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FULL PAPER

Fuzzy C-means clustering of magnetic resonance imaging on apparent diffusion coefficient maps for predicting nodal metastasis in head and neck cancer

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Objective: The present study evaluated and analyzed apparent diffusion coefficients (ADCs) from partitions through a fuzzy C-means (FCM) technique for distinguishing nodal metastasis in head and neck cancer.

Methods: MRI studies of 169 lymph node lesions, dissected from 22 patients with a histopathologically confirmed lymph node status, were analyzed using in-house software developed using MATLAB® (The MathWorks® Inc., Natick, MA). A radiologist manually contoured the lesions, and ADCs for each lesion were divided into two (low and high) and three (low, intermediate and high) partitions by using the FCM clustering algorithm.

Results: The results showed that the low-value ADC clusters were more sensitive (95.7%) in distinguishing malignant from benign lesions than the whole-lesion mean ADC values (78.3%), while retaining a high

specificity (approximately 90%). Moreover, receiver-operating characteristic curves demonstrated that the low-value ADC clusters used as a predictor of malignancy for lymph nodes could achieve a higher area under the curve (0.949 and 0.944 for two and three partitions, respectively).

Conclusion: The segmentation by ADC values of lesions through the FCM technique enables the efficient characterization of the lymph node pathology and can help distinguish malignant from benign lymph nodes.

Advances in knowledge: Tumour heterogeneity may degrade the prediction of metastatic lymph nodes that involves using mean region-of-interest ADC values. The clustering of ADC values in lesions by using FCM can improve the diagnostic accuracy of nodal metastasis and reduce interreader variance.

INTRODUCTION

Detecting whether cancers have spread to lymph nodes not only helps in cancer staging but also serves as an extremely crucial clinicopathological factor for evaluating the prognosis and survival as well as for treatment planning.^{1–3} Therefore, the ability to differentiate malignant from benign lymph nodes would be critical for optimizing head and neck cancer treatment.

Anatomical imaging through X-ray CT and MRI are well-established imaging tools for the initial diagnosis of head

and neck cancer and are widely used for treatment planning, monitoring and post-treatment follow-up assessment.⁴ However, the limited accuracy⁵ of visualizing the morphological characteristics (shape, size, internal architecture, extracapsular extension and vascular features or necrosis) in anatomical CT and MR images necessitates the use of advanced imaging techniques that have the potential to increase diagnostic accuracy.

Diffusion-weighted imaging (DWI) enables the visualization of the diffusion properties of water molecules in the

extracellular space of biological tissues by means of calculating apparent diffusion coefficient (ADC) maps.⁶ The ADC value is calculated using the equation $ADC = \ln(SI_1/SI_2)/b_2 - b_1$, where SI_1 and SI_2 are the signal intensity of diffusion-weighted images with different gradient factors of b_1 and b_2 , which reflect the strength and timing of the gradients. ADC values suggest that this imaging method has the potential for highly specific characterization of head and neck lesions.⁷ The use of ADC values based on an optimized threshold for distinguishing malignant from benign lymph nodes has been previously reported;^{7–12} in these studies, benign lymph nodes had higher ADC values than those of malignant lymph nodes. Sumi¹⁰ et al reported contrasting results that may be due to different region of interest (ROI) positions. Therefore, a careful selection of ROI positions within suspect lesions is required for measuring ADCs, because a variation in the positions affects study results.¹³

The fuzzy C-means (FCM) clustering method enables clustering one data set into various groups with common traits.^{14–16} We hypothesize that lesion classification into partitions through clustering analysis more efficiently distinguishes malignant from benign lesions than methods that entail using whole-lesion mean ADC values. We investigated this hypothesis on data from patients with diagnosis of head and neck cancer.

METHODS AND MATERIALS

Patient selection

This study was approved by the local institutional review committee. All patients gave their examination and research informed consent before MRI examinations, which included morphological MRI and DWI before undergoing surgery for tumour and lymph node removal between July 2009 and June 2010. A total of 26 patients were enrolled in this study; however, 4 patients whose images exhibited motion artefacts were excluded from analysis.

The remaining 22 patients (21 males and 1 female; median age, 51.5 years; range, 28–66 years) had primary cancer affecting the tongue (13 patients), buccal mucosa (2 patients), oropharynx (2 patients), hypopharynx (3 patients), oral floor (1 patient) and retromolar space (1 patient). In total, 169 nodes were dissected from 22 patients with a histopathologically confirmed lymph node status; 146 benign and 23 malignant lymph nodes were detected.

MRI

All MRI studies were performed on a 3.0-T MRI scanner (Verio, Siemens, Germany) by using a 12-channel head coil combined with a 4-channel neck coil, according to the following protocols. Before contrast administration, the patients underwent three MR sequences. The first sequence is the transverse T_2 weighted turbo spin-echo (TSE) MRI [repetition time (TR)/echo time (TE), 3500/88 ms; section thickness, 3 mm; intersection gap, 0.9 mm; field of view (FOV), 230 mm; image matrix, 314×448]. The second one is the transverse T_1 weighted TSE MRI (TR/TE, 700/10 ms; section thickness, 3 mm; FOV, 230 mm; intersection gap, 0.9 mm; image matrix, 314×448). The final one is DWI of the head and neck in the transverse plane by using a single-shot spin-echo echoplanar imaging

sequence (TR/TE, 8000/77 ms; section thickness, 3 mm; intersection gap, 0.9 mm; FOV, 230 mm; image matrix, 122×144 ; bandwidth, 880 Hz/Px; number of signal averages, three; diffusion scheme, bipolar). Optimal suppression of fat is achieved using spectral adiabatic inversion recovery (SPAIR). Diffusion-weighted images were obtained at b -factors of 0 and 800 s mm^{-2} for each section in the same sequence.¹² The scan range was from the skull base to the suprasternal notch. The ADC maps were automatically calculated on the scanner console.¹⁷

Contrast injection was then performed. After a bolus injection of 0.1 mmol kg^{-1} gadodiamide (Omniscan; GE Healthcare, Cork, Ireland), the patients underwent one scanning sequence: transverse fat-suppressed T_1 weighted TSE MRI (TR/TE, 700/10 ms; section thickness, 3 mm; FOV, 230 mm; intersection gap, 0.9 mm; image matrix, 314×448 ; number of signals acquired, one).

Pathological evaluation

The histologic results from surgical resection were treated as the reference standard for primary tumour metastasis to lymph nodes. Surgeons carefully reviewed the MR images on a picture archiving and communication system; intraoperatively, the specimens were matched with the lymph nodes as imaged on T_2 weighted and T_1 weighted contrast-enhanced MR images. To ensure that the node removed surgically during neck dissection was the same node as observed in MRI, the lymph nodes were excised adjacent to reference structures to determine the relationship between the excised nodes and the surrounding structures. After surgery, each node was carefully delineated and tagged for pathologic diagnosis. The histopathologic and radiologic findings were correlated on an individual nodal basis.

The size of the lymph node was a criterion for evaluating lymph node malignancy. Hence, we divided the lymph node specimens into subcentimetre and supracentimetre groups according to their minimal transverse diameters, which were measured by a radiologist on T_1 weighted contrast-enhanced MR images.

Image analysis

Diffusion-weighted imaging apparent diffusion coefficient calculation

DWI ADC maps were automatically calculated using standard software on the scanner console. The ROI position was based on T_2 and T_1 weighted contrast-enhanced MR images but was directly drawn on the ADC map for each node by a radiologist.^{12,18} Manual ROI measurements of the lymph nodes involved identifying the ROI of the largest solid tumour to avoid an obvious necrotic or cystic region, which may result in an ADC value variation from different components in the lymph node.

Fuzzy C-means technique

All MR images were analyzed and evaluated using in-house software implemented with MATLAB® (The MathWorks® Inc., Natick, MA). The voxels extracted from each ROI on the ADC map were clustered into k partitions through the FCM algorithm (Appendix A). This algorithm uses a clustering technique in

which a data set is grouped into c clusters with every data point in the data set belonging to every cluster to a certain degree. The algorithm attempts to identify natural groupings of data from the data set. Furthermore, the FCM algorithm was applied to the data obtained from each ROI, which included a whole lymph node. Cluster number determination is an essential step in the FCM algorithm,¹⁹ and the natural cluster number depends on lesion heterogeneity. We assumed that 2–3 partitions were sufficient for accommodating lesion heterogeneity, *i.e.* necrosis, solid nodule etc. Therefore, when two clusters were selected, ADC values of lesions were divided into low (ADC_{2-L}) and high (ADC_{2-H}) ADC clusters; when three clusters were selected, ADC values of lesions were divided into low (ADC_{3-L}), intermediate (ADC_{3-I}) and high (ADC_{3-H}) ADC clusters. For comparison, the whole-lesion mean ADC value (ADC_1), which constitutes a cluster of one, was analyzed.

Statistical analysis

Statistical analyses were performed using MedCalc® software (v. 9.4 MedCalc Software, Mariakerke, Belgium). A box-and-whisker plot was used for depicting the scatterplot of mean ADC values of benign and malignant lymph nodes for the three cluster models. An unpaired two-tailed Student's *t*-test was performed for all metrics— ADC_1 , ADC_{2-L} , ADC_{2-H} , ADC_{3-L} , ADC_{3-I} and ADC_{3-H} —and for determining differences in the mean of the benign and malignant lymph nodes.

After the histopathologic findings and processing results from the FCM technique for each lymph node were correlated, the optimal $ADC_b = 0.800$ threshold for differentiating malignant

from benign lymph nodes was determined using receiver-operating characteristic (ROC) analysis.¹² The sensitivity and specificity of the DWI method were then calculated for supra-centimetre and subcentimetre lymph nodes. A cut-off value was determined for predicting lesion malignancy by using the maximum value of the Youden index, calculated for every point on the ROC curve (sensitivity + specificity – 1). The corresponding area under the curve (AUC), sensitivity and specificity were calculated using 95% confidence intervals. Differences in the diagnostic performance among clustered ADC values were analyzed by comparing the ROC curves according to the method described by DeLong et al,²⁰ $p < 0.05$ was considered significant.

RESULTS

Figure 1 illustrates the lymph node of a patient with hypopharynx squamous cell carcinoma; a pathological examination revealed metastasis. As shown in Figure 1a, the hypointense area within the lymph node on the contrast-enhanced T_1 weighted image was a highly suspicious necrotic area. Figure 1b presents the corresponding calculated ADC map, whose ADC values are plotted as a colour-coded image for observing the suspicious necrotic area. Figure 1c shows the corresponding haematoxylin and eosin-stained histopathologic slide of the cervical lymph node with metastatic squamous cell carcinoma and tumour necrosis. The colour-coded cluster analysis of the same lymph node by using the two- and three-cluster models is shown in Figure 2, which illustrates lesion classification into partitions.

The box-and-whisker plot (Figure 3) presents the distribution of mean ADC values of benign and malignant lymph nodes across

Figure 1. A 60-year-old patient with pathologically proven squamous cell carcinoma of the hypopharynx. (a) The axial post-gadolinium T_1 weighted fast spin-echo MR image showing enlarged lymph nodes (arrow) with a heterogeneous signal intensity. (b) Malignant lymphadenopathy on apparent diffusion coefficient (ADC) maps revealing an inhomogeneous intensity with colour mapping. (c) The corresponding haematoxylin and eosin (H&E)-stained histopathologic slide showing a cervical lymph node with a normal lymphocyte (hollow arrowhead), metastatic squamous cell carcinoma (hollow black arrow) and tumour necrosis (white arrow). (H&E stain, $\times 40$).

Figure 2. Overlap of apparent diffusion coefficient (ADC) and cluster maps assuming one (a), two (b) and three (c) clusters and their corresponding histograms (e-f). H, high ADC cluster; I, intermediate ADC cluster; L, low ADC cluster.

all 169 lymph nodes grouped according to the pathological results among the various clusters. Figure 3 indicates that the low ADC clusters selected in the two- and three-cluster models yielded the most favourable separation of benign from malignant lymph nodes. Table 1 presents a summary of the detailed

data for various clusters according to the cut-off ADC within a cluster, mean ADC value, sensitivity, specificity, accuracy and AUC value. After the cut-off ADC value was determined according to the Youden index, the use of the low ADC clusters (ADC_{2-L} and ADC_{3-L}) for distinguishing malignant from benign

Figure 3. A box-and-whisker plot presenting the apparent diffusion coefficient (ADC) ($\times 10^{-3} \text{ mm}^2 \text{ s}^{-1}$) of benign (B) and malignant (M) lymph nodes in one-cluster (ADC_1), two-cluster (ADC_{2-L} and ADC_{2-H}) and three-cluster (ADC_{3-L} , ADC_{3-I} , and ADC_{3-H}) models.

Table 1. Apparent diffusion coefficient (ADC) in one-, two- and three-cluster models

Strategies	ADC cut-off value	ADC value		Sensitivity (%)	Specificity (%)	Accuracy (%)	<i>p</i> -value	AUC
		Benign	Malignant					
Lee et al ¹² (2013)	0.851	1.08 ± 0.22	0.7 ± 0.11	91.3	91.1	91.1	<0.0001	0.97
ADC ₁	0.881	1.14 ± 0.25	0.80 ± 0.11	78.3	91.1	89.3	<0.0001	0.915
ADC _{2-L}	0.804	1.02 ± 0.23	0.67 ± 0.10	95.7	90.4	91.1	<0.0001	0.949
ADC _{2-H}	1.101	1.28 ± 0.27	0.96 ± 0.15	87	71.9	74.0	<0.0001	0.867
ADC _{3-L}	0.764	0.98 ± 0.22	0.64 ± 0.11	95.7	90.4	91.1	<0.0001	0.944
ADC _{3-I}	0.884	1.14 ± 0.25	0.81 ± 0.11	82.6	89.0	88.2	<0.0001	0.920
ADC _{3-H}	1.241	1.34 ± 0.28	1.03 ± 0.17	91.3	59.6	63.9	<0.0001	0.832

AUC, area under the curve.

The unit of the value is $10^{-3} \text{ mm}^2 \text{ s}^{-1}$.

lesions revealed a higher sensitivity (95.7% and 95.7%, respectively) and accuracy (91.1% and 91.1%, respectively) than those obtained using the whole-lesion mean ADC value (sensitivity 78.3% and accuracy 89.3%), while retaining a high specificity (approximately 90%). The corresponding ROC curves for various clusters in the one-, two- and three-cluster models are illustrated in Figure 4. Of all the generated ROC curves, ADC_{2-L} (0.949) showed the highest AUC, followed by ADC_{3-L} (0.944), ADC_{3-I} (0.920), ADC₁ (0.915), ADC_{2-H} (0.867) and ADC_{3-H} (0.832). In this study, using of cluster number 2 in conjunction with the low-ADC values has resulted in the best sensitivity and an acceptable specificity (90.4% for ADC_{2-L}) (Table 1). Increasing the cluster number to 3 did not change the specificity (90.4% for ADC_{3-L}) (Table 1).

Overall, 18 lymph nodes (benign: 5 nodes; malignant: 13 nodes) were misclassified using the cut-off value of 0.881 in the whole-lesion mean ADC, and the misclassified cases could be reduced

to 15 (benign: 1 case; malignant: 14 cases) with a cut-off value of 0.804 in ADC_{2-L}.

All lymph nodes were divided into two groups according to their diameters:²¹ supracentimetre ($n = 58$) or subcentimetre ($n = 111$) lymph nodes. For subcentimetre lymph nodes, the sensitivities of ADC₁, ADC_{2-L} and ADC_{3-L} were 78.6%, 92.9% and 92.9%. The specificity and accuracy of ADC₁, ADC_{2-L} and ADC_{3-L} were similar (approximately 90%). For supracentimetre lymph node, the sensitivity and accuracy of ADC_{2-L} and ADC_{3-L} were higher than those of ADC₁. The detailed data are summarized in Table 2.

Figure 5 presents a comparison of the ROC curves of ADC₁, ADC_{2-L} and ADC_{3-L} for the one-, two- and three-cluster models, respectively; the corresponding AUC, sensitivity and specificity are reported in Table 2. Similar to the results presented in Table 1, benign and malignant lymph nodes were more efficiently distinguished in ADC_{2-L} for both the subcentimetre and supracentimetre groups, possibly because the limited resolution of DW images complicated the characterization of the heterogeneous appearance of small-sized tumours.²²

DISCUSSION

The ADC measurement for distinguishing benign from malignant lymph nodes in head and neck cancer has been substantiated as a strong predictor in several studies.^{9,11,17,23} A potential problem of using the ADC cut-off value to distinguish malignant lymph nodes is that metastatic nodes with necrotic areas might have higher ADC values because of necrosis and might be misidentified as benign. To prevent this bias, our previous study¹² calculated the ADC value from the ROI drawn manually on the solid part of the lymph nodes. In the present study, we developed the FCM clustering technique as a computed aid to help solve this problem. Various approaches have been adopted for analyzing the heterogeneity in MR images of tumours, including k-means clustering,^{24,25} texture analysis^{26,27} and fractal dimensions.^{28,29} To the best of our knowledge, this is the first study to use FCM for distinguishing malignant and benign lymph nodes in head and neck cancer.

FCM clustering involves an unsupervised classification without user-defined training classes and a prior model; it is a simple and

Figure 4. Receiver-operating characteristic curves obtained through fuzzy C-means analysis assuming cluster numbers of 1, 2 and 3. The area under the curve for ADC₁, ADC_{2-L}, ADC_{2-H}, ADC_{3-L}, ADC_{3-I} and ADC_{3-H} was 0.915, 0.949, 0.867, 0.944, 0.92 and 0.832, respectively.

Table 2. The sensitivity, specificity and area under the curve (AUC) with 95% confidence intervals (CIs) for diagnosing malignant lymph nodes for different lymph node sizes by using ADC₁, ADC_{2-L} and ADC_{3-L}

LN group	LN diameter (cm)	B/M	Strategies	Sensitivity (%)	Specificities (%)	Accuracy (%)	AUC (95% CI)
Subcentimetre	<1.0	97/14	ADC ₁	78.6	91.8	90.1	0.914 (0.845–0.959)
			ADC _{2-L}	92.9	89.7	90.1	0.937 (0.875–0.975)
			ADC _{3-L}	92.9	88.7	89.2	0.931 (0.867–0.970)
Supracentimetre	>1.0	49/9	ADC ₁	77.8	93.9	91.4	0.925 (0.825–0.978)
			ADC _{2-L}	100	93.9	94.8	0.968 (0.885–0.997)
			ADC _{3-L}	100	93.9	94.8	0.964 (0.878–0.995)

ADC, apparent diffusion coefficient; B/M, benign/malignant; LN, lymph node.

straightforward approach for separating the ADC value of identified suspicious lymph nodes into multiple clusters.

Figure 2 shows that the lymph node was classified from one to three clusters and presents different colour-coded histograms. Multiple clusters are efficient for classifying ADC values (low to high) according to the components of the lymph node.

ADC₁ indicates one ROI position in a whole lymph node that includes various components that affect the ADC values as mentioned. Therefore, the sensitivity in ADC₁ was lower than that in ADC_{2-L} and ADC_{3-L}; it was also lower than that reported by Lee et al¹² (91.3%). The sensitivities in ADC_{2-L} (95.7%) and ADC_{3-L} (95.7%) were higher than those reported by Lee et al (91.3%). The specificities in ADC_{2-L} and ADC_{3-L} were similar to those reported by Lee et al. In strategies of ADC_{2-L} and ADC_{3-L}, altering the ADC cut-off value decreased the false negatives but did not change the number of benign nodes classified as malignant.

A lymph node with a necrotic part has higher ADC values than a benign lymph node.¹⁰ Hence, while clinically measuring ADC values, radiologists must avoid positioning the ROI to encompass the necrotic area³⁰ by comparing the ADC maps with anatomical MR images (*T*₁ and *T*₂ weighted images). However, an ROI position avoiding the necrotic area in ADC value measurements is

subjective and depends on the experience of radiologists. The FCM clustering technique is a helpful tool for automatic lesion classification into clusters. Careful selection of the clusters can possibly avoid the necrotic areas and micrometastatic regions. These studies have shown that measuring the mean ADC values of low-ADC clusters is an alternative method for improving the diagnostic accuracy for both small and larger lymph nodes. Therefore, FCM clustering analysis of lymph node lesions can assist radiologists in predicting nodal metastasis.

When we set the cluster number at 1 in the FCM technique, the ROI extent included the whole lymph node (ADC₁) and revealed a sensitivity and specificity of 78.3% and 91.1%, respectively (Table 1). One ROI in a lymph node may include various components. However, the sensitivity and specificity improved in the groups of ADC_{2-L} and ADC_{3-L} when the cluster number was set at 2 and 3, respectively. The sensitivity and specificity in ADC_{2-L} were 95.7% and 90.4%, respectively, and 95.7% and 90.4%, respectively, in ADC_{3-L}. These improvements approached those of manual selection of ROI in the previous study (Lee et al,¹² sensitivity: 91.3% and specificity: 91.1%) and demonstrated even higher sensitivity. The present clustering method can effectively distinguish solid from necrotic components in a lymph node and may help distinguish malignant from benign lymph nodes.

Figure 5. Receiver-operating characteristic curves for ADC₁, ADC_{2-L} and ADC_{3-L} in (a) subcentimetre and (b) supracentimetre lymph nodes.

A limitation of the FCM clustering method is the requirement of a predetermined cluster number. Because of the low resolution of DW images and small size of lymph nodes, two or three partitions of the lesion area are sufficient for describing the complete lymph node. In this study, we achieved similar results with two and three clusters. No apparent difference was observed between ADC_{3-H} and ADC_{3-L}, possibly because the composition of lymph nodes may be limited to two components. Another limitation is that the study was conducted at a single institution and included a relatively low number of malignant lymph nodes. Additional studies enrolling more cases from different centres are required for confirming our findings and optimizing the cluster number. Some studies^{8,10–13} have investigated head and neck tumours with two *b*-values for ADC values. Although, two *b*-values are sufficient for creating an ADC image, selecting more *b*-values ensures a more accurate calculation of the ADC values. Padhani et al³¹ preferred *b* = 50 to *b* = 0, which can mitigate the contribution of perfusion to the calculation of ADC values. In the future, we will use more *b*-values and *b* = 50 as the SI₁ to investigate ADC images for optimization.

Padhani et al³¹ indicated that some studies have reported mean values from single or multiple ROIs placed on ADC maps, and these measures may be limited to detecting treatment-related

changes in ADC values such as cystic or necrotic areas. They used the cumulative frequency ADC histogram to present the percentile of ADC values. This method enables evaluating the complex changes in ADC values by separately assessing the spread of ADC data and presents tumour heterogeneity from the spatial distributions of ADC values. In the future, we can learn from this method to investigate ADC values and compare them with those from using the FCM technique. Such an investigation will provide a more sensitive method for physicians to treat head and neck cancers.

CONCLUSION

Applying the FCM technique to ADC maps can facilitate quantifying heterogeneous lesions and provide additional benefits in distinguishing benign from malignant neck pathologies compared with whole-lesion mean ADC values. Radiologists can use the output of clustering analysis for ROI classification and final decision-making. Therefore, we recommend the clinical application of this method for distinguishing malignant and benign lymph nodes.

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APPENDIX A

FCM clustering, proposed by Dunn¹⁵ in 1974 and extended by Bezdek et al,¹⁴ is commonly used for MRI segmentation¹⁶ as an iterative clustering algorithm for optimizing parameter partitioning by minimizing the squared error objective function. The objective function J is described by the following equation:

$$J = \sum_{i=1}^N \sum_{j=1}^c u_{ji}^m d^2(x_i, v_j), \quad m > 1 \quad (\text{A1})$$

Let x_i be the i th pixels used for clustering, N the total number of all pixels, v_j the j th cluster centre, c the number of clusters ($2 \leq c < N$), u_{ji} the degree of membership of the pixels x_i to the j th cluster and m the fuzzy coefficient. In this study, m was 2 and the iterative convergence threshold ε was 1×10^{-6} ; the fuzzy membership matrix $U = [u_{ji}]$ was randomly initiated. The variable $d^2(x_i, v_j)$ represents the distance between the data point x_i and cluster centre v_j . The fuzzy partitioning can be achieved by minimizing the objective function in the following iterative process. First, v_j is updated based on U and the following equation:

$$v_j^{(b)} = \frac{\sum_{i=1}^N \left(u_{ji}^{(b)}\right)^m x_i}{\sum_{i=1}^N \left(u_{ji}^{(b)}\right)^m} \quad (\text{A2})$$

where b is the iterative number. After obtaining v_j , the fuzzy membership matrix is updated based on the following equation:

$$u_{ji}^{(b+1)} = \frac{1}{\sum_{k=1}^c \left(\frac{d_{ji}}{d_{ki}}\right)^{2/m-1}} \quad (\text{A3})$$

The iterative process is terminated on the basis of the difference between the present and previous fuzzy membership matrices: when $\|U^{(b)} - U^{(b+1)}\| < \varepsilon$, the iterative process is terminated and the next iterative process begins with updating the v_j . At the end of the iteration, the centroid of a cluster representing the average values of all pixels weighted by their degree of belonging to the cluster is obtained and used for computing the degree of relationship to each cluster for each pixel. Subsequently, the defuzzification process is performed according to the membership matrices for determining the clusters with the highest degree of membership in each pixel:

$$C_i = \arg_j \{ \max \{ u_{ji} \} \} \quad \forall j, \forall k \quad (\text{A4})$$

where C_i represents the classification to which the i th pixels belongs.