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Research Article

Mobile diagnosis of thyroid based on ensemble classifier

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ABSTRACT

The thyroid gland plays a major role in many metabolic activities of the human body. Thyroid disease, which is quite common in humans, affects people's quality of life significantly. Early diagnosis is very important for taking precautions. The mobile diagnostic system can be the solution for early diagnosis especially in rural areas or without going to health institution. This study has been proposed to enable people with mobile devices to obtain quick information about the disease or to seek medical assistance in any matter without going to the hospital. Functional thyroid diagnosis system is designed using mobile device, Android based software application, Database (SQL) and Server (MATLAB based decision algorithms). With the system, functional thyroid disease can be diagnosed using an android based mobile device. Different classification algorithms were searched for the most accurate diagnosis and Ensemble method which has a high success rate for thyroid disease was used in the system. Ensemble classification technique reached a success rate of 99.06% and 99.08% for the first and second data group, respectively. These success rates were calculated by using gold standard test and results were compared with the literature. Obtained test results showed that, the proposed mobile diagnosis system could be used for the diagnosis of the functional thyroid. At the same time, this system can be developed for different diseases.

Introduction

Mobile devices enable people to benefit from the advantages of current technology independently of places. Cell phones in the field of communication, table computers in the field of education, hand terminals that collects orders in the commercial field, indexers used for electricity, water and gas billing are just a few examples. Mobil devices have also become popular in the field of health recently. Mobil health services are generally designed for two purposes. The first one is for the diagnosis, treatment or monitoring of the disease status of the sick people. The other produces solutions for the health system. For example, health expert support, patient data sharing, etc [1-5].

Some of the prefixes to new developments in mobile technology are as follows. Mobile applications such as devices and sensors that operate based on cloud systems and facilitate communication between health specialists in case of emergency were developed. Among these are devices which psychologically satisfy smoking addiction, inform family members and medical teams about the elderly living on their own in case of emergency, collect information about calorie burnt, blood oxygen amount and cardiac rhythm during exercises and monitor numerous vital activities in daily life. Many different software's are developed for mobile devices or hybrid systems. Sometimes systems (mobile and other systems) are designed to work together. Our study is an example of this.

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In this study, an accessible decision support system for functional thyroid diagnosis was developed. The Android application to be written in Android operating system was installed on a mobile device. The individual blood values (medical information) are entered on the designed system via a mobile device and sent to the database. The listener on MATLAB operating on the side of the server controls the database on regular intervals and receives the data to evaluate them via the algorithm based on the decision system. Following the evaluation, it sends these data from the database to the client device. Thus, the individual can reach preliminary information about whether s/he suffers from thyroid or not.

Various data classifications techniques are used in order to evaluate data on thyroid in the algorithm of mobile diagnosis system. This study uses ensemble classification technique which yields better accuracy rates. Ensemble method is based on the idea that the decisions made by multiple people (such as a society or council) instead of a single person will be more accurate [6].

Fulfilling a vital function in the human body, thyroid is a 25-gram endocrine gland located in the lower neck and anterior trachea in a healthy adult body. The thyroid gland regulating all organs in human body through its hormones, it is considered as the main regulator of the body's metabolism. Thyroid diseases are widespread around the world and poses an important problem for humanity. Medical screenings carried out demonstrate that thyroid diseases affect life quality. Similar to other endocrine diseases, females suffer more from thyroid diseases compared to males. In addition, thyroid diseases are directly proportional to aging [7, 8]. The diagnosis is usually made by medical specialists as normal, hypo or hyperthyroid, based on blood values. In this study, a decision support system has been proposed with the ensemble classifiers considering the decisions of the experts from the blood values. They will be able to see the results by entering their blood values on the web to the mobile decision support system which has been made ready for use.

Materials and Methods

Materials

The data belonging to thyroid disease used in this study were obtained from machine learning database of University of California (ftp://ftp.ics.uci.edu/pub/machine-learning-databases/thyroid-disease/). The thyroid datasets are divided into two groups as follows:

a) First Group Data: This group contains blood values obtained from 215 individuals. Five characteristics related to the thyroid disease exist in each sample. The data set is divided into three classes as Normal (euthyroid), Hyperthyroid, and Hypothyroid. As shown in Table 4, there are numerous studies on this data set in the literature.

First group data set consists of 150 normal (class 1), 35 hyper (class 2) and 30 hypo (class 3) data and each sample contains five feature consisting of blood values as follows.

Feature 1: Level of unsaturated thyroxine binding globulin in serum thyroxine level.

Feature 2: Total serum thyroxine level measured via isotopic displacement method.

Feature 3: Total serum triiodothyronine level measured via radioimmunoassay method.

Feature 4: Basal thyroid stimulating hormone measured via radioimmunoassay method.

Feature 5: The highest absolute difference between TSH and basal levels following a thyrotropic hormone (TSH) injection of 200 mg.

b) Second Group Data: This data set consists of 7200 samples/data belonging to three classes. There are seldom studies on this data set in the literature.

This data set consists of 166 normal (class 1), 368 hyper (class 2) and 6666 hypo (class 3) data.

Each sample contains 21 features. 1^{st} feature contains individual's age (between 0 and 1) from whom sample is obtained, and 2^{nd} to 16^{th} features (15 features) consist of 0 or 1 coded via binary number system. These features consist of responses regarding the individual's medical conditions such as gender, thyroxine, anti-thyroid drugs, thyroid, hypothyroid, hyperthyroid, pregnancy, diseases, tumor, lithium and goiter. 5 features between 17 and 21 have a value between 0 and 1. These features were obtained via blood test measurements during thyroid diagnosis. These tests consist of values obtained from blood tests such as TSH, T3, TT4, T4U, FTI and TBG.

Methods

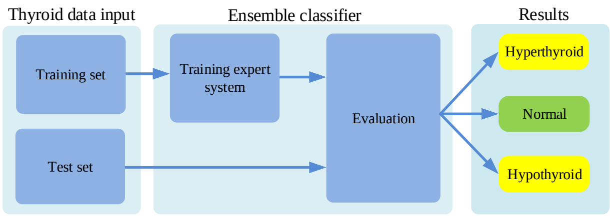


Figure 1. The flow diagram of the system operating on MATLAB in the host computer

Ensemble Classification

Ensemble technique is based on the idea that the decisions made by multiple people (such as a community or council) instead of a single person will be more accurate. Ensemble method can be also defined as a combination of models or mean of several different models. The mean of different models was developed with neural networks in early 1990s. The idea was put forward by Krogh, it was stated that generalization error of ensemble is lower than mean generalization error of single ensemble members. The ensemble technique forms a group of learners with a classification method and these learners are trained with '*x*' training data. The decision of each trained learner on the '*x*' test data is evaluated and the joint decision of the learners constitutes the final decision of the method [9-12].

The mathematical expression of the ensemble method for the test sample '*x*' can be written as follows;

$$class(x) = mode\{L_1(x), L_2(x), L_3(x) \ldots L_n(x)\} \quad (1)$$

where n is the number of learners in the ensemble. $L_n(x)$ is the final decision of the n-th learners in the ensemble [11].

Decision Trees (DT) method

Decision tree (DT) is a commonly used classification and pattern identification algorithm in the literature. This approach is very similar to human reasoning and is easy to understand. The decision trees method has ease of use, fast and high accuracy rate in data classification [13-16]. Due to the successful features of the decision tree method, it has been chosen as an individual decision-making algorithm for the diagnostic support system.

Application and Experimental Results

The data to be analyzed are entered by the user in Android based mobile device called client, and are stored in MSSQL database. The general structure of mobile decision-making system is described as shown in Figure 2. The listener on MATLAB operating on the side of the server controls the database on regular intervals. If there are new data in the database, the parameters sent by the user through the mobile client are used to operate algorithm. MATLAB sends the results (decisions) obtained from the algorithm to the database. Interacting with the database, the android application displays the decision and evaluates thyroid data via mobile diagnosis system.

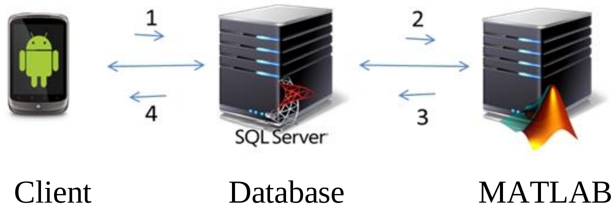


Figure 2. The general structure of mobile diagnosis system

Numbers 1, 2, 3 and 4 shown in Fig. 2 show the sequence and steps of the mobile diagnostic system. These; 1: The information entered by the user to the mobile device is sent to the Database (SQL). 2: Information received from the database is sent to the MATLAB for processing. 3: The decision resulting from the information processed on the MATLAB is sent to the Database. 4: The decision from the MATLAB is sent to the relevant mobile device. Thus, the user will be informed about his or her illness by looking at the decision of the trained algorithm received on the mobile device.

First stage

An Expert system designed in MATLAB medium that interprets incoming thyroid data and produces results. Ensemble classification method is the basis of the expert system. AdaBoostM2 was used as multiple classifier method and Decision trees were used as learner. Information on ensemble classification is readily available in the literature. It is therefore summarized here. Highest accuracy rate of Ensemble classification was obtained with 257 training cycles in the application with thyroid data (the first group data: 215 samples, the second group data: 7200 samples). Thyroid data was classified with optimized Ensemble classification. Table 1 shows the distribution of the first group of data and Table 2 shows the distribution of the second group of data. Table 3 shows the accuracy of Ensemble classification results according to the Gold Standard test system. In Table 4, the results of the model are compared with the literature.

Table 1. Application results for the first group data

215 samples	Normal	Hyper	Hypo	Total
150 Normal	148	2	0	150
35 Hyper	0	35	0	35
30 Hypo	0	0	30	30
Total				215
Error (%)				0.94
Accuracy (%)				99.06
The number of inaccurate diagnosis				2
The number of accurate diagnosis				213

As shown in Table 1, the accuracy rate of the first group data reached 99.06%. Here, the classifier diagnosed 2 out of 150 normal samples as Hyperthyroid. 35 Hyperthyroid and 30 Hypothyroid samples were diagnosed accurately. Only 2 out of 215 samples were inaccurately diagnosed.

7200 samples were used for the second group data. The classifier diagnosed 166 normal samples accurately. All of 368 hyperthyroid samples were diagnosed as hyperthyroid. Out of 6600 hypothyroid samples, 6600 samples were diagnosed accurately while 50 samples were diagnosed as hyperthyroid and 16 samples were diagnosed as the normal. The accuracy rate of the classifier was 99.08% for this dataset.

Table 2. Application results for the second group data

7200 samples	Normal	Hyper	Hypo	Total
166 Normal	166	0	0	166
368 Hyper	0	368	0	368
6666 Hypo	16	50	6600	6666
Total				7200
Error (%)				0.92
Accuracy (%)				99.08
The number of inaccurate diagnosis				66
The number of accurate diagnosis				7134

It is underlined in the medical literature that the function of thyroid gland can be best explored by the blood TSH level and that TSH upper limit is 4 *mIU/L* in the healthy youth population [17]. The present study yielded consistent results with this figure. The decision tree classifier used in this study determined the first branching criterion based on TSH attribute and measured its level as 3.7 *mIU/L*.

In this study, real diagnosis results were compared to get “gold standard test” [18] results in order to test the reliability of diagnosis performed pre-existing dataset.

Table 3. Gold standard test results of ensemble classification method for 1st and 2nd group data sets.

	1st Group dataset	**2nd Group dataset**
Sensitivity	1	0.9906
Specificity	0.9866	1
False positive rate	0.0133	0
False negative rate	0	0.0093
Positive predictive value	0.9701	1
Negative predictive	1	0.7155
Accuracy	0.9906	0.9908

When Table 1, 2 and 3 are analyzed, it can be noted that ensemble classification technique can yield quite accurate results for functional thyroid diagnosis. There are numerous studies on these data set in the literature, and the comparison results of the present study and recent studies are summarized in Table 4.

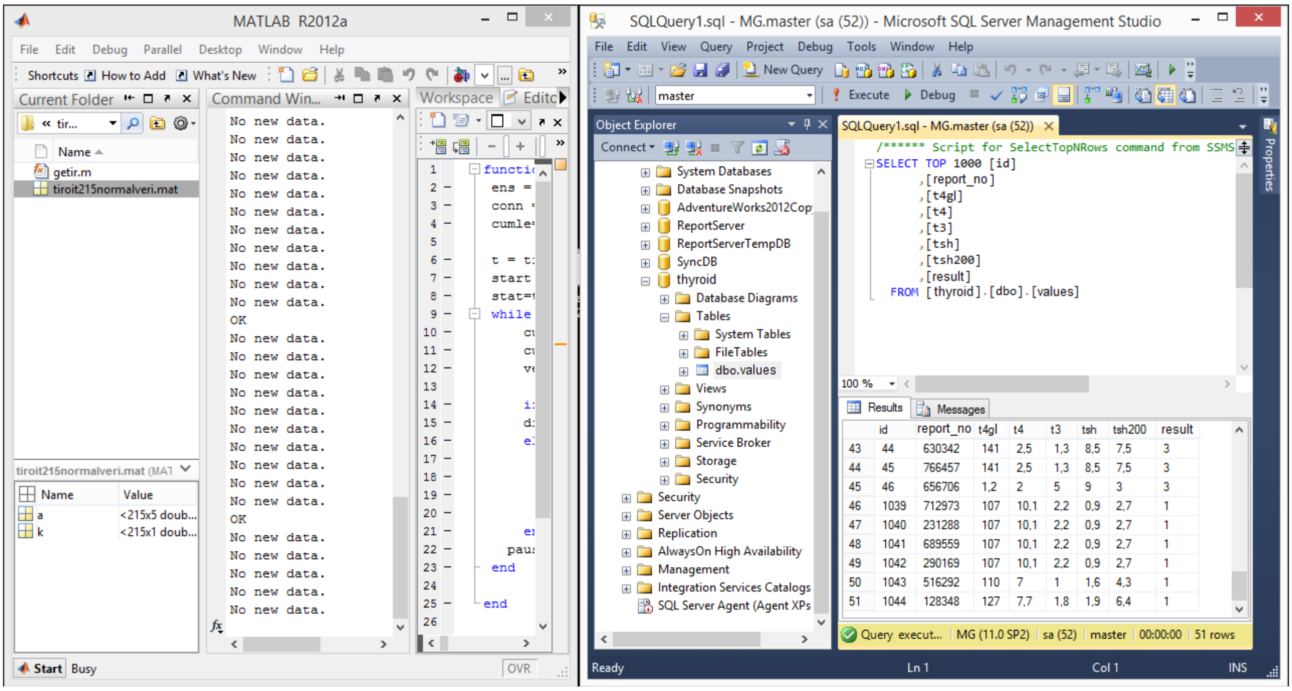
Table 4. The comparison of the present study and other studies in the literature carried out via 1st group data set

Author(s)	Method	Accuracy (%)
Serpen et al. [19]	MLP	36.74 (test data)
	LVQ	81.86 (test data)
	RBF	72.09 (test data)
	PPFNN	78.14 (test data)
Özyılmaz and Yıldırım [20]	MLP with back-propagation	86.33 (mean-3-fold-CV)
	MLP with fast back-propagation	89.80 (mean-3-fold-CV)
	RBF	
	CSFNN	79.08
		91.14
Pasi [21]	LDA	81.34 (test data)
	C4.5-1	93.26 (test data)
	C4.5-2	92.81 (test data)
	C4.5-3	92.94 (test data)
	MLP	96.24 (test data)
	DIMLP	94.86 (test data)
Polat et al. [22]	AIRS	81.00 (mean-10-fold-CV)
	AIRS with Fuzzy weighted pre-processing	8500 (mean-3-fold-CV)
Keleş and Keleş [23]	ESTDD	95.33 (10- fold -CV)
Kukkurainen and Luukka [24]	Level set classifier	96.44
Temurtaş [25]	MLNN with LM	92.96 (3-fold-CV)
	PNN	94.43 (3-fold-CV)
	LVQ	89.79 (3-fold-CV)
	MLNN with LM	93.19 (10-fold-CV)
	PNN	94.81 (10-fold-CV)
	LVQ	90.05 (10-fold-CV)
Kodaz et al. [26]	AIRS	94.82 (10-FCV)
	IG-AIRS	95.90 (10-FCV)
Doğantekin et al. [27]	ADSTG	93.77 (10-FCV)
Doğantekin et al. [28]	GDA-WSVM	91.86 (test data)
Chen et al. [29]	FS-PSO-SVM	97.40 (mean-10-fold-CV)
Liu et al. [30]	FKNN	98.82 (10-FCV)
Li et al. [31]	PCA-ELM	97.73 (mean-10-fold-CV)
		98.10 (10-fold-CV)
Dina et al. [32]	CBR	99.53
Kaya [33]	ELM (70-30% training-test)	96.79
The present study	ENSEMBLE Classification	99.06 (215 data set)
		99.08 (7200 data set)

After it was understood that the proposed system for thyroid diagnosis could be used in mobile applications, the next step was taken. The successful methodology was in the server in a trained state in order to classify new data to be evaluated. Users can send their blood values to the online database for diagnosis thanks to the Android application in their mobile devices. MATLAB in the host computer receives new data sent by the user via mobile devices and sends them back to the mobile media following the processing.

Second stage

At this stage, the system was operated thanks to the interaction between mobile devices, MATLAB and database.



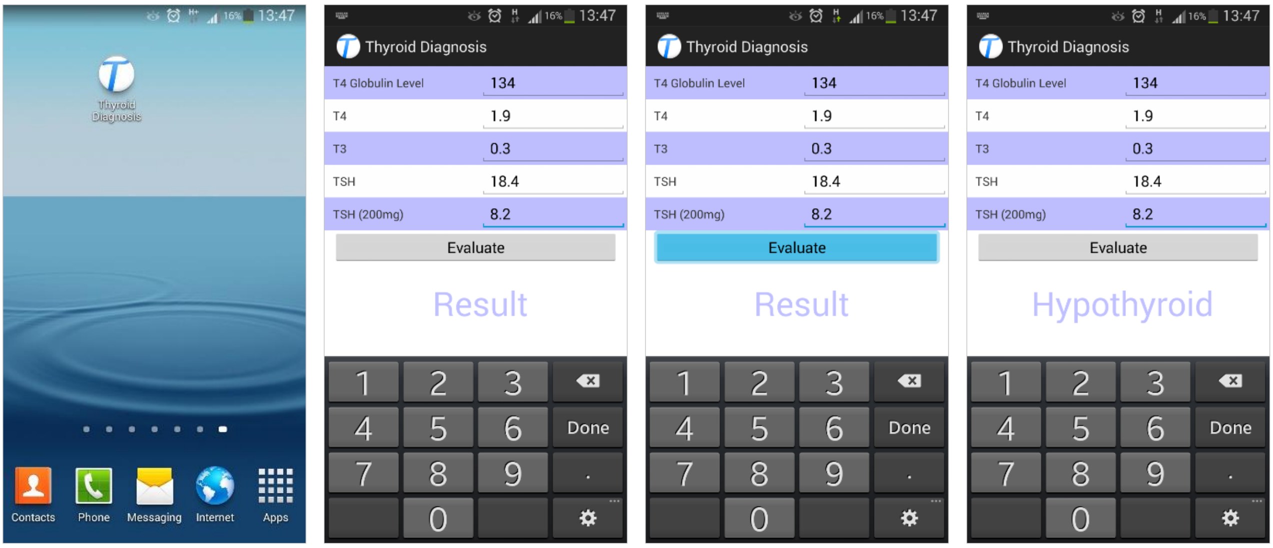
(a) (b)

Figure 3. Application for mobile system; a) Matlab program in the server, b) Information from the database.

Images taken from Matlab and database while mobile system is running were given in Figure 3 (a) and (b). Program codes prepared in Matlab environment, intervals and its control on the database are shown in Figure 3 (a). Figure 3 (b) shows the database where the evaluation results of the data entered via mobile devices are stored. The application system running on mobile device is developed with Linux based open source Android operating system. Database code is written in C language.

Third stage

The android based mobile software to be operated in the mobile device was written in the third stage. This application to be installed in the mobile device enables the user to enter data regarding the disease in the mobile device which will be evaluated by the system.



(a) (b) (c) (d)

Figure 4. Mobile device applications: a) Image of the mobile application logo on mobile device screen, b) Screen interface where the user enters data in the mobile application, c) Evaluation process of the system, d) Results displayed on the mobile device screen following the data evaluation.

Images of the mobile diagnosis system logo and interface are shown in Figure 4 (a), (b), (c) and (d). Thyroid data of each patient based on their blood values are entered in the related section of this application. When the user touches the "evaluate" button, the system sends the user's data to the database. MATLAB operating in the server controls the database on regular intervals, applies the decision making algorithm to the new data and sends the results to the database. The application operating on the client mobile device displays the related result sent by the database. Thus, the user's client mobile device can evaluate data regarding functional thyroid disease thanks to the mobile diagnosis system. The data on the application screen belong to the important blood values for the thyroid diagnosis.

Thanks to the methodology proposed in this study, a successful (nearly 99%) mobile decision support system for thyroid diagnosis was created using the thyroid data obtained from UCI database. The feasibility of the system was tested and the results indicated that it can be used in practical applications.

Discussion

Studies aimed at increasing the quality of life lead to the development of artificial intelligence and take more place in human life. This implies that in the near future biological data (informations on disease symptoms, pictures, sounds etc.) will be interpreted by artificial intelligence-based intelligent devices. In our work, it is aimed to evaluate live data by experts or specialized intelligent machines. For this purpose, the blood data about the thyroid disease were evaluated with the mobile device and accurate results were obtained.

With our application, the diagnosis of thyroid disease was successfully performed using a mobile device. It should be noted here that disease data is standard. Many studies have been done to show which algorithms used as decision mechanisms will be more successful in which disease. In this study, data set of thyroid functioning disease was evaluated online via mobile device. Our work has been done for multiple purposes. First, the most successful expert system for functional thyroid disease has been identified. Then a mobile application was written and a diagnostic system was created. This system allows the evaluation of disease data at another center in rural or undeveloped areas where no facilities are available. At the same time, the developed mobile diagnostic support system can be used for different diseases. The central labs integrated with the system can evaluate disease data with mobile devices. People can download the designed android application to their mobile device and use the system. In particular, doctors working in rural areas will be able to use this practice as a decision support system to assist physicians in evaluating disease data. With this system, any person can be informed about the disease through the mobile device if they have their blood data about thyroid disease. Our work will also provide additional information to the physicians who will evaluate the data obtained from the samples when they are installed on blood analyzers. So in fatigue, intensity or emergency situations, it may also reduce the possibility of making false interpretations of humans. Our work has the infrastructure to solve all the processes on the mobile device. However, current work requires internet access. Data standards are needed to evaluate disease data and it needs to be constantly updated to prevent over-learning of the algorithm.

Conclusion

In this study, mobile diagnostic system was created by using mobile devices, database and a server. With the designed mobile diagnostic system, functional thyroid disease data were evaluated and accurate diagnoses were made. The proposed system was developed via Linux based open source Android operating system. This application accurately evaluatesthe data entered via mobile devices and displays the evaluation results on the mobile device screen.

The classification accuracy of first and second data group for functional thyroid disease via ensemble classification technique are 99.06% and 99.08%, respectively. Highest accuracy rate of ensemble classification was obtained with 257 training cycles in the application for thyroid data. Ensemble classification system detected 2 of 215 samples incorrectly in the first data group. In the second data group, 66 of 7200 samples were detected incorrectly. The performance results of the proposed the functional thyroid diagnosis system is superior than the previous studies given in Table 4 [34-36].

This system can be used as a mobile health application and mobile support system for functional thyroid diagnosis or other diseases. Mobile diagnostic system can be developed and used for different diseases. When the mobile diagnostic system is operated in parallel with the blood analyzer, human-induced errors can be minimized by informing doctors of all possible diseases.

Table 5. Directory of abbreviations

SQL	:	Structured Query Language
MSSQL	:	Microsoft SQL Server
UCI or UC Irvine	:	The University of California, Irvine
DT	:	Decision Tree
MATLAB	:	Matrix Laboratory
X-ray	:	X-radiation, a form of high-energy electromagnetic radiation
MRI	:	Magnetic Resonance Imaging
TSH	:	Thyroid Stimulating Hormone
T3	:	Triiodothyronine
T4	:	Thyroxine
TBG	:	Thyroid Binding Globulin
FTI	:	Free Thyroxine Index
TT4	:	Total Thyroxine
T4U	:	Thyroxine Uptake

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Compliance with ethical standards

Conflict of interest

All authors read and approved the final manuscript. None of the authors had a conflict of interest.

Ethical approval

Ethics approval for the study protocol was obtained from the local area heath ethics committee.

Informed consent

Informed consent was obtained from all individual participants included in the study. In this study, real diagnosis results were compared to get “gold standard test” [18] results in order to test the reliability of diagnosis performed pre-existing dataset.

References

1. Electronic Mobile Health https://www.healthparliament.eu/wpcontent/uploads/2017/09/Electronic_mobile-health.pdf/19.09.2019
2. J. John, & C. Raju, (2018), "Design and Comparative Analysis of Mobile Computing Software Framework," *2018 Second International Conference on Inventive Communication and Computational Technologies (ICICCT)*. doi:10.1109/icicct.2018.8473350. 978-1-5386-1974-2/18/$31.00 ©2018 IEEE.
3. A. Uçar, & R. Özalp, (2017), "Efficient android electronic nose design for recognition and perception of fruit odors using Kernel Extreme Learning Machines," *Chemometrics and Intelligent Laboratory Systems*, vol. 166, pp 69–80. doi:10.1016/j.chemolab.2017.05.013.
4. S. A. Tuncer and A. Alkan, "Segmentation of thyroid nodules with K-means algorithm on mobile devices," *2015 16th IEEE International Symposium on Computational Intelligence and Informatics (CINTI)*, Budapest, 2015, pp. 345-348.
5. S. A. Tuncer and A. Alkan, "Abdominal image segmentation on Android based mobile devices," *2014 22nd Signal Processing and Communications Applications Conference (SIU*), Trabzon, 2014, pp. 806-809.
6. M. F. Amasyali, (2013), "A semi-random subspace method for classification ensembles," *21st Signal Processing and Communications Applications Conference (SIU).* doi:10.1109/siu.2013.6531301. 978-1-4673-5563-6/13/$31.00 ©2013 IEEE.
7. A. Maniakas, L. Davies, & M. E. Zafereo, (2018), "Thyroid Disease Around the World," *Otolaryngologic Clinics of North America, vol 51(3),* pp 631–642. doi:10.1016/j.otc.2018.01.014.
8. J. Longbottom & R. Macnab, (2014), "Thyroid disease and thyroid surgery," *Anaesthesia & Intensive Care Medicine*, vol. 15(10), pp 458–464. doi:10.1016/j.mpaic.2014.07.006
9. H. Kaneko, (2018), "Automatic outlier sample detection based on regression analysis and repeated ensemble learning," *Chemometrics and Intelligent Laboratory Systems*, vol. 177, pp 74–82.
10. M. Hosni, I. Abnane, A. Idri, J. M. C. de Gea, & J. L. F. Alemán, (2019), "Reviewing Ensemble Classification Methods in Breast Cancer", *Computer Methods and Programs in Biomedicine.* doi:10.1016/j.cmpb.2019.05.019.
11. U. Agrawal, D. Soria, C. Wagner, J. Garibaldi, I. O. Ellis, J. M. S. Bartlett, A. R. Green, (2019), "Combining Clustering and Classification Ensembles: A Novel Pipeline to Identify Breast Cancer Profiles." *Artificial Intelligence in Medicine*. doi:10.1016/j.artmed.2019.05.002.
12. Y. He, D. Chen, W. Zhao, (2006), "Ensemble classifier system based on ant colony algorithm and its application in chemical pattern classification, *Chemometrics and Intelligent Laboratory Systems*, vol. 80, pp. 39 – 49.
13. M. Czajkowski & M. Kretowski, (2019), "Decision Tree Underfitting in Mining of Gene Expression Data An Evolutionary Multi-Test Tree Approach," *Expert Systems with Applications*. doi:10.1016/j.eswa.2019.07.019.
14. H. Sun, & X. Hu, (2017), "Attribute selection for decision tree learning with class constraint," *Chemometrics and Intelligent Laboratory Systems*, 163, 16–23. doi:10.1016/j.chemolab.2017.02.004
15. N. Cerpa, M. Bardeen, C. A. Astudillo & J. Verner, (2016), "Evaluating different families of prediction methods for estimating software project outcomes," *Journal of Systems and Software*, 112, 48–64. doi:10.1016/j.jss.2015.10.011.
16. H. Sun & X. Hu (2017), "Attribute selection for decision tree learning with class constraint." *Chemometrics and Intelligent Laboratory Systems*, 163, 16–23. doi:10.1016/j.chemolab.2017.02.004.
17. Thyroid diseases diagnosis, treatment and follow-up guide, Turkey Endocrinology and Metabolism Society, ISBN No: ISBN: 978-605-4011-37-7, 2019.
18. https://www.statisticshowto.datasciencecentral.com/gold-standard-test/Accessed 20/09/2019.
19. G. Serpen, H. Jiang, L. Allred, (1997), "Performance analysis of probabilistic potential function neural network classifier," *In Proceedings of artificial neural networks in engineering conference*, St. Louis, MO, 7, pp. 471–476.
20. L. Ozyilmaz, T. Yildirim, (2002), "Diagnosis of thyroid disease using artificial neural network methods," *In Proceedings of ICONIP'02 nineth international conference on neural information processing*, Orchid Country Club, Singapore, pp. 2033–2036.
21. L. Pasi,(2004), "Similarity classifier applied to medical data sets," *International conference on soft computing*, Helsinki, Finland & Gulf of Finland & Tallinn, Estonia.
22. K. Polat, S. Sahan, S. Gunes, (2007), "A novel hybrid method based on artificial immune recognition system (AIRS) with fuzzy weighted pre-processing for thyroid disease diagnosis," *Expert Systems with Applications*, 32(4), pp. 1141–1147.
23. A. Keles, A. Keles, (2008), "ESTDD: expert system for thyroid diseases diagnosis," *Expert Systems with Applications*, 34(1), pp. 242–246.

24. P. Kukkurainen, P. Luukka, (2008), "Classification method using fuzzy level set subgrouping," *Expert Systems with Applications,* 34, pp. 859–865.
25. F. Temurtas, (2009), "A comparative study on thyroid disease diagnosis using neural networks," *Expert Systems with Applications*, 36(1) pp. 944–949.
26. H. Kodaz, S. Ozsen, A. Arslan, S. Gunes, (2009), "Medical application of information gain based artificial immune recognition system (AIRS): diagnosis of thyroid disease," *Expert Systems with Applications*, 36, pp. 3086–3092.
27. E. Dogantekin, A. Dogantekin, D. Avci, (2010), "An automatic diagnosis system based on thyroid gland: ADSTG," *Expert Systems with Applications*, 37, pp. 6368–6372.
28. E. Dogantekin, A. Dogantekin, D. Avci, (2011), "An expert system based on generalized discriminant analysis and wavelet support vector machine for diagnosis of thyroid diseases," *Expert Systems with Applications*, 38(1), pp. 146–150.
29. H. L. Chen, B. Yang, G. Wang, J. Liu, Y. D. Chen, D. Y. Liu, (2011), "A three-stage expert system based on support vector machines for thyroid disease diagnosis," *J. Med. Syst.*, http://dx.doi.org/10.1007/s10916-011-9655-8.
30. D. Y. Liu, H. L. Chen, B. Yang, X. En Lv, L. N. Li (2011), "Design of an enhanced fuzzy k-nearest neighbor classifier based computer aided diagnostic system for thyroid disease," *Journal of Medical Systems*, http://dx.doi.org/10.1007/s10916-011-9815-x.
31. L. N. Li, J. H. Ouyang, H. L. Chen, D. Y. Liu, (2012), "A computer aided diagnosis system for thyroid disease using extreme learning machine," *J. Med. Syst.*, 36, pp. 3327–3337, DOI 10.1007/s10916-012-9825-3.
32. A. Dina, Sharaf-El-Deen, İ. F. Moawad, M. E. Khalifa, (2014), "A new hybrid case-based reasoning approach for medical diagnosis systems," *J. Med. Syst.* 38(9), Doi 10.1007/s10916-014-0009-1.
33. Y. Kaya, (2014) "A Fast-Intelligent Diagnosis System for "Thyroid Diseases Based on Extreme Learning Machine," *Journal of Science and Technology A-Applied Sciences and Engineering,* 15(1), pp. 41-49. https://dergipark.org.tr/en/download/article-file/35611.
34. R. Solmaz, M. Günay, A. Alkan, (2013), "Uzman Sistemlerin Tiroit Teşhisinde Kullanılması," *Akademik Bilisim 2013 – XV. Akademik Bilisim Konferansı Bildirileri 23-25 Ocak 2013 – Akdeniz Üniversitesi, Antalya*, Türkiye, pp. 864-867, 2013. https://ab.org.tr/ab13/bildiri/268.pdf.
35. R. Solmaz, A. Alkan, (2013), "Kan Testi Tabanlı Sınıflandırma Yöntemlerinin Tiroit Tanısında Kullanılması," *6. Mühendislik ve Teknoloji Sempozyumu 25-26 Nisan 2013 I Çankaya Üniversitesi, Ankara, Türkiye, pp. 269-272. ISBN: 978-975-6734-155, https://zgrw.org/files/MTS6.pd*
36. R. Solmaz, M. Günay, A. Alkan, (2014), "Fonksiyonel Tiroit Hastalığı Tanısında Naive Bayes Sınıflandırıcının Kullanılması," *Akademik Bilişim'14 - XVI. Akademik Bilişim Konferansı Bildirileri 5 - 7 Şubat 2014 Mersin Üniversitesi*, Türkiye, pp. 891-897, 2014. https://ab.org.tr/ab14/kitap/solmaz_gunay_ab14.pdf.