Multifractal Analysis with L2 Norm Denoising Technique: Modelling of MS Subgroups Classification

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Abstract. Multifractal methods are employed to recognize the significant attributes through the removal of the noise in any dataset. Being a useful and sensitive technological tool, magnetic resonance imaging (MRI) is employed for the diagnosis of chronic diseases of the central nervous system, one of which is Multiple Sclerosis disease (MS). MS subgroups (Primary Progressive MS (PPMS), Relapsing Remitting MS (RRMS) and Secondary Progressive MS (SPMS)) were examined in this study. The dataset is based on the Expanded Disability Status Scale (EDSS) and MRI that belong to 139 individuals in total, 120 of whom have one of the MS subgroups, and 19 are healthy individuals. The stages of the study are as follows: (i) L2 Norm Denoising, which is a multifractal method was applied on the MS dataset, namely the MS dataset. From this application, the new dataset was formed. (ii) The new dataset (MS_L2 Norm dataset) which is comprised of the significant attributes was obtained as a result of the application in (i). (iii) K-means clustering algorithm was applied on both the MS dataset and MS_L2 Norm dataset for the classification of the MS subgroups. (iv) The classification accuracy rate for the K-means clustering algorithm in relation to the MS dataset and MS_L2 Norm dataset was compared both for patients with MS subgroups and healthy individuals. For the first time, through this study, the K-means classification has been performed by using multifractal denoising methods for the aforementioned dataset. The results of our study show that K-means algorithm and classification yielded more accurate results for the MS_L2 Norm dataset compared to the MS dataset in terms of classification. Overall, this study has aimed to bridge a gap in the literature.

Keywords: Multifractal Denoising method · K-means algorithm · MS subgroup · Clustering · MRI

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1 Introduction

Being common in nature, multifractal systems are a generalization of a fractal system where a single exponent, or the fractal dimension, proves is to be insufficient to describe its dynamics, thus, in a continuous spectrum of exponents is required [1]. Multifractal analysis employs the basis of mathematics to examine datasets, frequently accompanied by other fractal analysis methods. Besides being applied in various practical situations, multifractal analysis techniques are implemented for interpreting medical images, in finance sector, bioinformatics and areas concerning natural sciences. The multifractal denoising algorithm is utilized as a technique adapted to complex images and signals. This technique serves for improvement in the data in question [2,3].

Multifractal methods are employed neuroscience. Accordingly, they are used for the neurological disorders' identification and classification. One disease is Multiple Sclerosis (MS), a condition that involves the spinal cord and/or the brain, causing various symptoms. In addition, inflammatory lesions are detected in different regions of the Central Nervous System [4–7]. Some of the most frequently diagnosed MS subgroups are Relapsing-Remitting MS (RRMS), Secondary Progressive MS (SPMS), Primary Progressive MS (PPMS), Relapsing Progressive MS (RPMS), Benign MS, Spinal form of MS, CIS as well as RIS [5].

In this present study, the data from three MS subgroups were examined. These subgroups are RRMS, SPMS and PPMS. RRMS subgroup resembles the benign type and following seizures, a total recovery may be observed [6–9]. The research reports that more than eight in every ten diagnosed MS patients belong to the "Relapsing Remitting" subgroup. In another subgroup, Secondary Progressive MS (SPMS), the onset resembles the one in "Relapsing Remitting" subgroup. Following the early period of an average of 5–6 years, the disorder progresses. It is observed that there is less chance of recovery and more of disability [6–10]. Besides this, RRMS may evolve into SPMS in some patients. Thirdly, Primary Progressive MS (PPMS) may be a slow or rapid progression staring from the very beginning, and generally it does not show any improvement [5–10].

For the classification of MS, in recent years, early diagnosis has critical so that the disease can be taken under control early and treatment process can be initiated as early as possible. Concerning the MS subgroups' diagnosis and classification are examined, several studies can be cited. There are a number of studies concerning the use of linear models formed. A study by Karaca et al. [7] utilized linear model and obtained a 100% accuracy for the distinction of MS patients and healthy individuals. The accuracy rate for the classification of RRMS and SPMS/PPMS patients and RRMS/SPMS patients was 94% and 78.94%, respectively. For the determination and classification of MS subgroups, deep learning methods are also useful. In this regard, the study by [11] employed Support Vector Machines and Deep Learning to the classification of the 3 subgroups of MS, namely RRMS, PPMS and SPMS. Their results show that Deep Learning generated a more comprehensive system in the classification. Furthermore, the accuracy rate of Deep Learning algorithm is higher compared with

the accuracy obtained by multiclass SVM algorithm kernel types. Based on deep learning, this study aims to develop a convolutional neural network system that is improved. With the Convex Combination of Infinite Kernels model applied in their study, [6] realized the development of a clinical decision support system for the classification of the diagnostics of the patients. The study results demonstrate that the proposed model classifies MS subgroups' diagnosis level with a higher accuracy rate than the single kernel, artificial neural network and the other machine learning methods.

There are several studies on FCM and k-NN algorithms. To illustrate, [12] proposed a new clustering method using the k nearest neighbours and a density method based on k-nearest neighbours (k-NN) for the completion of the clustering process. The results of their experiments on the human face image data and synthetic data indicated that the algorithm at stake proved to be effective for the aim of their study. Another study by [13] worked on lung cancer, which aimed at identifying the pulmonary nodules in the lung computed tomography (CT) images by employing a hybrid intelligent approach. The authors utilized a type-II fuzzy algorithm and subsequently, a new segmentation algorithm based on fuzzy c-means clustering named as modified spatial kernelized fuzzy c-means (MSFCM) clustering. The researchers used three classifiers, including k-nearest neighbours (k-NN), Support Vector Machine (SVM) and Multilayer Perceptron (MLP) for the actual diagnosis and to determine if the nodule candidate is cancerous or healthy. The results obtained verified the potential useful performance of the proposed hybrid approach. Another relevant study was conducted by [14]. They proposed Computer-aided design (CAD) system, using the cascading of Fuzzy C-Means (FCM) and region-growing (RG) algorithm named FCMRG. As a result of their experiments, the classification accuracy was found out to be of 98.2% for the Mammographic Image Analysis Society (MIAS) dataset and the accuracy rate was found to be 95.8% for the Digital Database for Screening Mammography (DDSM). One more study that can be cited within this scope was conducted by [15] in which an algorithm for tumor delineation in positron emission tomography (PET) was presented. A local active contour algorithm was used to achieve segmentation, and k-nearest neighbour (k-NN) classification method was utilized for the integration and optimization. The approach proposed by the authors considered the delineation of cancers afflicting various body parts such as neck, brain, lung and head. The novel aspect of their approach is related to a novel form of energy. The results of their investigation demonstrate that it is possible to use the proposed method in clinical settings through the attainment of a reasonable level of accuracy in real-life instances.

There has been a major interest in the handling of medical data by means of fractal and multifractal techniques over the recent years. In the studies [16–19], the importance of fractal and multifractal techniques for data analysis in medicine has been highlighted. Apart from these, They [1] have studies with the datasets comprised of MS patients' Magnetic resonance imaging (MRIs). In one of their studies, Brownian motion Hölder regularity functions (polynomial, periodic (sine), exponential) for 2D image were applied to the dataset.

They performed an MS classification based on the multifractal method by the Self-Organizing Map (SOM) algorithm. As a result, a cluster analysis was obtained by identifying pixels from the afflicted regions revealed MRIs through the multifractal methods. Regarding the multifractal fractals, the study by [20] is concerned with the ANN fractal. The MS dataset examined in that study was comprised of MRI's of the patients diagnosed to have one of the MS subgroups is to identify the homogenous and self-similar pixels. For this purpose, Diffusion Limited Aggregation (DLA) was applied to the MRI's. The results show that by means of the application of ANN algorithms, identification of the most significant pixels was possible with the DLA. The study concerning stroke dataset by [21] highlights the significance of multifractal denoising techniques. By using K-means and FCM clustering algorithms. The results demonstrate that the 2D mBd technique is the most accurate feature descriptor in terms of classification accuracy rates.

The approach we adopted in this study focuses on identifying the significant attributes based on the MRI's and EDSS scores of MS patients by applying L2 norm multifractal denoising technique, which is one of the multifractal techniques. The MS dataset includes 139 individuals (76 RRMS, 38 SPMS, 6 PPMS, 19 Healthy). For the detection of the significant attributes in the dataset, the following steps were followed. First, L2 Norm Denoising was applied on the MS dataset. Then, the new dataset (MS_L2 Norm dataset) including the significant attributes was obtained through the application in the first step. Afterwards, K-means clustering algorithm was applied both the MS dataset and MS_L2 Norm dataset to classify the MS subgroups. Finally, the classification accuracy rate for the K-means clustering algorithm based on the MS dataset and MS_L2 Norm dataset was compared for patients with the MS subgroups and healthy individuals. When compared with other relevant studies in the literature, [16–21], in this present study of ours, K-means classification has been conducted by utilizing the multifractal denoising methods for our dataset. The results of the study reveal that the K-Means algorithm yielded more accurate results in terms of classification for the MS_L2 Norm dataset compared to the MS dataset.

The paper is organized as follows: Sect. 2 is concerned with Data and Methods. Section 3 is on Experimental Results and Discussion. Finally, the Conclusion summarizes the experimental results of our study.

2 Data and Methods

2.1 Patient Details

In this study, MRI's of the individuals with subgroups of MS, namely RRMS, SPMS, PPMS, aged between 18 and 65, with the definite clinical MS according to McDonald criteria [6]. The patients were tracked at Hacettepe University (Ankara, Turkey), Faculty of Medicine, Department of Neurology and Radiology and also the EDSS scores of these patients related to those years have been included.

Magnetic Resonance Imaging
Magnetic Resonance Imaging is a significant tool used particularly in medicine for the imaging of the internal structure of living things. With a high level of magnetism, living tissues are monitored through reflection method. The image is formed based on the intensity of the hydrogen atoms and their movements. All the images form in the digital medium and MR is much different from the other imaging methods.

In the present study, MRI is used for displaying soft tissues in the spinal cord and the brain. The MRI data have been taken from the three regions of the brain (upper cervical region, upper brainstem and also corpus callosum–periventricular region). MRI from the 120 patients diagnosed with the subgroups of MS (76 patients who have RRMS, 38 patients who have SPMS and 6 patients who have PPMS) and 19 healthy individuals have been analysed in three different years.

Expanded Disability Status Scale
Expanded Disability Status Scale (EDSS) is based on the measurements regarding the central nervous system. The scale measures the degree of impairment, for instance, temporary numbness or visual impairment of the face and the fingers [6–10] (for further details on EDSS, the readers may resort to reference numbered [22].

The MS dataset in this study has a dimension of (139×228), and consists of the number of lesion diameters and EDSS scores obtained from the MR images of 120 MS patients with the aforementioned subgroups as well as 19 healthy individuals.

2.2 Methods

The method used in our study is based on the steps specified below:

(i) As a multifractal method, L2 Norm Denoising was applied on the MS dataset which is based on MRI and EDSS. From this application, the new dataset was generated.
(ii) The new dataset named the MS_L2 Norm dataset which includes the significant attributes was obtained.
(iii) K-means clustering algorithm was applied both on the MS dataset and MS_L2 Norm dataset for the classification of the MS subgroups.
(iv) The classification accuracy rate for the K-Means clustering algorithm in relation to the MS dataset and MS_L2 Norm dataset was compared both for patients with MS subgroups and healthy individuals.

For the calculations and figures, Matlab and FracLab [23] environment were utilized.

2.2.1 Analysis Related to the Hölder Regularity

Structural details for the MS data can be identified and classified using fractal dimension approaches [18]. Fractional Brownian motion with the Gaussian process yields zero mean, and covariance function equals to number (1) [23].

$$\operatorname{cov}\left\{B_H(s), B_H(t)\right\} = \frac{1}{2}\left\{|s|^{2H} + |t|^{2H} - |s-t|^{2H}\right\} \tag{1}$$

W denotes the Wiener process that resembles the signal. It also has intervals with the steady increments [21,23–25]. The Hurst base (H) has significance for signal continuity and also for the signal dependency properties [22–25]. Instead of Hurst exponent as $0 < H(t) < 1$, t can be denoted by Hölder function $H(t)$. Therefore, Hölder function replaces the stochastic integral by the integral that has an upper bound of t taken in the mean square sense. For Multi-fractional Brownian Motion, the increments are not stationary, and the signal resembles itself [22–28].

The Hölder exponent offers information on the most significant parts of the singular and irregular signals for the 2-D analysis. In that way, the Hölder base measures the variations in characterization in different areas of the signal processor. Represented by a signal $X(t)$, for a positive measurement, the Hölder exponent specifies the singularity force at $t = t(0)$ [21]. (detailed definition of the Hölder exponent and the related equations thereof can be found at [22,27–29].

In which H refers to the Hurst exponent, $H - a/2$ and $a \in (0,1)$ [20]. Fractional Brownian motion is stated in line with (2) by a stochastic integral.

$$\begin{aligned} B_H(t) = \tfrac{1}{\Gamma(H+1/2)} \times & \left\{ \int_{-\infty}^{0} \left[(t-s)^{H-\left(\frac{1}{2}\right)} - (-s)(t-s)^{H-\left(\frac{1}{2}\right)}\right] \right\} dW(s) \\ & + \int_{\infty}^{0} \left[(t-s)^{H-\left(\frac{1}{2}\right)} dW(s)\right] \end{aligned} \tag{2}$$

2.2.2 Multifractal Analysis

Multifractal analysis is performed statistically via analysing a huge deviation. This paper concentrates on this method that requires to examine an amount that is coined as the large deviation multifractal data [21,22], [28]. This information can be put expressed as: think about a stochastic procedure. It is accepted not losing any generality that $T = [0,1]$. $N_n^{\in}(\alpha)\#\left\{s : \alpha - \varepsilon \le \alpha_n^s \le \alpha + \varepsilon\right\}$ where α_n^s is the coarse-grained Hölder exponent which refers to dyadic interval $I_n^s = [s2^{-n}, (s+1)2^{-n}]$ that is shown as follows based on [6]:

$$\alpha_n^s = \frac{\log |Y_n^s|}{-\log n} \tag{3}$$

One can see that Y_n^s is some number that calculates the variation of X in the interval I_n^s. $Y_n^s := X((s+1)2^{-n}) - X(s2^{-n})$, resulting in the most basic forms of analytical calculations. One can also have a different way of doing it. One needs to take Y_n^s to be the wavelet coefficient $x_{n,s}$. Referencing the information of X without citation to the selected analysing wavelet may not look logical. Large deviation data $f_g(\alpha)$ are described conforming to (7) [22,26,27].

$$f_g(\alpha) = \lim_{\varepsilon \to 0} \lim_{n \to \infty} \sup \frac{\log N_n^{\varepsilon}(\alpha)}{\log n} \tag{4}$$

It is quite clear that whatever the choice of Y_n^s, f_g ranges in $\Re^+ \cup \{-\infty\}$ at all times [26].

2.2.3 L2 Norm Multifractal Denoising Technique

Regularization serves as a significant method in machine learning so that we can avoid overfitting. It contributes a *regularization term* that helps us to avoid the coefficients to fit in such a flawless way to overfit in mathematical terms [25–27].

While applying machine learning, we could encounter an option of the unknown. L2-norm yields non-sparse coefficients. L2 regularization on least squares as (8) [28–32].

$$w^* = \arg\min_w \left(\sum_j (t(x_j) - \sum_i w_i h_i(x_j)) \right)^2 + \lambda \sum_{i=1}^{k} w_i^2 \tag{5}$$

L2-norm loss function is recognised as least squares error (LSE) as well. What it means is essentially keeping the total number of the square of the differences of the target value (y_i) and the estimated values $f(x_i)$ as (9) to the minimum.

$$S = \sum_{i=1}^{n} ((y_i - f(x_i))^2 \tag{6}$$

In this current study, multifractal denoising (L2 Norm) technique is applied to MS dataset's (139×228) attributes which belong to MS Subgroups and Healthy control group. MS dataset $(\hat{X})$ was applied on FracLab program to regularity-based enhancement $(\hat{X})$ from multifractal L2-Norm denoising technique. Regularity-based enhancement of MS_L2 Norm dataset has been clustered to K-means algorithm. As a result, the most correct clustering has been accomplished for MS Subgroups and Healthy.

2.2.4 K-Means Algorithm

$X = (x_1, x_2, \ldots, x_n)$ nd-dimensional data should be clustered into a set of K clusters, $C = \{c_k, k = 1, \ldots, K\}$. This algorithm aims at finding groups in the data, with the number of groups which the variable k represents. The working of the algorithm is in a repetitive manner so as to assign each data point to one of k groups depending on the features that are presented. The clustering of the data points are done depending on the feature similarity. With μ_k being the mean of cluster c_k, the squared error between μ_k and the points in cluster c_k can be defined based on (10) [21,22,33–35]

$$J(c_k) = \sum_{x_i \in c_k} \|x_i - \mu_k\|^2 \tag{7}$$

K-means is to keep the total of the squared error over all K clusters to the minimum conforming to (11).

$$J(C) = \sum_{k=1}^{K} \sum_{x_i \in c_k} \|x_i - \mu_k\|^2 \tag{8}$$

K-means is inserted with a primary partition with K groups, it also allocates patterns to groups so that it makes it possible to decrease the squared error. The squared error always declines with a rise in the number of clusters K (with $J(C) = 0$ when $K = n$, it could be minimized only at a fixed number of clusters [31]. Below are the major steps for the K-means algorithm [21,22] (Fig. 1):

Algorithm: K-means
Input:
The dataset with n number of samples
$X = (x_1, x_2, ..., x_n)$
Method:
1. From the $C < X$ dataset, c number of cluster centres are selected.
2. **while** (it is also possible that the cluster centres do not change below a certain threshold level)
3. The distances to all cluster centres are calculated for each sample in the dataset.
4. According to the following relation, the distance of each sample to the cluster centre is calculated.
Output:
Information on clustering of the n number of samples in the whole dataset

Fig. 1. K-means algorithm general structure

MS dataset $X = (x_1, x_2, \ldots, x_{139\times228})$ and MS_L2 Norm dataset $\hat{X} = (\hat{x}_1, \hat{x}_2, \ldots, \hat{x}_{139\times228})$ were applied to K-means algorithm to be able to cluster MS subgroups (RRMS, SPMS, and PPMS) and Healthy.

3 Experimental Results and Discussion

In this study, the application has been conducted based on the two datasets. The steps regarding the application of the K-means algorithm to the MS dataset are as presented in Fig. 2. In this study, for the clustering procedure of RRMS, SPMS, PPMS, Healthy, K-means algorithm was applied onto the MS dataset (see Fig. 2(a)). The clustering was performed for the classification of MS subgroups, which are RRMS, SPMS, PPMS, as well as of the Healthy individuals (the details are provided below in Fig. 2(a) (iii).

L2 Norm Denoising technique was applied onto the MS dataset. The steps are presented in Fig. 2(b). The new dataset was generated from this application. The new dataset was named the MS_L2 Norm dataset and it includes the significant

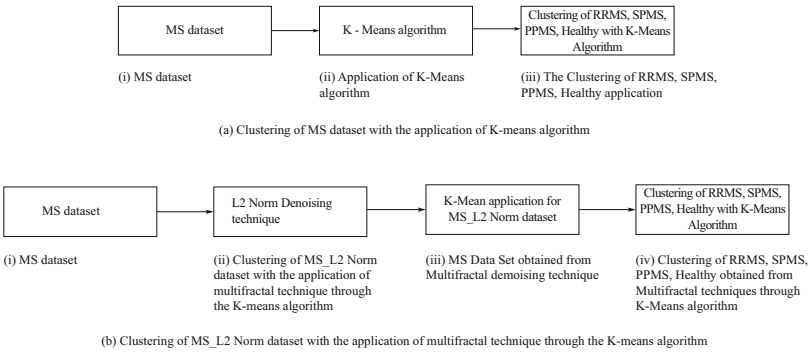

Fig. 2. The Procedural Steps with the K-means Algorithm Applications (a) on the MS dataset (b) on the MS_L2 Norm dataset.

attributes obtained. K-means clustering algorithm was applied both on the MS dataset and MS_L2 Norm dataset to classify MS subgroups (see Fig. 2(b) (iii)). As the final step, the classification accuracy rate for the K-means clustering algorithm regarding to the MS dataset and MS_L2 Norm dataset was compared, and this comparison was conducted both for the patients with MS subgroups and the healthy individuals (see Fig. 2(b) (iv)).

3.1 The Application of the K-Means Algorithm

The K-means algorithm applied on the MS dataset and MS_L2 Norm dataset are shown in Table 1, with the parameters used and which has yielded the most accurate result.

Table 1. Parameters for the K-means clustering algorithm

Parameters	Parameters value
K clusters	4
Maximum number of iterations	1000

As regards the most accurate results yielded by the K-means clustering algorithm with 1000 iterations, Fig. 3(a) provides the results for the MS dataset, and Fig. 3(b) indicates the results for the MS_L2 Norm dataset. Computation for classification is terminated at the 1000th iteration as there is no change in centroid values compared to the previous iteration. Figure 3(a) shows the MS dataset (139×228), with the application of the K-means algorithm, which yielded the best total sum of distance for the centroid values (J (C)) did not change after 0.7 (for 1000 iterations). Figure 3(b) provide the MS_L2 Norm dataset (139×228), with the application of the K-means algorithm, which yielded the best total

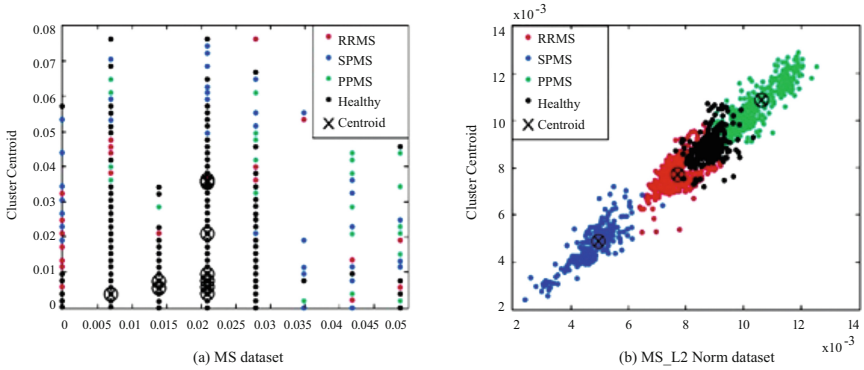

Fig. 3. The Analyses for clustering the K-means Algorithm based on the (a) MS dataset (b) MS_L2 Norm dataset.

sum of distance account for it did not change after 0.1 value. The iteration is terminated here (1000th iteration) since there is no change in the classification calculation after 1000 iterations from the previous iteration. According to the computed best total sum of distance result (see Fig. 3), the K-means clustering performance of the MS_L2 Norm dataset proved to be more accurate than of the MS dataset.

3.2 The Results of the K-Means Algorithm

The results of the classification accuracy rates have been obtained by means of the K-means algorithm application onto the MS dataset and the MS_L2 Norm dataset (see Fig. 2).

In this study, the K-means algorithm was applied on the MS dataset and MS_L2 Norm dataset for the classification the three MS subgroups (RRMS, SPMS, PPMS) and Healthy individuals. The results of the application are presented below in Table 2.

Table 2. Clustering results of the K-means algorithm

MS subgroups	MS dataset (%)	MS_L2 Norm dataset (%)
RRMS	68.9	88
SPMS	67.7	78.4
PPMS	78	86
Healthy	85	89.6

4 Conclusion

The principle contribution of this study is to classify the subgroups of MS through K-means algorithm by selecting and identifying the significant and efficient attributes from the MS dataset by L2 Norm Denoising technique, which is one of the multifractal methods. For the MS dataset, MRI and EDSS scores of the MS patients have been made use of. When compared with other works in the literature [16–21], our study, for the first time, has performed a medical classification for the three subgroups of (Primary Progressive MS (PPMS), Relapsing Remitting MS (RRMS) and Secondary Progressive MS (SPMS). Secondly, on mathematical scale, these particular methods have also been used for the first time in this study for the MS dataset. The study utilized the following steps to get the accuracy performance results for classification: Firstly, L2 Norm Denoising was applied on the MS dataset. From this application, the new dataset was formed. Next, the new dataset, named MS_L2 Norm dataset, which includes the significant attributes was obtained. Afterwards, K-means algorithm was applied on both of the datasets for the classification of the MS subgroups. And finally, the classification accuracy rate for the K-means algorithm as regards the MS dataset and MS_L2 Norm dataset was compared both for MS patients and healthy individuals. Through this study, the K-means classification has been performed by using multifractal denoising methods for the relevant dataset for the first time. The results of our study show that K-means algorithm and classification yielded more accurate results for the MS_L2 Norm dataset compared to the MS dataset with regard to classification. It has also been demonstrated that L2 Norm Denoising technique as one of the multifractal methods play an important role for the classification of the disease and identifying the significant attributes in the dataset. The classification of the MS subgroups also assists medical doctors in their diagnostic processes for early diagnosis and accurate prediction.

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