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Chapter 29
Evaluation of a Support Vector Machine Based Method for Crohn's Disease Classification

S. Franchini, M. C. Terranova, G. Lo Re, S. Salerno, M. Midiri and Salvatore Vitabile

Abstract Crohn's disease (CD) is a chronic, disabling inflammatory bowel disease that affects millions of people worldwide. CD diagnosis is a challenging issue that involves a combination of radiological, endoscopic, histological, and laboratory investigations. Medical imaging plays an important role in the clinical evaluation of CD. Enterography magnetic resonance imaging (E-MRI) has been proven to be a useful diagnostic tool for disease activity assessment. However, the manual classification process by expert radiologists is time-consuming and expensive. This paper proposes the evaluation of an automatic Support Vector Machine (SVM) based supervised learning method for CD classification. A real E-MRI dataset composed of 800 patients from the University of Palermo Policlinico Hospital (400 patients with histologically proved CD and 400 healthy patients) has been used to evaluate the proposed classification technique. For each patient, a team of radiology experts has extracted a vector composed of 20 features, usually associated with CD, from the related E-MRI examination, while the histological specimen results have been used as the ground-truth for CD diagnosis. The dataset composed of 800 vectors has been used to train and validate the SVM classifier. Automatic techniques for feature space reduction have been applied and validated by the radiologists to optimize the proposed classification method, while *K*-fold cross-validation has been used to improve the SVM classifier reliability. The measured indexes (sensitivity: 97.07%, specificity: 96.04%, negative predictive value: 97.24%, precision: 95.80%, accuracy: 96.54%, error: 3.46%) are better than the operator-based reference values reported in the literature. Experimental results also show that the proposed method outperforms the main standard classification techniques.

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29.1 Introduction

Crohn's disease (CD) is a chronic, disabling disease that causes inflammation of the gastrointestinal tract. Epidemiological data analysis suggests that the incidence and prevalence rates of CD have been rapidly increasing during the past decades. CD is most often diagnosed in people between 15 and 25 years old, although it can appear at any age. CD has a complex etiopathogenesis; its development results from the effect of environmental factors in genetically predisposed subjects. This condition consists in the granulomatous inflammation of the intestinal walls from the mucosal to the serosa layer, and it is also characterized by extra-luminal and extra-intestinal manifestations. The disease presents heterogeneous behaviors in terms of location and extent of the interested bowel tracts and can involve different healing and relapses events during its course [1–3]. Because of these heterogeneous manifestations of CD, its diagnosis is a challenging issue that requires a combination of radiological, endoscopic, histological, and laboratory investigations [4]. Medical imaging allows for a first-step non-invasive clinical evaluation of CD [5–8]. Recent studies have explored the use of enterography magnetic resonance imaging (E-MRI) as a valid and accurate diagnostic technique for CD activity and extension assessment [1, 2, 5] showing sensitivity and specificity indexes of 93% and 90%, respectively [9]. E-MRI-based diagnosis relies on the evaluation of typical E-MRI features that have been demonstrated to be associated with CD [2, 10, 11]. However, the manual classification process by expert radiologists is time-consuming and expensive. Conversely, automated learning techniques that classify patients into positive or negative classes with respect to CD starting from E-MRI images can allow for early diagnosis of CD and reduce the high-economic costs of such a widespread disease.

29.1.1 Related Works

Automated learning methods include supervised and unsupervised machine learning techniques. Supervised learning consists in building a predictive model that can map a set of input variables to a response, while unsupervised learning looks for natural patterns within the dataset without reference to a response or true result. Unsupervised learning methods, including k-means algorithm, as well as self-organizing maps (SOM), are used for clustering tasks. Classification tasks are usually performed by using supervised learning algorithms or feed-forward neural networks. Supervised classification methods include K-Nearest Neighbor (KNN), Decision Trees, Naïve Bayes, Discriminant Analysis, and Support Vector Machines (SVM). Recently, several approaches to classify MRI images into positive or negative with respect to some kind of disease have been proposed. A supervised learning method, namely K-Nearest Neighbor, is used in [12] for MR brain tissue classification, while in [13] another, supervised learning technique, based on a Support Vector Machine, is used to classify MR brain images. Other approaches use unsupervised methods,

such as fuzzy C-means [14] and self-organizing maps (SOM) [13] to classify MR brain images. When compared to other supervised classification methods, Support Vector Machines present advantages such as elegant mathematical treatment, direct geometric interpretation, and high accuracy. An SVM classifier with leave-one-out cross-validation has been presented in [15] for predicting medication adherence in heart failure (HF) patients. In [16] a Kernel Support Vector Machine (KSVM) with Radial Basis Function (RBF) kernel, has been used to classify MR brain images as either normal or abnormal. This hybrid method uses digital wavelet transform to extract features and principal component analysis (PCA) [17] to reduce the feature space dimension and, consequently, the computational cost. The KSVM with five-fold cross-validation is then applied for classification. To the best of our knowledge, SVM-based approaches for CD classification starting from E-MRI images have not been proposed in literature.

29.1.2 Our Contribution

This paper proposes the evaluation of a Support Vector Machine based method for Crohn's disease classification using Enterography MRI images. An E-MRI dataset composed of 800 patients from the University of Palermo Policlinico Hospital (400 patients with histologically proved CD and 400 healthy patients) has been used to evaluate the proposed classification technique.

Preliminary results of this approach have been presented in [18] for a dataset of 300 patients. In the study presented in [18], 22 features, usually associated with CD, have been extracted by a team of radiologists starting from the E-MRI examination of each patient. However, two of these features, namely activity and pattern, are composite features that require radiology expertise to be derived. Regarding the pattern, CD can show different patterns and, on the basis of MR features, the radiologists define the CD subtype: 1. Active Inflammatory Subtype: high contrast enhancement, both full-thickness and stratified. Mucosal layer appears hyper-intense in T2W fat saturated images and shows cobblestone appearance due to ulcers and pseudo-polyps. Multiple lymph nodes, comb sign, and mesenteric edema may be present; 2. Fibrostenotic Subtype: Chronic fibrotic walls are typically hypo-intense on both T1W and T2W images, with inhomogeneous enhancement. Mesenteric edema, lymph nodes, and comb sign are usually not present; 3. Fistulizing Subtype is defined when sinus or fistulas occur, usually together with active inflammation features. Fibrostenotic subtype can be overlapped as well. When more than one pattern is simultaneously present, the radiologists assign the more severe pattern [10]. Regarding the activity, it is defined on the basis of the total summa of the following features: wall thickening greater than 4 mm, intramural and mesenteric edema, mucosal hyperemia, wall enhancement (and enhancement pattern), transmural ulceration and fistula formation, vascular engorgement, and inflammatory mesenteric lymph nodes [11]. Therefore, activity and pattern values strongly depend on the subjective evaluation of the radiologist and are subject to great variability.

For this reason, in this work we have excluded activity and pattern from the feature set and considered only the remaining 20 parameters so as to avoid operator dependence. Furthermore, in this paper, the CD classification method has been refined by feature space reduction techniques, tested on a larger dataset (800 patients instead of 300) and evaluated by a performance comparison with the conventional classification methods. A team of radiology experts has extracted from each E-MRI image the vector composed of the typical E-MRI features associated with CD-affected patients. Based on the histological specimen results, which are the ground-truth for CD diagnosis, each patient has been classified as either positive or negative with respect to CD. The 800 observations have been then used to train and validate different classifiers. Experimental results have demonstrated that the SVM-based method shows a better performance with respect to the other standard classification algorithms. Different kernels have been compared, while *K*-fold cross-validation has been used to improve the classifier reliability. Feature space reduction techniques, such as principal component analysis (PCA), have been applied to reduce feature space dimensionality. The following indexes have been measured using 20 features and a 15-fold cross-validation scheme: sensitivity: 97.07%, specificity: 96.04%, negative predictive value: 97.24%, precision: 95.80%, accuracy: 96.54%, and error: 3.46%. These results are better than the manual reference methods reported in literature [9].

The rest of the paper is organized as follows: Sect. 29.2 describes the dataset used to train and validate the SVM classifier, while the proposed classification method is presented in Sect. 29.3. Section 29.4 outlines the experimental results and Sect. 29.5 concludes the paper.

29.2 Materials

The proposed classification method has been tested and evaluated using a real dataset containing medical data related to 800 patients from the University of Palermo Policlinico Hospital. The dataset is composed of 800 magnetic resonance (MR) enterography examinations of 800 patients (427 females, 373 males, mean age 30.1 years): 400 patients with histologically proven Crohn's disease and 400 healthy patients. The following sequences have been used: DWI—axial plane, HASTE thick slab—coronal plane, Single Shot Fast Spin Echo (T2 SPAIR)—axial and coronal planes, Contrast 3D Spoiled Gradient Echo (T1 e-Thrive)—axial and coronal planes, Steady State Free Precession (BFFE)—axial and coronal planes. Starting from this dataset, a team of radiology experts has extracted for each patient a set of features that have been proven to be associated with Crohn's disease [2, 10, 11].

29.3 Methods

This paper proposes the evaluation of an automated tool for the classification of CD-affected patients that uses a supervised machine learning method based on a Support Vector Machine.

29.3.1 Classification Methods Comparison

First, the study presented in [18] related to a dataset of 300 patients has been extended to a larger dataset composed of 800 patients. Different classification methods, namely Support Vector Machines (SVM), *K*-Nearest Neighbor (KNN), Naïve Bayes (NB), and Feed-Forward Neural Network (FFNN) have been compared and evaluated. These classifiers have been trained and validated using the dataset presented in Sect. 29.2, composed of 800 observations each containing the 22 features used in [18]. The comparison results, shown in Table 29.1, demonstrate that the SVM-based classification technique achieves a better performance with respect to the other three methods. Based on these results, the SVM-based method has been chosen for the classification of CD-affected patients. The following subsections describe the different phases of the classification process as well as the methods used in each phase.

Table 29.1 Comparison of different classification methods: Support Vector Machine (SVM), *K*-Nearest Neighbor (KNN), Naïve Bayes (NB), Feed-Forward Neural Network (FFNN)

	Classification method			
	SVM (%)	KNN ($K = 10$) (%)	NB (%)	FFNN (%)
True Positive (TP)	46.46	46.21	46.34	47.43
True Negative (TN)	50.70	49.80	49.29	48.71
False Positive (FP)	1.02	1.92	2.43	0.64
False Negative (FN)	1.79	2.05	1.92	3.20
Sensitivity (Eq. 29.1)	96.27	95.74	96.01	93.67
Specificity (Eq. 29.2)	98.01	96.27	95.28	98.70
Negative predictive value (Eq. 29.3)	96.57	96.03	96.24	93.82
Precision (Eq. 29.4)	97.83	96.00	95.00	98.66
Accuracy (Eq. 29.5)	97.18	96.03	95.64	96.16
Error (Eq. 29.6)	2.82	3.97	4.36	3.84

29.3.2 Feature Extraction

For each E-MRI image, a set of 20 parameters, based on the typical E-MRI features associated with CD-affected patients [2, 10, 11], have been derived by expert radiologists. Starting from the 22 parameters considered in [18], we have excluded the composite features activity and pattern, which require great radiology expertise to be derived, and have used only the remaining 20 features. This choice allowed us to avoid operator dependence and to exclude two features that are subject to great variability among different teams of radiologists since they strongly depend on the radiologist subjective evaluation. The 20 considered features are listed in Table 29.2.

29.3.3 Feature Reduction Techniques

The extracted features will be used as the predictive variables to train and test the SVM model. Reducing the number of predictors can have significant benefits on computational time and memory consumption. Furthermore, a reduced number of predictors results in a simpler model that is easier to interpret and can be generalized. Automated methods for feature space dimensionality reduction can find noisy or highly correlated predictive variables. These methods include feature transformation methods, such as principal component analysis (PCA) [17], which transform the coordinate space of the observed variables, and feature selection methods [19], which choose a subset of the observed variables to be included in the model. PCA transforms an n-dimensional feature space into a new n-dimensional space of orthogonal components. The principal components are ordered by the variation explained in the data. PCA can therefore be used for dimensionality reduction by discarding the components beyond a chosen threshold of explained variance. We have applied both the PCA technique and a sequential forward feature selection algorithm to reduce the number of predictors. The sequential forward feature selection algorithm selects the subset of predictors by incrementally adding predictors to the model as long as the prediction error is decreasing. Different SVM models with different numbers of predictors have been trained, validated, and compared. Results are reported in Sect. 29.4.

29.3.4 Support Vector Machines

Support Vector Machines (SVM) perform data classification by finding the best hyperplane that separates all data points [20, 21]. This optimization problem consists in finding the boundary that is as far as possible from any of the observations, namely maximizing the margin, i.e., the distance between the boundary and the nearest

Table 29.2 Features extracted from Enterography MR images

Sequence types	Features	Values
DWI	Water diffusion restriction (DWI)	0: Free and physiological diffusion, no hyper-intensity on DWI; 1: Mild hyper-intensity; 2: Severe hyper-intensity
HASTE thick slab	Bowel cleaning protocol	0: No sufficient preparation; 1: Adequate bowel loops cleaning and distention
	Bowel distention protocol	0: No sufficient bowel distention, only stomach or duodeno-jejunal loop; 1: PEG has reached the ileocecal junction
T2 SPAIR	Lumen	0: No changes in lumen caliber; 1: Stenosis/sub-stenosis
	Pseudo-polyps	0: No; 1: yes
	T2W imaging	0: No mural edema; 1: Mild mural edema; 2: Severe hyper-intensity due to noticeable edema
Post-contrast T1 e-Thrive	Breathing/peristalsis artifacts	0: No; 1: yes
	Lymph nodes	0: No; 1: yes
	Post-contrast T1 imaging	0: No wall enhancement; 1: Layered enhancement; 2: Transmural enhancement
T2 SPAIR/post-contrast T1 e-Thrive/BFFE	Complications	0: No; 1: yes
	Fat wrapping	0: Normal mesenteric adipose tissue; 1: Mesenteric hyperplasia
	Fistulas	0: No; 1: yes
	Free fluid	0: No; 1: yes
	Intestinal obstruction	0: No; 1: yes
	Length	Length (in cm) of the affected gastrointestinal tract/tracts
	Mucosal layer	0: No mucosal involvement; 1: edema and post-contrast enhancement; 2: Inflammatory changes and pseudo-polyps
	Single lesion/skip lesions	1: Single tract involved; 2: Multiple tracts involved
	Sinus	0: No; 1: yes

(continued)

Table 29.2 (continued)

Sequence types	Features	Values
	Surgery	0: No; 1: yes
	Terminal ileum thickening	0: None or less than 3 mm thickening; 1: Thickening greater than 3 mm

observations (support vectors). Since real noisy data can be not linearly separable, the optimization problem is modified to maximize the margin, but with a penalty term for misclassified observations. This is reduced to a quadratic optimization problem that is solved by quadratic programming. Many classification problems are not linearly separable in the space of the input data, but they might be separable in a higher-dimensionality feature space. Support Vector Machines can be still used for non-linear classification problems by applying appropriate kernel functions that map the input data into a higher-dimensional space where the classes are linearly separable. Three common kernels, namely linear, Gaussian, and polynomial, have been used in this work.

29.3.5 K-*Fold Cross-Validation*

Cross-validation can provide a more robust and reliable estimate of the classification accuracy [22]. To evaluate a classification model performance, input data are divided into training and test data. The classification model is first fitted to the training data and then validated using test data. The learning algorithm accuracy is therefore calculated for that specific test data. The classifier could not generalize well to other data. To solve this problem, *K*-fold cross-validation randomly divides input data into K sets or folds. The training and testing process is repeated K times, each time reserving a different fold for the testing and using the rest of the data for the training. The average error from all the folds is the overall *K*-fold error. When K is equal to the number of observations, then a single observation is used each time for validation. This is known as leave-one-out cross-validation. As described in Sect. 29.4, a cross-validation strategy has been integrated into the proposed SVM classifier in order to obtain a more robust estimation of its generalization capabilities.

29.4 Results and Discussions

The classification method described in Sect. 29.3 has been evaluated using the medical dataset presented in Sect. 29.2.

29.4.1 Performance Evaluation

The following standard metrics have been used to measure the classifier performance.

Sensitivity measures the percentage of actual positives that are correctly classified:

$$\text{Sensitivity} = \frac{\text{TP}}{\text{TP} + \text{FN}} \tag{29.1}$$

Specificity measures the percentage of actual negatives that are correctly classified:

$$\text{Specificity} = \frac{\text{TN}}{\text{TN} + \text{FP}} \tag{29.2}$$

Negative Predictive Value measures the probability that subjects classified as negatives truly do not have the disease:

$$\text{Negative Predictive Value} = \frac{\text{TN}}{\text{TN} + \text{FN}} \tag{29.3}$$

Precision measures the probability that subjects classified as positives truly have the disease:

$$\text{Precision} = \frac{\text{TP}}{\text{TP} + \text{FP}} \tag{29.4}$$

Accuracy measures the percentage of correctly classified cases among the total number of cases examined:

$$\text{Accuracy} = \frac{\text{TP} + \text{TN}}{\text{TP} + \text{FP} + \text{FN} + \text{TN}} \tag{29.5}$$

Error measures the percentage of misclassified cases among the total number of cases examined:

$$\text{Error} = \frac{\text{FP} + \text{FN}}{\text{TP} + \text{FP} + \text{FN} + \text{TN}} \tag{29.6}$$

Table 29.3 lists classification results obtained using the linear SVM kernel for four different cross-validation schemes, while the comparison of three different SVM kernels with 15-fold cross-validation is reported in Table 29.4. The best results are obtained by the linear kernel SVM with 15-fold cross-validation, which achieves an accuracy of 96.54% with an error of 3.46%.

Table 29.3 Linear SVM classifier with *K*-fold cross-validation: comparison for different values of K (the classification method has been applied to the dataset composed of 800 vectors each containing the 20 features listed in Table 29.2)

	Linear SVM			
	K-fold cross-validation (%)			Leave-one-out cross-validation (%)
	$K = 5$	$K = 10$	$K = 15$	
True Positive (TP)	46.54	46.67	46.79	46.54
True Negative (TN)	49.74	49.61	49.74	49.74
False Positive (FP)	2.05	2.17	2.05	2.05
False Negative (FN)	1.66	1.53	1.41	1.66
Sensitivity (Eq. 29.1)	96.54	96.81	97.07	96.54
Specificity (Eq. 29.2)	96.04	95.79	96.04	96.04
Negative predictive value (Eq. 29.3)	96.76	97.00	97.24	96.76
Precision (Eq. 29.4)	95.78	95.54	95.80	95.78
Accuracy (Eq. 29.5)	96.29	96.29	96.54	96.29
Error (Eq. 29.6)	3.71	3.71	3.46	3.71

Table 29.4 SVM classifier with 15-fold cross-validation: comparison of 3 different kernels (the classification method has been applied to the dataset composed of 800 vectors each containing the 20 features listed in Table 29.2)

	15-Fold Cross-Validation		
	SVM kernel		
	Linear (%)	Gaussian (%)	Polynomial (%)
True Positive (TP)	46.79	46.79	46.15
True Negative (TN)	49.74	49.36	49.61
False Positive (FP)	2.05	2.43	2.17
False Negative (FN)	1.41	1.41	2.05
Sensitivity (Eq. 29.1)	97.07	97.07	95.74
Specificity (Eq. 29.2)	96.04	95.30	95.79
Negative predictive value (Eq. 29.3)	97.24	97.22	96.03
Precision (eq. 29.4)	95.80	95.05	95.49
Accuracy (Eq. 29.5)	96.54	96.16	95.77
Error (Eq. 29.6)	3.46	3.84	4.23

29.4.2 Feature Space Reduction Techniques

Different feature space dimensionality reduction methods have been applied.

Principal Component Analysis (PCA)

The PCA technique described in Sect. 29.3 has been applied to the original dataset composed of the 22 features of [18]. Figure 29.1 reports the variance values explained by principal components, while Fig. 29.2 depicts the classification error for different PCA reduced SVM models that use a different number of principal components. The first 16 principal components explain approximately 97% of the variance and

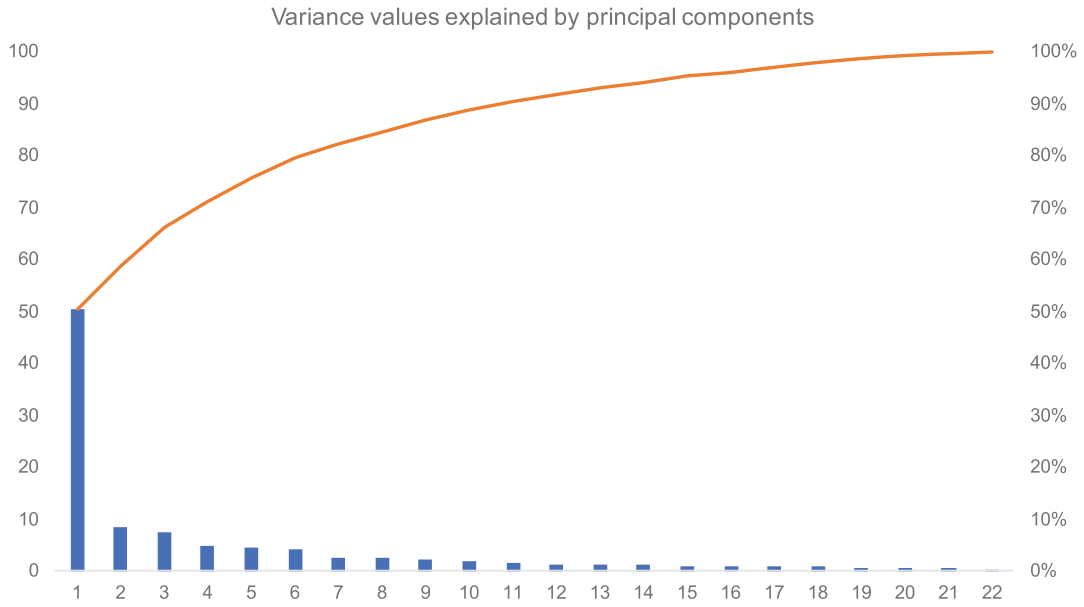

Fig. 29.1 Principal component analysis

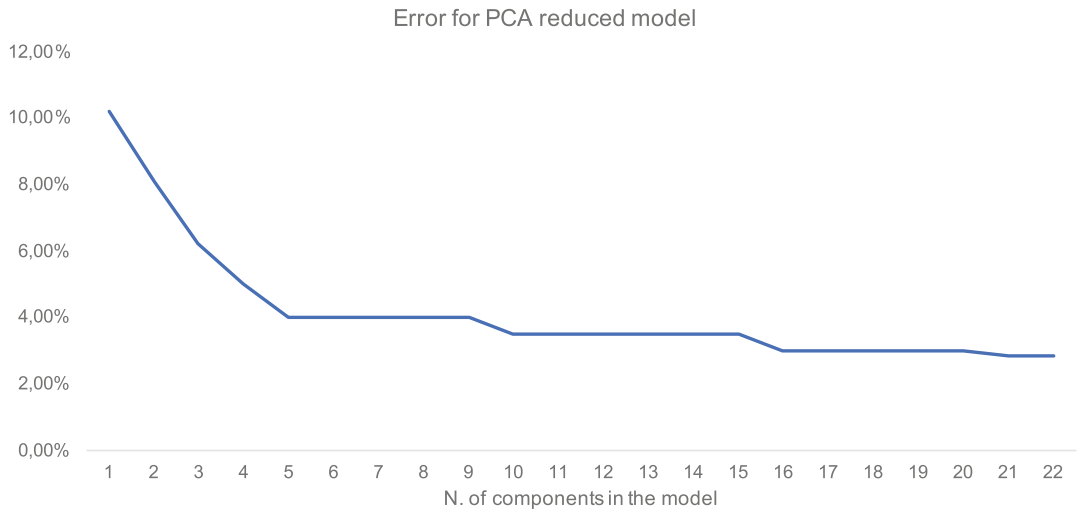

Fig. 29.2 Error for different PCA reduced SVM models

Table 29.5 Sequential feature selection results

10 selected features	SVM reduced model error
Activity, bowel distention protocol, fat wrapping, length, lumen, lymph nodes, pattern, post-contrast t1 imaging, single lesion/skip lesions, T2W imaging	3.33%

the corresponding SVM model, obtained by discarding the components beyond this threshold, shows an error of 2.97%, comparable to the complete model error (2.82%). It can be also observed that the PCA reduced model based on the first 5 principal components shows a classification error of about 4%.

Sequential Feature Selection (SFS)

A sequential feature selection algorithm, as described in Sect. 29.3, has been also used to select the features that are the most important for creating an accurate model. Table 29.5 shows the 10 selected features and the related classification error of the reduced SVM model.

29.4.3 Radiologist Driven Reduction Techniques

Based on the radiologist expertise, the 5 features that have the higher importance have been manually selected and the related error of the reduced SVM model has been measured. Results are reported in Table 29.6.

The latter result confirms that activity and pattern are the two most important and significant predictors. It can be observed that the 5 selected predictors shown in Table 29.6, which include activity and pattern, allow to achieve a classification error (3.72%) comparable to that achieved using the 20 predictors other than activity and pattern listed in Table 29.2 (3.46%). We can therefore conclude that the 20 predictors excluding activity and pattern still give an acceptable classification accuracy allowing us at the same time to avoid the operator dependence and variability given by these two composite features.

Figure 29.3 reports the errors measured for the five different SVM classifier models: the full model that uses the 22 features including activity and pattern considered in [18], the PCA reduced model that uses the first 16 principal components, the sequential feature selection (SFS) reduced model that uses the 10 features reported in Table 29.5, the manually reduced model that uses the 5 features manually selected by the radiologists and reported in Table 29.6, and finally, the model based on the 20 features excluding activity and pattern reported in Table 29.2 and used in this work.

Table 29.6 Most important feature selection based on the radiologist expertise

5 selected features	SVM reduced model error
Activity, DWI, lymph nodes, pattern, T2W imaging	3.72%

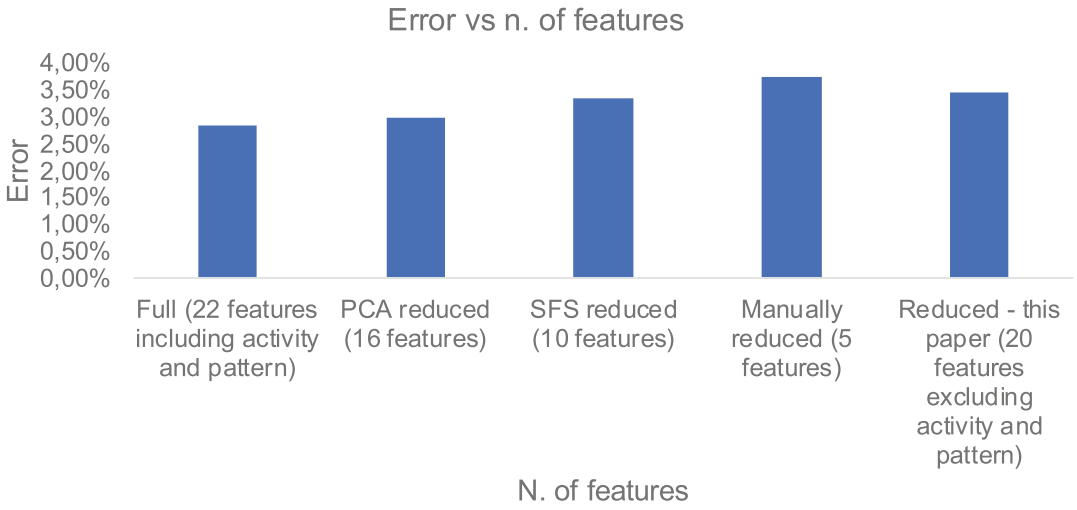

Fig. 29.3 Comparison of different SVM models: full model (based on the 22 features including activity and pattern), PCA reduced model (based on the first 16 principal components), sequential feature selection (SFS) reduced model (based on the 10 features of Table 29.5), manually reduced model (based on the 5 features of Table 29.6), and reduced model (based on the 20 features excluding activity and pattern used in this work)

29.5 Conclusions

The evaluation of an SVM-based method for classifying Crohn's disease affected patients has been presented. A real dataset composed of E-MRI images of 800 patients from the University of Palermo Policlinico Hospital has been used to evaluate the proposed method. A team of radiology experts has extracted for each patient two vectors: The first composed of 22 parameters and the second composed of 20 parameters. Principal component analysis and feature selection techniques have been applied to verify the possibility to reduce feature space dimensionality, while a *K*-fold cross-validation strategy has been integrated into the classifier to better measure results accuracy. Classification results have been compared with the histological specimen results, which are the adopted clinical ground-truth for CD diagnosis. It has been proven that the proposed SVM-based classification method outperforms the main standard classification techniques. Furthermore, the performance metrics measured using 20 parameters and a 15-fold cross-validation (sensitivity: 97.07%, specificity: 96.04%, negative predictive value: 97.24%, precision: 95.80%, accuracy: 96.54%, error: 3.46%) are better than the operator-based reference values reported in literature [9], namely sensitivity: 93% and specificity: 90%.

Future work will focus on the design of a multi-class SVM classifier able to not only detect the presence/absence of the Crohn's disease, but also grade the disease activity and classify patients into different classes according to the disease activity level (mild, moderate, or severe).

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