition, and artificial intelligence, radiologists have an opportunity to ease their burden with the second opinion provided by computer-aided diagnosis (CAD) systems. The CAD system has become one of the most important research subjects in medical imaging and diagnostic radiology. In fact, it has been reported that the readers’ sensitivity can be increased by 10% on average with the assistance of the CAD systems [3]. There are several topics in the development of mammographic CAD systems, including detections and classifications of micro-calcification clusters (MCCs), masses, and architectural distortions [1].

* Graduate School of Biomedical Engineering, Tohoku University, Sendai, Miyagi 980-8579, Japan
** National Institute of Technology, Sendai College, Sendai, Miyagi 989-3128, Japan
*** Tohoku University Graduate School of Medicine, Sendai, Miyagi 980-8575, Japan
**** Tohoku University Hospital, Sendai, Miyagi 980-8574, Japan
E-mail: zhangzhang@dc.tohoku.ac.jp
(Received July 4, 2019)
(Revised December 9, 2019)
classify the MCCs into benign and malignant types [10]–[16]. However, for a cogent second opinion, there is a medical requirement to classify the MCCs into more detailed categories of several degrees of malignancy according to mammographic anatomy such as spatial distributions and shapes. CAD methods for extracting the shape features have been reported [17]. On the other hand, there was no statistical method applied to analyze MCCs’ spatial distribution quantitatively. Thus, we focus on the spatial distribution of MCCs in this study based on a statistical method. Figure 2 illustrates five different spatial distribution categories of MCCs used in the breast imaging-reporting and data system (BI-RADS) categories. These distributions refer to the arrangement of the calcifications inside the breast and, relative to the probability of malignancy [4]. To analyze the spatial distribution of MCCs, we have proposed an adaptive Gaussian mixture model (GMM) method, which can classify three types of spatial distributions, including linear, diffuse, and grouped, effectively but has a shortcoming that the method is not capable of distinguishing regional and segmental MCCs [18]. The cause of the shortcoming is that the difference between segmental and regional MCCs not only depends on the spatial distributions but also relates to ducts architecture. According to BI-RADS categories, the main difference between segmental and regional MCCs is that segmental MCCs are developed along with the breast ducts while regional MCCs are not.

In this study, to complete the analysis and further classify the remaining two types of spatial distribution of MCCs, we propose a novel method that takes into account the duct feature [19]. The new feature is integrated into the adaptive GMM method, and the novel method can analyze the features of all the five types of MCCs’ spatial distributions. Experimental evaluation using clinical datasets demonstrates that the proposed method can classify all the five types of MCCs into spatial distribution categories.

2. Proposed Method

The proposed method consists of four major procedures: the pre-processing to enhance the MCs, the adaptive GMM method [18] to model the MCCs’ spatial distributions, MCC detection, and spatial distribution categorization by using the GMM method and the duct feature.

2.1 Pre-Processing

Since most mammograms have a low-intensity contrast between MCs and surrounding tissue, pre-processing techniques are necessary in order to enhance MCs in the image [20].

In this study, we use a top-hat transform method, which is based on a morphological technique to enhance the MC candidates by removing the smooth background and extracting the small bright blobs. The formula of the top-hat transform is given by

\[ t = f - f \circ b, \]  
(1)

where \( f \) is the original image, \( \circ \) denotes the opening operation, and \( b \) is a disk structuring element [21]. The bright blobs, most of them are MCs in mammograms, can be suppressed by the opening operation. The subtracting operation yields an image in which only the bright blobs fitting to the structuring element remain. Figure 1 shows an original mammogram, and Fig. 3 shows the result of the top-hat transform. In Fig. 3, the MCs are enhanced against the breast region. After we enhance the MCs, individual MC candidates can be segmented by using thresholding [22]. In this study, we determined a threshold \( T \) based on experiments:

\[ T = \mu + 4\sigma, \]  
(2)

where \( \mu \) is the mean gray value of \( t \) within the breast region, and \( \sigma \) is the standard deviation of the gray value of \( t \) within the breast region. Figure 4 shows an example of the MC candidates’ detection result; the bright points are the MC candidates.
2.2 MCC Modeling Using an Adaptive GMM

GMM is a robust and simple model that is capable of providing spatial distribution information. The robustness of GMM makes the result unaffected by small variations of misdetected non-MC candidates. In view of the above-mentioned reasons, we use the GMM method to cluster MC candidates and then obtain the parameters to extract the spatial features.

In this study, the spatial coordinates of MCs can be modeled as a GMM. The MCCs can be detected and categorized based on the statistical characteristics of the GMM subsequently. Let \( y = [y_1, \ldots, y_n]^T \) represent the coordinates of MCs where \( n \) is the number of MC candidates. The distribution of MCs’ coordinates can be approximated by the following probability density function:

\[
p(y|\theta) = \sum_{m=1}^{k} \alpha_m p(y|\theta_m), \tag{3}
\]

\[
p(y|\theta_m) = p(y|\mu_m, \Sigma_m) = \frac{1}{2\pi|\Sigma_m|^{\frac{1}{2}}} \exp \left( -\frac{(y - \mu_m)^T \Sigma_m^{-1} (y - \mu_m)}{2} \right), \tag{4}
\]

where \( k \) is the number of components, \( \alpha_1, \ldots, \alpha_k \) are the mixture weights, \( \theta_m \) is the set of the mean \( \mu_m \) and covariance matrix \( \Sigma_m \) defining the \( m \)-th component, and \( \theta \equiv \{\theta_1, \ldots, \theta_k\} \) is the complete set of parameters needed to specify the Gaussian mixture, respectively.

The expectation-maximization (EM) algorithm is an iterative method to estimate the parameters of the GMM. The number of components \( k \) needs to be estimated because it is a necessary input of the EM algorithm, but the number of MCCs in a mammogram is generally unknown.

We employ the minimum message length (MML) criterion [23] to estimate the number of components. The message length is a value to evaluate model fit. To calculate the message length of model parameters \( \theta \) and dataset \( y \), Wallace and Dowe (2000) and Baxter and Oliver (2000) gave the formula as follows:

\[
\text{Length} \equiv - \log p(\theta) - \log p(y|\theta) + \frac{1}{2} \log |F(\theta)| + c \left( 1 + \frac{\log \frac{1}{12}}{2} \right), \tag{5}
\]

where \( c \) is the dimension of \( \theta \), \( F(\theta) \) is the expected Fisher information matrix, and \( |F(\theta)| \) denotes its determinant [24],[25]. The estimation of the number of components is carried out by finding the minimum with respect to the parameters of the message length.

The adaptive GMM method can be described by the flow chart in Fig. 5. Instead of using model selection criteria to choose one among a set of candidate models, the adaptive GMM method integrates estimation and model selection in a single algorithm. Firstly, we determine a maximum and a minimum number of components. Secondly, we make a random initialization of the components’ parameters. Thirdly, we use the following formulas to calculate posterior probability \( \omega_m^{(i)} \) which can be considered as the posterior probability that point \( y_i \) belongs to the \( m \)-th component and then update the parameters:

\[
\omega_m^{(i)} = \frac{\alpha_m p(y_i|\mu_m, \Sigma_m)}{\sum_{j=1}^{k} \alpha_j p(y_i|\mu_j, \Sigma_j)}, \tag{6}
\]

\[
\alpha_m = \frac{\sum_{i=1}^{n} \omega_m^{(i)}}{n}, \tag{7}
\]

\[
\mu_m = \frac{1}{\sum_{i=1}^{n} \omega_m^{(i)}} \sum_{i=1}^{n} \omega_m^{(i)} y_i, \tag{8}
\]

\[
\Sigma_m = \frac{1}{\sum_{i=1}^{n} \omega_m^{(i)}} \sum_{i=1}^{n} \omega_m^{(i)} (y_i - \mu_m)(y_i - \mu_m)^T, \tag{9}
\]
where \( n \) is the number of MC candidates. The fourth step is to calculate the message length when we use the updated model to fit the data. We repeat the third step and the fourth step until the message length converges. Then we decrease the number of the component by 1 and repeat the steps until the number of the component equals the minimum number. Finally, we find the minimum message length and output the best model.

### 2.3 MCC Detection

After obtaining the GMM model of the MCCs, we can analyze the distribution of the models.

The analysis is based on the distribution features, which can be calculated by the estimated GMM parameters. The weight \( \alpha_m \) can be used to describe the number of MC candidates in each component. The mean \( \mu_m \) of the component is the spatial coordinate of the components’ central point, so we can obtain the location of the components. We use singular-value decomposition (SVD) to transform the covariance matrix \( \Sigma_m \) of the GMM into two matrices as shown in the following formula:

\[
\Sigma_m = U E U^{-1},
\]

where \( U \) is a unitary matrix and \( E \) is a diagonal matrix. As shown in the following formulas, \( U \) contains direction information of the component, and the elements of \( E \) positively correlate to axes of the component:

\[
E = \begin{bmatrix}
\frac{l_1^2}{4} & 0 \\
0 & \frac{l_2^2}{4}
\end{bmatrix},
\]

\[
U = \begin{bmatrix}
\sin \phi_1 & -\cos \phi_1 \\
\cos \phi_1 & \sin \phi_1
\end{bmatrix},
\]

where \( l_1 \) and \( l_2 \) are semi-major axis and semi-minor axis of the component, respectively, and \( \phi_1 \) represents the angle between the component direction and the vertical direction. Then, we can obtain the component’s size and shape information as shown in the following formulas:

\[
S = \pi l_1 l_2,
\]

\[
e = \frac{l_1}{l_2},
\]

where \( S \) is the area of the component and \( e \) is the eccentricity of the component.

Then we begin to detect MCCs. Because not all the components correspond to MCCs, we need to remove the non-MCC components. Most of non-MCC components have a small weight, and some non-MCC components have a large eccentricity. In view of the above reasons, we calculate a ratio \( r \) as follows:

\[
r = \frac{\alpha_m}{e}.
\]

The components with large \( r \) are detected as MCC components, and others are seen as non-MCC components.

### 2.4 Spatial Distribution Categorization

The final stage is to categorize the MCCs into five categories by using their spatial distributions and the duct feature. According to BI-RADS categorization [4] shown in Fig. 2, a basic idea of the proposed method to represent the anatomical features of each type of MCC distributions is as follows. Let us define the thresholds \( T_{P1}, T_{P2}, T_e, T_e \) and the area of breast region \( S_b \). As shown in Fig. 2, only the grouped MCCs have small area percentage (\( \frac{S_b}{S} < T_{P1} \)), and only the diffuse MCCs have large area percent of the breast region (\( \frac{S_b}{S} > T_{P2} \)). Thus, these two MCC distributions can be classified by the feature of areas. Only the linear MCCs have large eccentricity (\( e > T_e \)); thus, they can be classified by the feature of eccentricity. The segmental MCCs are developed along with the breast ducts’ directions. As shown in Fig. 6, the breast ducts in mammograms can roughly be simulated as the exponential curves [19], and the direction can be calculated as follows:

\[
f(x) = e^{Bx},
\]

\[
\phi_2 = \arctan(Be^{\phi_1}),
\]

where \( f(x) \) is the exponential curve for the simulated duct, \( B \) is the parameter of the exponential curve, and \( \phi_2 \) represents the duct direction. Thus, segmental MCCs can be classified by the difference between the MCCs’ direction and the breast ducts’ direction (\( |\phi_1 - \phi_2| < T_\phi \)). Figure 7 shows the flowchart of the categorization process. The thresholds \( T_{P1}, T_{P2}, T_e, T_e \) were selected in experiments.

### 3. Experimental Results

To evaluate the performance of the proposed method, we conducted an experiment on mammograms with MCCs. In the experiment, 100 mammograms with 111 MCCs are selected from an image database acquired from 2006 to 2010 in Tohoku University Hospital. The size of the digital mammograms is \( 6,880 \times 9,480 \) pixels. Among the 111 MCCs in mammograms,
there were 66 grouped MCCs, 8 diffuse MCCs, 19 segmental MCCs, 6 linear MCCs, and 12 regional MCCs diagnosed by radiologists.

In order to evaluate the detection results, we computed the free-response receiver operating characteristic (FROC) analysis, of which the test variable is \( r \). The true-positive (TP) rate is defined as the rate of the number of correctly detected MCCs over the total number of MCCs, and false positives (FPs) are defined as the number of mis-detected MCCs in the experiment. The FROC curve is a plot of the TP rate (y-axis in Fig. 8) versus the average number of FPs per image (x-axis in Fig. 8). By counting the TP rate and FPs per image, the proposed method achieves a TP rate of 80% with 1.2 FPs per image and a TP rate of 90% with 1.7 FPs per image.

Cohen's kappa value [26], a statistic which measures inter-rater agreement for categorical items, is utilized to evaluate the categorization result. It is generally thought to be a more robust measure than simple percent agreement calculation, as it takes into account the possibility of the agreement occurring by chance. Figure 9 shows the histogram of area percentage, Fig. 10 shows the histogram of eccentricity, and Fig. 11 shows the histogram of the direction difference between MCCs and the simulated breast ducts. The manual thresholds \( T_{P1}, T_{P2}, T_e, \) and \( T_\phi \) selected by maximization of classification accuracy are shown in the histograms. Table 1 shows the categorization result with the manual thresholds. The accuracy was nearly 70% with Cohen's kappa value of 0.52, corresponding to a moderate agreement.

4. Discussion

To develop a CAD system that can classify MCCs into BI-RADS categories, it is necessary to analyze MCCs' mammographic anatomy such as spatial distributions and shapes. Although there are several conventional methods for the evaluation of MCCs' shapes, this study is the first attempt for categorization of MCCs' spatial distributions to the best of our knowledge.

The experimental results have suggested that the semi-automatic categorization with manual thresholding can classify MCCs' spatial distributions according to BI-RADS categories. However, it is necessary for a clinically useful CAD system to provide an appropriate automatic categorization. Taking this problem into account, we used Gaussian mixtures to fit the distributions of each feature as shown in Figs. 12, 13, and 14. We calculated the parameters of the Gaussian mixtures by using the EM algorithm. Corresponding to the manual thresholding, histograms of the area percentage, the eccentricity, and the direction difference are shown in Fig. 12, 13, and 14. Table 1 shows the result of categorization with manually thresholds.
Fig. 12 Histogram of the area percentage with the Gaussian mixture fit.

Fig. 13 Histogram of the eccentricity with the Gaussian mixture fit.

Fig. 14 Histogram of the direction difference between MCCs and the simulated breast ducts with the Gaussian mixture fit.

differe
tion difference were fitted by 3 Gaussian distributions, 2 Gaussian distributions, and 2 Gaussian distributions, respectively. From the Gaussian mixture fits and the MCC components' features, we can calculate the likelihood of the MCC components belonging to each category as follows:

\[
p(\text{Gro.}) = \frac{f_{p1}(\frac{x}{s_{b}})}{\sum_{m=1}^{3} f_{pm}(\frac{x}{s_{b}})},
\]

(18)

\[
p(\text{Dif.}) = \frac{f_{p2}(\frac{x}{s_{b}})}{\sum_{m=1}^{3} f_{pm}(\frac{x}{s_{b}})},
\]

(19)

\[
p(\text{Seg.}) = \frac{f_{p2}(\frac{x}{s_{b}}) f_{e1}(e)}{\sum_{m=1}^{3} f_{pm}(\frac{x}{s_{b}}) \sum_{n=1}^{2} f_{en}(e) \sum_{m=1}^{2} f_{dm}(\phi)},
\]

(20)

\[
p(\text{Reg.}) = \frac{f_{p2}(\frac{x}{s_{b}}) f_{e1}(e) f_{d2}(\phi)}{\sum_{m=1}^{3} f_{pm}(\frac{x}{s_{b}}) \sum_{n=1}^{3} f_{en}(e) \sum_{m=1}^{2} f_{dm}(\phi)}.\]

(21)

\[
p(\text{Lin.}) = \frac{f_{p2}(\frac{x}{s_{b}}) f_{e2}(e)}{\sum_{m=1}^{3} f_{pm}(\frac{x}{s_{b}}) \sum_{n=1}^{2} f_{en}(e) \sum_{m=1}^{2} f_{dm}(\phi)},
\]

(22)

where \(S_{b}\) is the area of breast region, \(f_{p1}, f_{p2},\) and \(f_{p3}\) are the Gaussian mixture fits of the area percentage histogram, \(f_{e1}\) and \(f_{e2}\) are the Gaussian mixture fits of the eccentricity histogram, and \(f_{d1}\) and \(f_{d2}\) are the Gaussian mixture fits of the direction difference histogram. Table 2 shows the automatic categorization result according to the most likelihood. The accuracy was 66% with Cohen's kappa value of 0.47. In addition, if the two categories that achieve the most and the second most likelihood are both seen as the result of the cogent second opinion for reference, the accuracy can reach 83%.

To test the robustness of the proposed method, we used the Gaussian mixture fits to categorize 59 MCCs in other 55 mammograms from Tohoku University Hospital dataset. Among the 59 MCCs in mammograms, there were 46 grouped MCCs, 1 diffuse MCC, 3 segmental MCCs, 3 linear MCCs, and 6 regional MCCs diagnosed by radiologists. Table 3 shows the automatic categorization result according to the most likelihood. The accuracy was 68%, and the result showed that the proposed method is robust.

Deep learning-based methods may achieve better results in benign and malignant categorization. However, there are several disadvantages of deep learning-based methods in this research. First, we need an explainable system for radiologists in clinical situations to explain why the system makes the decision. Neural networks work in a black-box fashion, so it is difficult to explain a decision made by a deep learning-based system. In addition, it is very difficult to use a deep learning-based method for MCC detection because the spatial distribution information of very little MCs may be removed in pooling steps. Last, deep learning-based methods need a large number

| Number | Truth | Diff. | Gro. | Seg. | Reg. | Lin. |
|--------|-------|-------|------|------|------|------|
| Diff.  | 8     | 3     | 3    | 4    | 2    |      |
| Gro.   | 0     | 50    | 5    | 1    | 2    |      |
| Seg.   | 0     | 4     | 8    | 2    | 0    |      |
| Reg.   | 0     | 6     | 2    | 5    | 0    |      |
| Lin.   | 0     | 3     | 1    | 0    | 2    |      |

| Number | Truth | Diff. | Gro. | Seg. | Reg. | Lin. |
|--------|-------|-------|------|------|------|------|
| Diff.  | 1     | 4     | 0    | 0    | 0    |      |
| Gro.   | 0     | 32    | 1    | 1    | 1    |      |
| Seg.   | 0     | 2     | 1    | 1    | 0    |      |
| Reg.   | 0     | 6     | 4    | 0    | 0    |      |
| Lin.   | 0     | 2     | 0    | 0    | 2    |      |

\[
p(\text{Lin.}) = \frac{f_{p2}(\frac{x}{s_{b}}) f_{e2}(e)}{\sum_{m=1}^{3} f_{pm}(\frac{x}{s_{b}}) \sum_{n=1}^{2} f_{en}(e) \sum_{m=1}^{2} f_{dm}(\phi)},
\]

(20)

\[
p(\text{Seg.}) = \frac{f_{p2}(\frac{x}{s_{b}}) f_{e1}(e) f_{d1}(\phi)}{\sum_{m=1}^{3} f_{pm}(\frac{x}{s_{b}}) \sum_{n=1}^{3} f_{en}(e) \sum_{m=1}^{2} f_{dm}(\phi)},
\]

(21)

\[
p(\text{Reg.}) = \frac{f_{p2}(\frac{x}{s_{b}}) f_{e1}(e) f_{d2}(\phi)}{\sum_{m=1}^{3} f_{pm}(\frac{x}{s_{b}}) \sum_{n=1}^{3} f_{en}(e) \sum_{m=1}^{2} f_{dm}(\phi)}.\]

(22)
of labeled mammograms, but the preparation of labeled data is difficult. Therefore, it is difficult to use a deep learning-based method in this research.

Moreover, it should be noted that there is a great potential for improvement of the categorization accuracy. Firstly, the remained non-MC candidates may affect the modeled MCC components’ shapes or locations. Utilizing another method or structure element for the top-hat transform may make a better segmentation [27]. Secondly, because of the limitation of the duct simulation method [19], the simulation can make errors, which is the reason for miscategorization in some cases. An accurate simulation may improve the accuracy of the categorization. Last of all, the accuracy may change with either more cases or better feature selection. The features used to categorize MCCs in this study are selected according to the BI-RADS categorization, but there are some other morphological features and texture features [12] not used here, which may be useful to classify MCCs.

5. Conclusion

Diagnosis of MCCs in mammograms is a difficult task even for expert radiologists. Spatial distributions of MCCs can provide valuable information for radiologists to diagnose MCCs. In this paper, an adaptive GMM method for diagnosis of MCCs in mammograms has been developed. The proposed method can model the MCCs in mammograms and classify them into spatial distribution categories.

Except for the spatial distribution of MCCs, each shape of individual MCs is another important information of mammographic anatomy. In future work, we will make experiments on more mammograms including both mammograms with MCCs and normal cases for detection and spatial distribution categorization, classify the MCCs into shape categories. Then, we can classify the MCCs into BI-RADS categories by combining the shape and spatial distribution information.

Acknowledgments

This work was supported by JSPS KAKENHI Grant Number JP17K17582, JP17H04117, JP18K19892.

References

[1] M. Baum and C. Henderson: Classic Papers in Breast Disease, pp. 162–180, CRC Press, 2004.

[2] H.D. Cheng, X. Cai, X. Chen, L. Hu, and X. Lou: Computer-aided detection and classification of microcalcifications in mammograms: A survey, Pattern Recognition, Vol. 36, No. 12, pp. 2967–2991, 2003.

[3] R.N. Strickland: Image-Processing Techniques for Tumor Detection, pp. 135–157, CRC Press, 2002.

[4] P.L.A. Hernández, T.T. Estrada, A.L. Pizarro, M.L.D. Cisternas, and C.S. Tapia: Breast calcifications: Description and classification according to BI-RADS, 5th edition, Rev. Chil. Radiol., Vol. 22, pp. 80–91, 2016.

[5] H. Strange, Z. Chen, E.R. Denton, and R. Zwiggelaar: Modelling mammographic microcalcification clusters using persistent mereotopology, Pattern Recognition Letters, Vol. 47, pp. 157–163, 2014.

[6] R.M. Nishikawa, M.L. Giger, K. Doi, C.J. Vyborny, and R.A. Schmidt: Computer-aided detection of clustered microcalcifications on digital mammograms, Medical and Biological Engineering and Computing, Vol. 33, No. 2, pp. 174–178, 1995.

[7] B. Caputo, E. La Torre, S. Bouattour, and G.E. Gigante: Detection: Spin glass-Markov random fields, Health Data in the Information Society: Proceedings of MIE2002, Vol. 90, p. 30, 2002.

[8] G. Lemaur, K. Drouiche, and J. DeConinck: Highly regular wavelets for the detection of clustered microcalcifications in mammograms, IEEE Transactions on Medical Imaging, Vol. 22, No. 3, pp. 393–401, 2003.

[9] L. Wei, Y. Yang, R.M. Nishikawa, and Y. Jiang: A study on several machine-learning methods for classification of malignant and benign clustered microcalcifications, IEEE Transactions on Medical Imaging, Vol. 24, No. 3, pp. 371–380, 2005.

[10] Y. Wu, M.L. Giger, K. Doi, C.J. Vyborny, R.A. Schmidt, and C.E. Metz: Artificial neural networks in mammography: Application to decision making in the diagnosis of breast cancer, Radiology, Vol. 187, No. 1, pp. 81–87, 1993.

[11] J.Y. Lo, J.A. Baker, P.J. Kornguth, J.D. Iglehart, and C.E. Floyd, Jr.: Predicting breast cancer invasion with artificial neural networks on the basis of mammographic features, Radiology, Vol. 203, No. 1, pp. 159–163, 1997.

[12] H.P. Chan, B. Sahiner, K.L. Lam, N. Petrick, M.A. Helvie, M.M. Goodsett, and D.D. Adler: Computerized analysis of mammographic microcalcifications in morphological and texture feature spaces, Medical Physics, Vol. 25, No. 10, pp. 2007–2019, 1998.

[13] A.P. Dhawan, Y. Chitre, C. Bonasso, and K. Wheeler: Radial-basis-function based classification of mammographic microcalcifications using texture features, Proceedings of 17th International Conference of the Engineering in Medicine and Biology Society, Vol. 1, pp. 535–536, 1995.

[14] R.J. Ferrari, P.M. Azevedo-Marques, A.F. Frère, S.K. Kinoshita, and L.A.R. Spina: Characterization of breast cancer using statistical approaches, Proc. Computer-Aided Diagnosis in Medical Imaging, pp. 281–286, 1999.

[15] W.J. Veldkamp, N. Karssenmeier, J.D. Otten, and J.H. Hendriks: Automated classification of clustered microcalcifications into malignant and benign types, Medical Physics, Vol. 27, No. 11, pp. 2600–2608, 2000.

[16] O.R. Zaiane, M.L. Antonie, and A. Coman: Mammography classification by an association rule-based classifier, Proceedings of the Third International Conference on Multimedia Data Mining, pp. 62–69, 2002.

[17] H. Soltanian-Zadeh and F. Rahee-Rad: Comparison of multiwavelet, wavelet, Haralick, and shape features for microcalcification classification in mammograms, Pattern Recognition, Vol. 37, No. 10, pp. 1973–1986, 2004.

[18] Z. Zhang, X. Zhang, K. Ichiji, M. Osanai, and N. Homma: Computer-aided diagnosis of microcalcification clusters in mammograms using an adaptive GMM, Proceedings of SS12018, SS17-02, 2018.

[19] N. Homma, T. Handa, T. Ishibashi, Y. Kawasumi, and N. Homma: Breast cancer detection system, breast cancer detection method, breast cancer detection program, and computer-readable recording medium having breast cancer detection program recorded thereon, U.S. Patent 9,808,217, 2017.

[20] S.K. Bandyopadhyay: Pre-processing of mammogram images, International Journal of Engineering Science and Technology, Vol. 2, No. 11, pp. 6753–6758, 2010.

[21] R.C. Gonzalez, R.E. Woods, and S.L. Eddins: Digital Image Processing Using MATLAB, 3rd edition, Prentice Hall, 2004.

[22] X. Zhang, N. Homma, S. Goto, Y. Kawasumi, T. Ishibashi, M. Abe, N. Sugita, and M. Yoshizawa: A hybrid image filter method for computer-aided detection of microcalcification clusters in mammograms, Journal of Medical Engineering, Vol. 2013, pp. 1–8, 2013.

[23] M.A.T. Figueiredo and A.K. Jain: Unsupervised learning of finite mixture models, IEEE Transactions on Pattern Analysis and Machine Intelligence, Vol. 24, No. 3, pp. 381–396, 2002.

[24] C.S. Wallace and D.L. Dow: MML clustering of multi-state,
Poisson, von Mises circular and Gaussian distributions, Statistics and Computing, Vol. 10, No. 1, pp. 73–83, 2000.

[25] R.A. Baxter and J.J. Oliver: Finding overlapping components with MML, Statistics and Computing, Vol. 10, No. 1, pp. 5–16, 2000.

[26] K.J. Berry and P.W. Mielke, Jr.: A generalization of Cohen’s kappa agreement measure to interval measurement and multiple raters, Educational and Psychological Measurement, Vol. 48, No. 4, pp. 921–933, 1998.

[27] M. Wirth, M. Fraschini, and J. Lyon: Contrast enhancement of microcalcifications in mammograms using morphological enhancement and non-flat structuring elements, Proc. 17th IEEE Symposium on Computer-Based Medical Systems, pp. 134–139, 2004.

Zhang Zhang

He received his B.S. degree from Beihang University, China in 2016. He received his M.S. degree from Tohoku University, Japan, in 2018. He is currently a Ph.D. student at Tohoku University. His research interests include imaging processing.

Xiaoyong Zhang

He received his Ph.D. degree from Tohoku University, Japan, in 2011. He is currently an Assistant Professor of National Institute of Technology, Sendai College. His research interests include artificial intelligence and imaging processing. He is a member of IEICE. He is a Senior member of IEEE.

Kei Ichiji (Member)

He received his Ph.D. degree from Tohoku University, Japan, in 2014. He is currently an Assistant Professor of Tohoku University Graduate School of Medicine. His research interests include radiation therapy. He is a member of IEEE and AAPM.

Yumi Takane

She received her Ph.D. degree from Tohoku University, Japan, in 2015. In 2016, she joined Tohoku University Hospital. Her research interests include image analysis and image quality evaluation of medical images.

Satoru Yanagaki

He received his B.S. degree from Tohoku University, Japan, in 2014. He is currently a Ph.D. student at Tohoku University.

Yusuke Kawasumi

He received his Ph.D. degree from Tohoku University, Japan, in 2008. He is currently an Associate Professor of Tohoku University Graduate School of Medicine. His research interests include radiation image diagnosis.

Tadashi Ishibashi

He received his B.S. degree from the Faculty of Medicine, Tohoku University, Japan, in 1978. He is currently a Professor Emeritus of Tohoku University Graduate School of Medicine. His research interests include diagnostic radiology and interventional radiology.

Noriyasu Homma (Member)

He received his Ph.D. degree from Tohoku University, Japan, in 1995. He is currently a Professor of Tohoku University Graduate School of Medicine. His research interests include complex systems and brain functions. He is a member of IEEE and AAPM.