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Prediction of the Success of Wart Treatment Methods

Siğil Tedavi Yöntemlerinin Başarısının Tahmini

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Abstract

The wart is a dermatosis originated by Human Papilloma Virus. People can be infected by direct or indirect contact. Almost all age groups, especially children and young adults suffer from warts. Recently, new treatment methods including cryotherapy and immunotherapy have been developed as alternatives to conventional methods. Although the treatment decision process is very important, there is no validated decision strategy yet except for only a few studies. In this study, an expert system is proposed to predict whether the selected wart treatment method will be successful or not. The publicly available datasets are applied to the Multi-Layer Perceptron and the Extreme Learning Machine classification algorithms. We compute the classifier performances by the 10-fold cross-validation method. As a result, the multi-layer perceptron approach results in 78.95% of sensitivity, 98.60% of specificity, and 94.45% of accuracy to predict the success of a wart treatment method.

Keywords: Cryotherapy, Extreme learning machine, Human papilloma virus, Immunotherapy, Prediction, Multi-layer perceptron, Wart treatment

Öz

Siğil, insanlara doğrudan veya dolaylı temastan bulaşabilen human papilloma virüsü kaynaklı bir cilt hastalığıdır. Neredeyse tüm yaş grupları, özellikle çocuklar ve genç yetişkinler siğile katlanmaktadır. Son zamanlarda, geleneksel yöntemlere alternatif olarak kriyoterapi ve immünoterapi gibi yeni tedavi yöntemleri geliştirilmiştir. Tedavi karar süreci çok önemli olmasına rağmen, sadece birkaç çalışma dışında henüz geçerliliği kabul edilen bir karar stratejisi yoktur. Bu çalışmada, seçilen siğil tedavisi yönteminin başarılı olup olmayacağını tahmin etmek için uzman bir sistem önerilmiştir. Açık erişime sahip veri setleri, Çok Katmanlı Algılayıcı ve Aşırı Öğrenme Makinesi sınıflandırma algoritmalarına uygulanmıştır. Sınıflandırıcı performansını 10 kat çapraz doğrulama yöntemiyle hesaplanmıştır. Sonuç olarak, önerilen çok katmanlı algılayıcı yaklaşımının, siğil tedavisi yönteminin başarısını tahmin etmede %78,95 duyarlılık, %98,60 özgüllük ve %94,45 hassasiyete sahip olduğu tespit edilmiştir.

Anahtar Kelimeler: Kriyoterapi, Aşırı öğrenme makinesi, İnsan papiloma virusü, İmmunoterapi, Kesitirim, Çok katmanlı algılayıcı, Siğil tedavisi

1. Introduction

The wart is a dermatosis originated by Human Papilloma Virus (HPV), with which people can be infected by direct or indirect contact (air, tools, etc.) (James et al. 2011, Carman et al. 2013). Warts can be seen in any part of the body especially on hands and feet. Most of them are benign although they are epidemic and to contaminate to people easily (James et al. 2011). Warts are divided into four main groups according to their differences about colors, sizes, and constitutional structure: Common warts, Plantar warts, Flat warts, and Genital warts. Common and plantar warts are the most common types among them. Common warts are a type of wart seen on hands, fingers, and nails. They are harmful but painless. Plantar warts are painful warts embedded in the skin in single or multiple groups (Hosrik 2010).

Almost all age groups, especially children and young adults (between 10 and 20 years of age) suffer from warts. It is estimated that about 10% of the public population suffer from warts in Turkey (Carman et al. 2013, Hosrik 2010). To eliminate this type of dermatoses, several treatment methods have been developed. Surgical treatment, cryotherapy,

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laser, electrocautery, and surgical excision methods can be applied only by specialist physicians but salicylic acid and podophyllin methods can be applied by patients themselves (McGibbon 2006).

There are many different treatment methods and processes depend on different factors (such as repetition, easy and quick application, economical efficiency, low side effects). However, none of these methods have achieved superior success yet (Lipke 2006). The required time for a wart treatment process depends on the age of the patients, their immunity, their financial situation, and the number of warts and the preference of the doctor. The treatment longs more than 3 weeks in general (Varol 1998). Therefore, to decide which treatment method may be successful at first sight is very important.

Moreover, new treatment methods including cryotherapy and immunotherapy have been developed as alternatives to the methods mentioned above. Cryotherapy and immunotherapy are the most commonly used methods among wart treatment methods. Cryotherapy or known as "freezing" treatment in the society is a form of treatment method based on the principle of freezing and destroying abnormal tissues and lesions. The treatment consists of a tube with liquid nitrogen or carbon dioxide, and this tube is attached to the cuff. This treatment method has many advantages such as applicable to all ages, having few complications, short treatment elapsed time; notwithstanding, it has many disadvantages such as being painful, not responding in one time (Khozeimeh et al. 2017a, Khozeimeh et al. 2017b). In immunotherapy, the patient's immune system is strengthened by using an agent that is allergic. Immunity is activated by the help of special medicine given either orally or by injection.

Over the last two decades, there are many researches related to determine the effects of these wart treatment methods (Russell et al. 2010, Clifton et al. 2003, Nofal and Nofal 2010, Horn et al. 2005, Maronn et al. 2008, Gamil et al. 2010, Silverberg et al. 2000). On the other hand, only a few studies have focused on determining whether these methods will become successful or not before starting the treatment. In the first study, authors have provided that the immunotherapy method can be applied in wart treatment using statistical evidence levels (Khozeimeh et al. 2017a). Khozeimeh et al. (2017b) created Fuzzy Logic-based rule tables for these two wart treatment methods and they achieved the average performance of 80%. In another study, Uzun et al. (2018a) investigated the performances of these two wart treatment methods with Naive Bayes and k-nearest neighbor classifier algorithms. They found a similar classifier performance by using the 7-nearest neighbor classifiers. They also obtained higher classifier performances of (85.46%) by using the support vector machine (Uzun et al. 2018b). Abdar et al. (2019) proposed a new computer-aided diagnosis (CAD) system, which is combined by improved adaptive particle swarm optimization algorithm and artificial immune recognition system, using machine learning to classify the wart treatment methods. They used different partitioning number of cross-validation to measure their proposed model performance. They obtained the maximum accuracy of 90.00% on the combined dataset. Akben (2018) used decision trees method to decide which treatment method is more appropriate. The accuracy rates of decision trees used for cryotherapy and immunotherapy treatment methods are 94.4% and 90.0%, respectively. Khatri et al. (2018) investigated the J48 classification algorithm and the feature selection based on Genetic Algorithm (GA) on predicting the success of wart treatment methods. They obtained the classification performances of 82.22% and 96.66% for Immunotherapy and Cryotherapy methods using the J48 algorithm alone, respectively. Besides, they reported the best classification performances of 93.33% and 98.88% for Immunotherapy and Cryotherapy methods using the J48 algorithm with the selected features only, respectively. Putra et al. (2018) proposed a boosting-algorithm to select the wart treatment method and achieved the classifier accuracy of 96.6% and 91.1% in cryotherapy and immunotherapy datasets, respectively. Talabani and Avci (2018) investigated four different kernel functions to enhance the learning capacity of support vector machine algorithm for classifying wart treatment methods. They obtained the best classification performance by using Pearson VII Function-based Universal Kernel (PUK) with 97.77% accuracy for cryotherapy and 81.11% accuracy for immunotherapy separately. Rahmat et al. (2019) achieved the accuracy of 88.03% by using the k-nearest neighbor classifier. Also, they investigated the classifier performances for each dataset separately and combining in a single dataset together similar to our study. They found that the classifier performance is less than performances of separate classifiers. In a recent study, Jia et al. (2019) achieved 80.73% accuracy for the success prediction of only Immunotherapy method by using the C4.5 algorithm. Most of these studies are based on determining successes of each treatment by using distinct classifiers trained to the corresponding treatment method.

In this study, the success of cryotherapy and immunotherapy methods, which are commonly used wart treatment techniques, was predicted by a single classifier. Two different artificial neural network models of multi-layer perceptron (MLP) and extreme learning machine (ELM) were examined for this purpose. MLP has very common use in the machine learning literature and ELM has become very popular thanks to its fast learning phase. The features given in the inputs of classifiers are taken from the freely-available online datasets from UCI (Khozeimeh et al. 2017a, Khozeimeh et al. 2017b).

2. Material and Methods

2.1. Data

In this study, two datasets of *Immunotherapy Dataset* and *Cryotherapy Dataset*, which have open-access via the Internet at https://archive.ics.uci.edu/ml/datasets/Immunotherapy+Dataset and https://archive.ics.uci.edu/ml/datasets/Cryotherapy+Dataset+ respectively, were utilized. These datasets were acquired from the patients who had suffered from the plantar and common warts. These datasets were collected in the dermatology clinic of Ghaem Hospital in Mashhad from January 2013 to February 2015 (Khozeimeh et al. 2017a, Khozeimeh et al. 2017b).

The first dataset contains seven features from the patients who were treated by using the cryotherapy method. The other dataset consists of eight features from the patients who were treated by using the immunotherapy. These features were listed in Table 1 for both datasets. The feature of *Response to Treatment* from these datasets is the desired output of the proposed system. Khozeimeh et al. (2017a) analyzed these features using the independent t-test and discovered the existence of statistical evidence between datasets.

These two datasets were combined and the treatment method was added as a feature. The feature of *Induration diameter* was excluded from the study since it was recorded for only Immunotherapy method. If the output of the proposed system is successful, the selected method should be applied to the patient. Otherwise, the other method should be applied to them.

2.2. Classification

Machine learning (by covering the concepts of data mining, pattern recognition, and decision making) allows us to investigate a huge amount of data, to make it meaningful by reaching the information inside, to evaluate them, and to make predictions (Duda et al. 2000). The principal area in machine learning is classification. Recently, machine learning methods have attracted researchers in many biomedical applications including the classification of skin diseases (Lamminen et al. 2001, Bunte et al. 2011, Giotis et al. 2015, Mirzaalian et al. 2016, Sumithra et al. 2015, Jain et al. 2015, Oliveria et al. 2016, Flores and Scharcanski 2016, Shrivastava et al. 2015).

Table 1. Features employed in both the cryotherapy and immunotherapy methods.

Features	Cryotherapy Group		Immunotherapy Group	
	Values	Mean±SD[a]	Values	Mean±SD[a]
Response to treatment	Yes (48) No (42)		Yes (71) No (19)	
Gender	Male (47) Female (43)		Male (41) Female (49)	
Age (Year)	15-67	28.6±13.36	15-56	31.04±12.33
Time before treatment (Months)	0-12	7.66±3.4	0-12	7.23±3.10
Number of warts	1-12	5.51±3.57	1-12	6.14±4.2
Types of warts (Count)	1- Common (54) 2- Plantar (9) 3- Both[b] (27)		1- Common (47) 2- Plantar (22) 3- Both[b] (21)	
Surface area of the biggest wart (mm^2)	4-750	85.83±131.73	6-900	95.7±136.61
Induration diameter of initial test[c] (*mm*)			5.70	14.3±17.22

[a]Standard deviation; [b]Patients have both types of common and plantar warts; [c]This feature is available only for the immunotherapy method.

In the literature related to prediction of the success of wart treatment method, classifier algorithms of Fuzzy Rules (Khozeimeh et al. 2017b), support vector machines (Uzun et al. 2018a), Naive Bayes (Uzun et al. 2018b) and k-Nearest Neighbors (Uzun et al. 2018b) were used previously. We explored the use of multi-layer perceptron and extreme-learning machine on solving this problem.

2.2.1 Multi-Layer Perceptron (MLP)

MLP has become the most favorite method among artificial neural network algorithms. It is commonly used in a wide range of applications including the diagnosis of several diseases in biomedicine (Pan et al. 2012, Kocer and Canal 2011). The three-layer structure is preferred in almost all of MLP related studies: the input layer, the hidden layer, and the output layer. The number of neurons in the input layer is the number of features, which is 7 in this study. The hidden layer is constituted through a various number of neurons to obtain the optimal classifier performance, which was varied between 5 and 50 with the activation of the "hyperbolic tangent **(**tanh)" function. The output layer obtains the classifier's answer. Network weights, which connect these layers, are updated using the error back-propagation learning method. In this method, the mean square error between the calculated network output and the actual output is obtained and this error value is used to update network weights. This routine is repeated until the mean square error is reduced to a certain threshold value (Duda et al. 2000).

2.2.2 Extreme Learning Machine (ELM)

ELM has become popular among single-hidden-layer feedforward networks. ELM has superior regression and classification performances with much faster learning speed than other some traditional artificial neural networks (Huang et al. 2012). The input weights of the algorithm are chosen randomly and the output weights are determined analytically (Huang et al. 2004). ELM pretends giving good generalization performance at extremely fast learning speed (Huang et al. 2006). There is a website that hosts well-prepared resources and codes for different programming languages and detailed information about the algorithm can be found in (http://www.ntu.edu.sg/home/egbhuang/elm_codes.html).

2.2.3 Validation and Performance Measures

In this study, the 10-fold method is preferred as a cross-validation method. First, the data is divided into 10 groups. One of the groups is used for test and other groups are used for training the classifier. This process is repeated until each group is used for the test purpose. Consequently, true-positive (TP), true-negative (TN), false-positive (FP), and false-negative (FN) were found where true means correct classification, false means wrong classification, positive means patient, and negative means normal subjects.

The performance of the classifier is determined by some metrics including sensitivity (SEN), specificity (SPE), and accuracy (ACC). SEN gives the correctly classified ratio of positive decisions among total positive answers. Similarly, SPE gives the ratio of exact negative decisions among all negative answers. Finally, ACC is the ratio of total correct decisions of the classifier to the total number of subjects (Duda et al. 2000):

$$SEN = \frac{TP}{TP + FN} \quad \textbf{(1a)}$$

$$SPE = \frac{TN}{TN + FP} \quad \textbf{(1b)}$$

$$ACC = \frac{TN + TP}{TN + TP + FP + FN} \quad \textbf{(1c)}$$

3. Results and Discussion

Two databases are combined in a single dataset in this study. We constructed the feature set of the study as follows: gender, age, time elapsed before treatment, the number of warts, type of warts, the surface area of the biggest wart, treatment method. *The induration diameter of the initial test* was excluded from the study since it was not recorded for both methods. These features were applied to the inputs of the classifier. The classier output is the *Response to treatment* (Figure 1).

The number of neurons in the hidden layer of the ELM algorithm was changed from 2 to 100. We repeated the classifier algorithm 10 times for each configuration and noted the highest classifier performances in Figure 2. We compute the classifier performances by the 10-fold cross-validation method. This ELM-based approach results in 36.85% sensitivity, 90.15% specificity, and 78.89% accuracy.

The number of neurons in the hidden layer of the MLP algorithm was changed from 5 to 50. We repeated the classifier algorithm 10 times for each configuration and noted the highest classifier performances in Figure 3. This MLP-based approach results in 78.95% sensitivity, 98.60% specificity, and 94.45% accuracy. This method results in

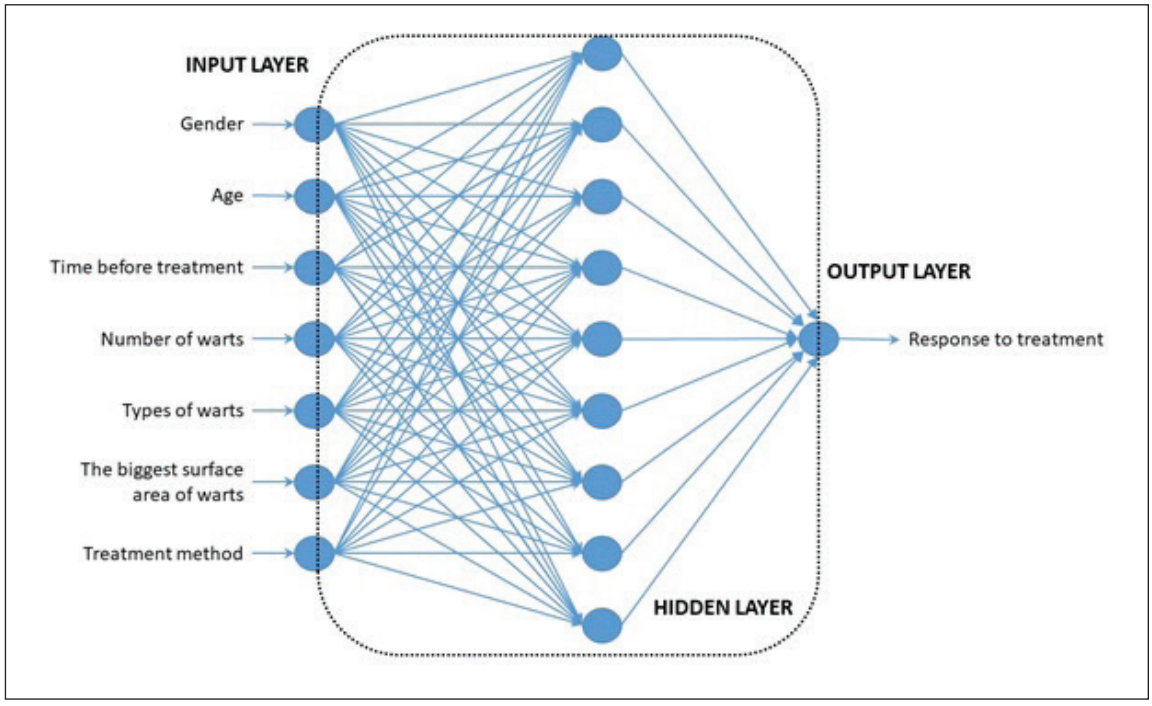

Figure 1. Multi-layer perceptron to detect the performance of the wart treatment methods.

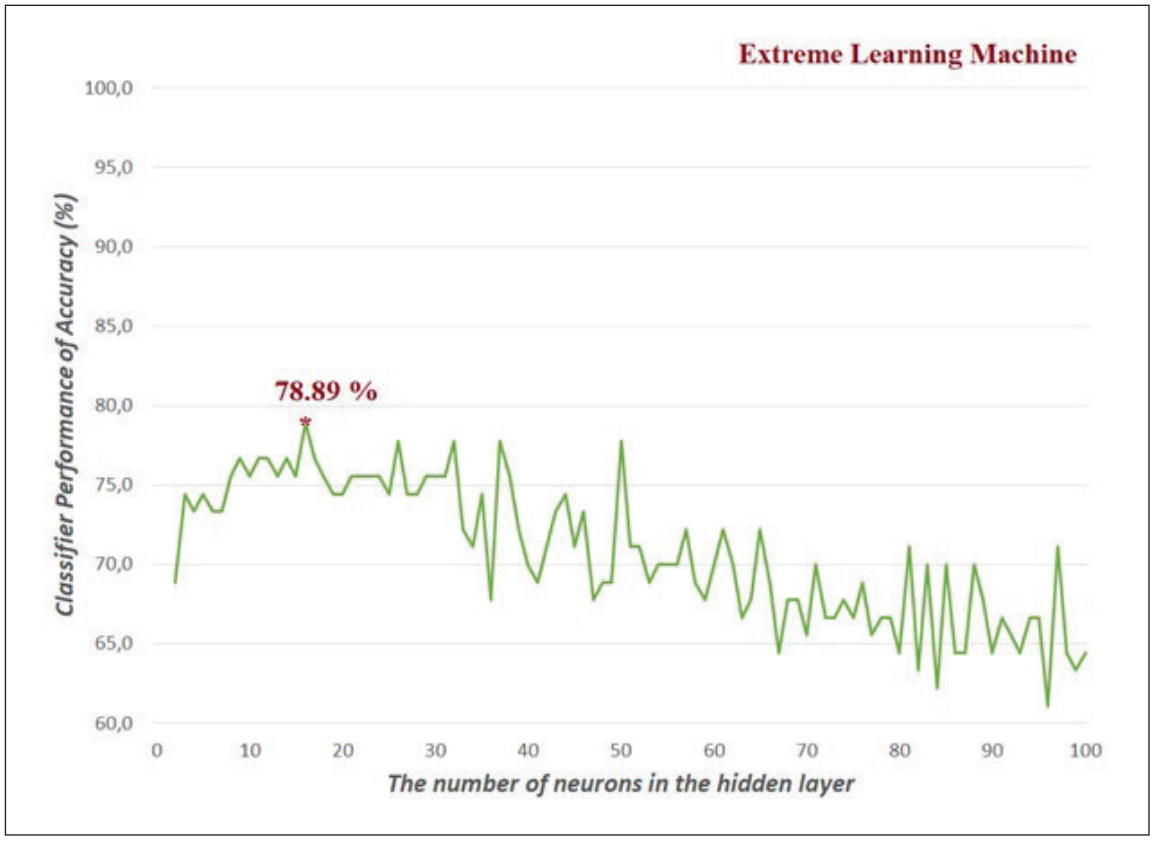

Figure 2. Extreme learning machine performance results of accuracy. The highest accuracy value is emphasized by a star sign.

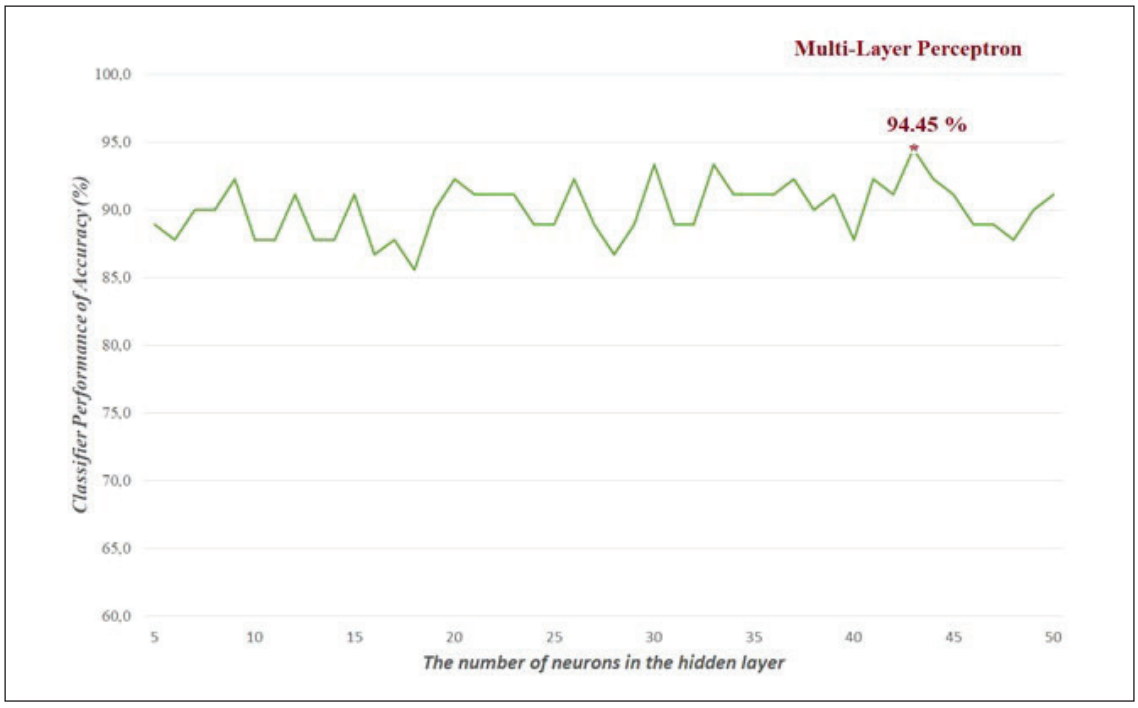

Figure 3. Multi-Layer Perceptron performance results of accuracy. The highest accuracy value is emphasized by a star sign.

better classification performance than similar studies in the literature.

We summarized the recent literature related to predicting the performance of a selected treatment method in Table 2. If a study reported the performances separately for both datasets, we combined both into a single performance by calculating performances from TP, TN, FP, and FN values given in the related study. Khozeimeh et al. (2017b) prepared the database and obtained prediction accuracies of 83.3% for immunotherapy method and 80.7% for cryotherapy method. Uzun et al. (2018a, 2018b, 2019) used Naive Bayes, k-Nearest Neighbors, Support Vector Machines, Logistic Regression, and Decision Tree on the same database and reached the maximum classification performance of an accuracy of 85.56%, a sensitivity of 52.63%, and a specificity of 94.37% for Decision Tree algorithm. Talabani and Avci (2018) compared SVM classifiers of four different kernels (Normalized Polynomial Kernel (NP), Polynomial Kernel (PK), Radial Basis Function Kernel (RBF), and Pearson VII function based Universal Kernel (PUK)) and achieved the maximum classification performance of an accuracy of 89.44%, a sensitivity of 77.05%, and a specificity of 89.06% with the PUK kernel. Putra et al. (2018) proposed the AdaBoost algorithm to determine the success of the selected wart treatment method and achieved the maximum classification performance of an accuracy of 93.89%, a sensitivity of 96.64%, and a specificity of 93.10%. Khatri et al. (2018) investigated the J48 classification algorithm and the feature selection based on Genetic Algorithm (GA) on predicting the success of wart treatment methods. They obtained the best classification performance of an accuracy of 88.03%, a sensitivity of 93.60%, and a specificity of 84.50% by using the J48 algorithm with the selected features only. Rahmat et al. (2019) compared three different classifiers (Decision Tree, Random Forest, and k-Nearest Neighbors) and achieved the maximum classification performance of an accuracy of 88.03%, a sensitivity of 93.60%, and a specificity of 84.50%. Consequently, the proposed method based on MLP classifier in this study results in an acceptable classification performance than similar studies in the literature.

Two artificial neural network models were experimented to decide whether the selected wart treatment method will be successful or not in this paper. The achieved results highlighted that MLP-based expert system has a great potential to decrease the cost of treatment by reducing the time before deciding the treatment method for patients drastically. According to these results, we may propose that our approach based on multi-layer perceptron provides a better tool to predict the success of wart treatment methods. The benefits of this system are multifold: assisting physicians in selecting the treatment method, saving time for patients, reducing the treatment cost, and improving the quality of treatment.

Table 2. The comparison of classifier performances of sensitivity (SEN), specificity (SPE), and accuracy (ACC). The algorithm-specific value (the number of neurons in the hidden layer, the number of neighbors, etc.) is given in the parenthesis if available.

Study	Methods	SEN (%)	SPE (%)	ACC (%)
Khozeimeh et al. 2017a	Fuzzy Rules	-	-	83.33
Uzun et al. 2018a	Naive Bayes	68.43	67.61	67.78
Uzun et al. 2018b	KNN (k=7)	15.79	97.19	80.00
	SVM	47.37	95.78	85.46
Talabani & Avci 2018	Pearson Function Based Universal Kernel (PUK)	77.05	89.06	89.44
Putra et al. 2018	AdaBoost (CART)	**96.64**	93.10	93.89
Khatri et al. 2018	J48	81.97	90.76	87.78
	J48 + GA	95.08	**97.52**	**96.72**
Abdar et al. 2019	IAPSO + IARS	-	-	90.00
Uzun et al. 2019	Logistic Regression (n=10, 14)	26.32	94.37	80.00
	Decision Tree (n=14)	52.63	94.37	85.56
Rahmat et al. 2019	KNN (k=1)	93.60	84.50	88.03
This study	ELM (n=16)	36.85	90.15	78.89
	MLP (n=43)	**78.95**	**98.60**	**94.45**

4. Conclusion

The experimental studies conducted on the combined dataset of cryotherapy and immunotherapy datasets show that the multi-layer perceptron (MLP) algorithm can provide higher performance than previous studies. The study that results in a better performance than our study applied feature selection algorithms. For future works, we will apply feature selection algorithms and other well-known classifiers.

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