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Conflict of Interest Statement

TO: Professor Edward Ciaccio
Editor in Chief, Computers in Biology and Medicine Journal
Columbia University, New York, New York, USA

May 6, 2016

Subject: Conflict of Interest

Dear Editor,

We hereby confirm that we have no conflict of interest for the manuscript entitled "*Mining Balance Disorders' data for the development of Diagnostic Decision Support Systems*" jointly written by *T.P. Exarchos, G. Rigas, A. Bibas, D. Kikidis, C. Nikitas, F.L. Wuyts, B. Ihtijarevic, L. Maes, M. Cenciarini, C. Maurer, N. Macdonald, D.-E. Bamiou, L. Luxon, M. Prasinou, G. Spanoudakis, D. D. Koutsouris and myself*, to be considered for publication in the *Computers in Biology and Medicine Journal*.

We remain at your disposal for any further details or clarifications.

Yours sincerely,
Dimitrios I. Fotiadis
Professor of Biomedical Engineering

Editor in Chief

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Response 1: We have made every effort to revise the manuscript for copying. It should be mentioned that only the main long text parts changes are marked in the marked version of the revised manuscript.

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Response 1: We thank the reviewer for his valuable comments that helped to improve the quality of the manuscript.

Mining Balance Disorders' data for the development of Diagnostic Decision Support Systems

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Abstract— In this work we present the methodology for the development of the EMBalance diagnostic Decision Support System (DSS) for balance disorders. Medical data from patients with balance disorders have been analysed using data mining techniques for the development of the diagnostic DSS. The proposed methodology uses various data, ranging from demographic characteristics to clinical examination, auditory and vestibular tests, in order to provide an accurate diagnosis. The system aims to provide decision support for general practitioners (GPs) and experts in the diagnosis of balance disorders as well as to provide recommendations for the appropriate information and data to be requested at each step of the diagnostic process. Detailed results are provided for the diagnosis of 12 balance disorders, both for GPs and experts. Overall, the reported accuracy ranges from 59.3 to 89.8% for GPs and from 74.3 to 92.1% for experts.

Index Terms—Balance disorders, data mining, decision support systems, vestibular system

I. INTRODUCTION

Human balance requires vision, joint and muscle proprioception and the vestibular system. The integration of the above input and motor output to the visionary and muscle systems are required in order to achieve balance. If one of the three above mentioned systems or their integration fails, this could lead to several different pathologies that can cause balance disorders. The reasons that can cause balance disorders can be many and different [1]. In approximately 5%, the causes are mainly neurological; in 5% are medical; in 15% are psychological; in more than 50% the causes are related to diseases of the inner ear while in the rest 25%, the causes are multiple. Balance disorders can lead to falls [2], which can subsequently lead to other complications

The diagnosis of balance disorders is challenging, sometimes even for the expert otolaryngologists or expert neurologists [3]. A systematic history taking, followed by appropriate clinical examinations chosen on a patient and symptom specific basis are the cornerstones of diagnosis and are tasks where a Decision Support System (DSS) could be of great help, facilitating the diagnostic process, especially for medical practitioners with less expertise in balance disorders such as GPs. Only a few DSS have been developed in the past regarding the diagnosis of vestibular disorders. Mira et. al. [4] proposed an automated diagnosis system, VERTIGO, which is based on rules. CAMISEL is another DSS [5], which is based on a two-step approach for reaching a diagnosis. In the first step, the system suggests a potential diagnosis based on initial evidence, while in the second step the system confirms or rejects the diagnosis, taking into account information from the patient's history and clinical examinations. Galactica is a machine learning approach [6, 7] which learns and develops diagnostic decision rules using data from 564 patients with vertigo, with as primary diagnoses Menière's disease, vestibular schwannoma, traumatic vertigo, sudden deafness, benign paroxysmal positional vertigo (BPPV) and vestibular neuritis. OtoNeurological Expert (ONE) [8,9] developed diagnostic rules using 815 neuro-otology patients, which included the same diagnosis as Galactica and subsequently tested for 1030 cases, including cases with benign recurrent vertigo, vestibulopathia and central lesion. The best total classification accuracies using the combined knowledge bases with machine learning knowledge and experts' knowledge, classified 82.5–84.7% of cases correctly within

the first and second diagnostic suggestion. NetSet has been developed using 815 patient cases with the same primary diagnoses [10]. NetSet showed a sensitivity, specificity, positive predictive value and total accuracy for all six diagnostic classes 85%, 83%, 96% and 95%, respectively.

Miettinen and Juhola [11], employed Bayesian probabilistic models for the diagnosis of six otoneurological diseases. Additional experiments with the ONE diagnostic system were also presented in [12,13], using different machine learning methods, such as the k-nearest neighbor method, the Naïve Bayes classifier and Support Vector Machines. Finally, Dong *et al.* [14] developed a diagnostic system, through dynamic uncertain causality graphs. The graphs were developed using medical knowledge and validated in 60 patient cases, resulting in an average accuracy ranging from 81.7 to 88.3%.

A newly developed diagnostic DSS is part of an integrated system, EMBalance (<http://www.embalance.eu/>), which is a system for the management of patients with balance disorders in terms of diagnosis, treatment and disease evolution. The EMBalance diagnostic platform goes beyond current state of the art in several directions. All previous works focus only on the development of data mining models for classifying patients in different diagnostic categories. The proposed methodology aims to provide a recommendation tool which is able to guide the GPs and experts in requesting the appropriate information for reaching the diagnosis. Another innovative feature of the proposed DSS is that due to the several data mining models developed for each one of the diagnoses, it can provide more than one diagnosis for each patient. An additional benefit of the EMBalance DSS is that while in previous systems, the patients' data used for training and testing the algorithms contained approximately 10-240 features, the EMBalance repository characterizes patients using approximately 350 features. This exhaustive patient characterization coupled with extensive experiments with feature selection algorithms enables the EMBalance DSS to identify the critical information needed for the diagnosis of the different pathologies. Finally, the proposed DSS has two different modules, one for expert use and the other for GP use, which utilize different features which are determined by the access that each of the two groups (GPs and

experts) has to specialized equipment and tests. Previous systems assumed only experts usage, judging on the features used by them for diagnosis.

II. MATERIALS AND METHODS

A. Dataset

Data from 985 patients were collected from the National Hospital of Neurology and Neurosurgery, Queen Square, UK, the 1st Otolaryngology University Clinic of Athens, Greece, the University of Antwerp, Belgium and the University Clinic of Freiburg, Germany. These data contained more than 350 features (variables), including epidemiological information, detailed medical history, disease related history, clinical findings and laboratory examination results (<http://www.embalance.eu/>). Furthermore, detailed information on different balance related types of symptoms together with symptom duration, symptom free intervals, association between symptoms and relevant triggers was collected, since these are important features for the diagnosis of vestibular disorders. It should be noted that in the GP case, only features corresponding to personal disease history, symptoms and clinical examinations were utilized, whereas in the expert case, all the above mentioned features were used. Diagnostic outcomes were classified into more than 100 diagnoses, using the standard ICD10 code, as well as additional, not as yet specified in the ICD code, diagnostic categories based on the Bárány Society proposed International Classification of Vestibular Disorders (see <http://www.jvr-web.org/Barany-feedback.html>). The study has been approved by the respective ethics committees of each Institute according to local/national regulations. Following numerous experiments and detailed analysis and collaboration with medical experts, 12 diagnostic categories shown in Table I, along with the corresponding recommendation for specific features are supported by the proposed DSS. Diagnostic categories with a very small number of patients (i.e. less than 20) were excluded because it was not feasible to be analysed. The proposed DSS is based on the above described dataset and provides diagnosis for 12 different diseases as they are described in Table I.

B. Methods

B1. Training

To develop the DSS for the diagnosis of 12 balance disorders, a three stage methodology was implemented which is shown in Fig. 1. In the first step, preprocessing of the dataset was performed; this included the removal of features with more than 50% missing values and the development of the datasets per class. Due to the large number of target classes (12), 12 different binary classification models have been developed instead of a 12-class classification model. A different dataset was thus prepared per diagnostic category; each dataset per class contained all records from the target class and randomly the same number of records from the rest of the database.

In the second step, feature selection was performed. Two different data mining frameworks have been tested for each diagnostic category (Fig. 1). In the first (upper part of Fig. 1), feature selection was applied separately in each category of features (Personal disease history, symptoms, vertigo-instability symptoms, tinnitus symptoms, clinical examinations, auditory tests, video-nystagmography, questionnaires, vestibular tests, imaging data) and selected features were collected at the end for the diagnostic process. In the second category (lower part of Fig. 1), feature selection was applied in all features from all categories and the optimal subset was used for the diagnostic process. Feature selection was applied on the training set of each diagnostic category (10 times since 10-fold cross validation was used). In our case, we employed feature subset selection methods, that consider the overall set of features collectively, compared to feature ranking methods that assess each feature independently. Further to that, feature subset selection methods can be classified into two categories: the filter [15], where the feature subset selection is independent of the training algorithm and removes irrelevant and high correlated features and the wrapper [16], where the feature subset selection is applied as a wrapper with the training algorithm and the optimal feature subset is identified based on its accuracy with the specific training algorithms.

Finally, in the third step, classification algorithms were applied. The reduced subset of features from the second step is used as input to predict the target class. The best results were obtained using the second data mining framework (overall feature subset selection in all available features) with the combination of wrapper feature

selection (second step) and decision trees enhanced with a boosting algorithm, Adaboost (third step). Wrapper feature selection performs an exhaustive search within the space of available features, targeting the optimization of the accuracy of the selected classification algorithm. Decision trees are one of the most common data mining techniques, employed in several different domains, including clinical applications [9]. A key element of the decision trees that makes their usage appealing in the medical domain is that they can be transformed to rules and provide transparency and interpretation in the decisions made (in contrast for example to neural networks or support vector machines). Given an initial dataset, with instances characterized by features, there are exponentially different decision trees that can be induced. For the development of diagnostic models for each of the diagnoses, decision trees were used as basic models, induced using the C4.5 algorithm. The C4.5 algorithm for decision tree induction creates a tree structure form with nodes, edges and leaves. The nodes correspond to features, the edges to different values or ranges of values of the features of the nodes and the leaves are the decisions of the tree.

In order to identify which feature to have in which node and in which values to divide this feature, the notion of information gain was considered. Details can be found in [17,18]. After the induction of the decision tree, the tree is pruned in order to avoid overfitting in leaves where only a small number of instances applies. Boosting is a procedure performed in an iterative manner and is used to change the distribution of the training instances so that the base classifier, in our case the decision tree induced using the C4.5 algorithm, focuses more on examples that are difficult to classify correctly. Boosting assigns weight to each training instance and then tunes the weight of all instances; instances easily classified receive a reduced weight, while instances not classified correctly receive an increased weight.

The assigned instance weights are then used in the sampling distribution in order to draw a set of bootstrap sample from the original dataset. A specific type of boosting is the algorithm Adaboost, which works as follows: Let $\{(x_j, y_j) | j = 1, 2 \dots N\}$ denote the set of N training instances, where x_j are the features characterizing record j and

y_j is the class. Adaboost assigns different weights in the base classifiers C_i , depending on the error rate of each classifier, given as:

$$\epsilon_i = \frac{1}{N} \left[\sum_{j=1}^N w_j I(C_i(x_j) \neq y_j) \right], \quad (1)$$

where $I(p) = 1$ if part p is true and 0 otherwise. i is the number of base of classifier. The weight of the C_i is given by:

$$a_i = \frac{1}{2} \ln \left(\frac{1-\epsilon_i}{\epsilon_i} \right), \quad (2)$$

which is used to define also the weight of the training instances as follows:

$$w_i^{(j+1)} = \frac{w_i^{(j)}}{Z_j} \times \begin{cases} e^{-a_j} & \text{if } C_j(x_i) = y_i \\ e^{a_j} & \text{if } C_j(x_i) \neq y_i \end{cases}, \quad (3)$$

where Z_j is the normalization factor that ensures that $\sum_i w_i^{(j+1)} = 1$. The weight equation (Eq. 3) increases the weight of the instances classified incorrectly and decreases the weight of those instances that are classified correctly. After the definition of the weights of the instances and of the base classifiers, the classification is performed according to the weight of each base classifier. In this way, base classifiers with low accuracy rate receive less weight and are used less in the classification.

It should be noted that several different combinations of classification schemes were tested prior to the resulting wrapper-decision trees and Adaboost approach. Besides wrapper, also filter based approaches were tested for feature selection. Due to the requirement of the collaborating clinicians and vestibular experts to provide the ability for interpretation for the decisions made, several classification methodologies were not selected (artificial neural networks, support vector machines, k-nearest neighbors) or due to their reduced reported results compared to decision trees and Adaboost (ripper algorithm [19], ridor algorithm [20], naïve Bayes algorithm). Moreover, instead of Adaboost, bagging and random forests were also tested. Additionally, due to the large number of classes, the 12 binary classification models approach was selected compared to the multiclass classification problem. An additional advantage to select binary diagnostic models was the nature of the vestibular diagnosis

problem; several subjects present with more than one pathology at the same time. A multiclass classification setting would not be able to address this requirement and assign two or more classes at the same time for a subject. The utilization of binary diagnostic models allows addressing this, by providing more than one diagnosis at the same time. For the C4.5 algorithm, the initial settings for pruning were set to 0.25 pruning factor and minimum instances per leaf to 5. The second value was tuned in each of the diagnostic categories. Adaboost was set to 10 different iterations and thus resulted in the generation of 10 decision trees per category.

B2. Testing

Fig. 2 shows the diagnostic (test) process which involves: (a) a recommendation tool that guides the GPs and experts in requesting the appropriate information (features), and (b) the diagnostic DSS, which has a different model/tree for each one of the 12 diagnoses. The recommendation system, based on the identified informative features for each diagnosis, recommends to the GP/Expert which parameter, clinical examination, and/or test to request in order to continue the diagnostic process. Specifically, the recommendation system proposes to the GP/Expert the feature identified in the respective path of the decision tree that is needed each time for the continuation of the tree parsing until the diagnosis is reached (Table I).

III. RESULTS

The 10-fold cross validation was used to evaluate the DSS. Sensitivity, specificity, positive predictive value, negative predictive value and accuracy were estimated for each diagnosis. Table II presents the results obtained for each different diagnosis considered, for both GPs and experts (since experts have access to specialized equipment and thus additional information compared to GPs). The first line of the results corresponds to the results obtained for the GPs, while the second line corresponds to the results for the experts. Also, the two columns, Features for GPs, Features for Experts, correspond to the resulting reduced subset of features identified for each diagnosis, for GPs and experts, respectively. This is due to the fact that GPs usually do not have access to the necessary equipment to perform specific tests (e.g. videonystagmography, auditory tests and vestibular tests).

For this reason, the first column (Features for GPs) contains only features made available to the GPs during the diagnostic process. The second column (Features for experts), contains additional features that can be acquired using sophisticated equipment, available only to expert settings. It should be noted that these two DSS modes were obtained and finalized after a series of experiments with different algorithms and different parameters. The reported results range in terms of all metrics in the different diagnoses taken into consideration, as well as, in terms of the features used. Overall, the metrics used for GPs are quite lower from the corresponding results of the experts. This is an expected finding, since the DSS developed for the experts, contains more sophisticated features (audiological and vestibular tests, imaging). When these test features are added, the corresponding metrics, as well as the diagnostic abilities, are improved in almost all cases.

The developed EMBalance DSS addresses the 4 most prevalent balance disorders (Migrainous vertigo, Typical Benign paroxysmal positional vertigo, Vestibular Neuritis and Menière's disease), as well as another 8 less prevalent (Possible Benign paroxysmal positional vertigo, Unilateral Peripheral Dysfunction/Failure, Psychological Disorders, Bilateral Vestibular failure/dysfunction, Cerebellar/Pontine lesion, CPA Acoustic neuroma, Chronic Subjective Dizziness Persistent Postural-Perceptual Dizziness, Vestibular Paroxysmia). For the 4 most prevalent diseases except Vestibular neuritis, quite high results have been reported, both for the GP and expert DSS modules. The best results were reported for Menière's disease, reaching an accuracy of 92.1% for the experts, while the lowest ones were reported for Unilateral Peripheral Dysfunction/Failure, with an accuracy of 59.3% for the GPs.

Based on the different number of records for each of the 12 classes, the classification framework used (feature subset selection, boosting, training of decision trees), required maximum 1 minute (in the case of Migrainous Vertigo, expert model). Regarding the testing time, decision trees are efficient classification structures and the testing time for a new record is negligible.

IV. DISCUSSION

The diagnosis of balance disorders is a difficult task, not only for the GPs but also for the experienced medical professionals which include otolaryngologists, audiovestibular physicians, neurologists, and audiologists. For those lacking the specialised medical training and the long clinical experience, the diagnostic process of vestibular disorders can be fraught with difficulties, and it may not be possible to gather all necessary information or to interpret such information meaningfully in order to conclude in the correct diagnosis. A DSS that would successfully address diagnosis of such disorders would address a significant public health need. The impact of this achievement includes better diagnostic outcomes and consequently improved quality of life for a large patient group, reduction of falls and fall related injuries, equity in health services access and cost reduction via referrals and follow up assessment decrease.

In this work we have presented the EMBalance diagnostic DSS for balance disorders, which includes one GP and one expert module, which reflect the availability of sophisticated tests and equipment in primary vs. secondary/tertiary clinical setups. According to Table II, for the unilateral peripheral dysfunction/failure, the diagnostic accuracy results for the GP mode are quite low. However, the diagnostic accuracy results are increased substantially in the expert module when the audiological test characteristics, which are very informative for unilateral diseases are added to the diagnostic process. Since audiological equipment is usually not available for the GPs, audiometry tests were not taken into consideration in this specific analysis for the GP DSS module. In the case of psychological disorders, the same simple models have been developed both for the GP and for the expert module, taking into consideration anxiety and/or depression validated questionnaire score levels and the existence or not of visual vertigo symptoms. For the Bilateral Vestibular failure/dysfunction case, the same models with quite accurate results have been developed for both GPs and experts, taking into consideration the same simple clinical history and examination features. In the Cerebellar/Pontine lesion case, the addition of vestibular tests improves the results from the GP to expert case, proving that vestibular tests are quite essential for this diagnosis. When considering the cerebellopontine angle (CPA) acoustic neuroma case, in the GP module, the

sensitivity obtained was quite low, which was increased substantially in the expert module, when the results of imaging tests are added. According to the medical expert module results, imaging and especially magnetic resonance imaging (MRI) is required to clearly identify a CPA acoustic neuroma. Nevertheless, in the GP module, results show that even with more easily acquired features, CPA lesions can be identified with satisfactory sensitivity. For Chronic Subjective Dizziness Persistent Postural-Perceptual Dizziness (PPPD), the results for GPs and experts are quite similar. Furthermore, the addition of the Videonystagmography (VNG) caloric test (canal paresis) category (a laboratory examination which is not available to the GPs) increases the accuracy for the identification of this diagnosis. In the vestibular neuritis case, the results are quite low in both modules. Still it can be seen that the addition of the VNG caloric test canal paresis category, improves the results for this diagnosis. In Menière's disease, quite high results are reported both for GPs and experts. Still, the addition of some auditory test results (low frequency 250-500 Hz hearing loss) increases the accuracy of the DSS for Menière's disease. Migrainous vertigo (vestibular migraine) is an important balance disorder, not addressed by most of the previous DSS in the literature [9-13]. For this diagnosis, the same model was developed and used for GP and expert DSS modules.

The diagnostic accuracy results for Vestibular paroxysmia are quite low in the case of the GPs, however those are substantially increased in the expert module, especially with the addition of the imaging results which are a key diagnostic feature for this disorder. Finally, the results for the posterior canal BPPV, both typical and atypical have been presented. The differentiation between typical and atypical BPPV depends on the existence or not of nystagmus in the Dix Hallpike examination. With a positive Dix Hallpike, i.e. typical posterior BPPV, the obtained results are quite satisfactory both for GPs and experts. In the case of the negative Dix Hallpike and the atypical posterior BPPV, the two modules report the same results.

Our work goes beyond the state of the art in many ways: A much more detailed feature vector has been formulated, accounting for more than 350 features including parameters regarding the medical history, symptoms, clinical examinations, audiological and imaging findings, questionnaire and, posturography results. In addition, an

advantage compared to the previously developed DSSs is that the EMBalance diagnostic DSS harnessed several different data mining models with a different model developed for each disease, which allowed the extraction of more than one diagnosis for each patient, since this is often required for patients with balance disorders. Through the decision tree based diagnostic DSSs, the medical professionals are thus able to obtain decision support in two tasks: (i) acquisition of patient's data, through the recommendation tool that has been developed based on the parsing of the decision trees, by requesting the specific features and in the correct order and, (ii) interpretations for the decisions made due to the decision tree based nature. More specifically, for each diagnosis made through the diagnostic decision support system, the corresponding rules that were applied for each patient case are presented to the medical expert.

Table III presents a summary of the current and of previous related works reported in the literature for the diagnosis of balance disorders including detailed accuracy for the common diagnosis (Benign Paroxysmal Positional Vertigo, Vestibular Neuritis and Menière's Disease) and high risk diagnosis (Vestibular Schwannoma-CPA acoustic neuroma). A direct comparison cannot be performed due to the different datasets and different methodologies (ranging from expert systems developed using expert knowledge [12] to more sophisticated modelling of knowledge with dynamic uncertain causality graphs [14], Bayesian networks analysis [11], artificial neural networks [10] etc.) that were employed by the different research groups. However, as it can be seen in Table III, the strength of the EMBalance DSS compared to DSSs presented in the literature include: (i) the number of different features used to inform the diagnostic process, allowing for a more detailed analysis of all available features and identification of the most informative ones per pathology. All previous works started their analysis from a smaller set, not taking into consideration several important features that the proposed DSS and analysis does. (ii) The number of different diagnostic classes considered. The proposed DSS can provide diagnosis for 12 different pathologies. All previous works reach up to 9 pathologies, limiting the exploitation of the DSS by a vestibular expert. An exception is the methodology presented in [14], which, however, was tested in a limited set of 60 patient cases, limiting its credibility in larger populations. Apart from the larger number of classes considered, the proposed DSS can provide simultaneously two or more diagnosis, which is typical for

several patients suffering from vestibular disorders. (iii) The comparable number of patient cases. As it is presented in Table III, the number of patient cases range from 60 to 1283; the 985 cases, using 10-fold cross validation used in our approach allows to consider the reported results credible and the DSS reliable. (iv) The availability of both GP and expert modules. This is an innovative point of the proposed DSS, compared to previous works that consider only usage by experts. In several healthcare systems, GPs are the first point of patient access for diagnosis; the GP mode of the proposed DSS allows GPs to perform the diagnostic process, helping them also during data acquisition.

In the future, the EMBalance DSS will be clinically evaluated in a multi-centre proof of concept clinical trial that will be conducted on a minimum of 200 prospective patients. Additionally, since in some of the diagnostic categories (Bilateral Vestibular failure/dysfunction, CPA Acoustic neuroma, Chronic Subjective Dizziness Persistent Postural-Perceptual Dizziness and Vestibular Paroxysmia), the number of available records was relatively small and the data highly skewed, in the future, when the EMBalance DB increase in terms of samples in these categories, retraining will be performed. Moreover, techniques for oversampling will be tested (e.g. Wilcoxon signed-rank, Friedman's, Iman-Davenport post hoc tests, Synthetic Minority Oversampling Technique) in order to address the relatively small number of records in the specific cases.

V. CONCLUSIONS

A methodology based on data mining techniques (feature selection, boosting algorithms, decision trees) has been employed for the development of a recommendation tool and a diagnostic DSS for 12 balance disorders, to assist GPs and experts, firstly in requesting the necessary information from the patients to reach a potential diagnosis and secondly to support the diagnosis of balance disorders. The reported results in most of the cases are satisfactory and the features used for each diagnosis are in line with clinical knowledge and guidelines. An increase in overall accuracy is presented, from the GP to the expert module, which is attributed to the additional

and more sophisticated features used by the experts. Further application of the diagnostic DSSs in real clinical settings could reveal the potential of the proposed approach.

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Figures and Tables

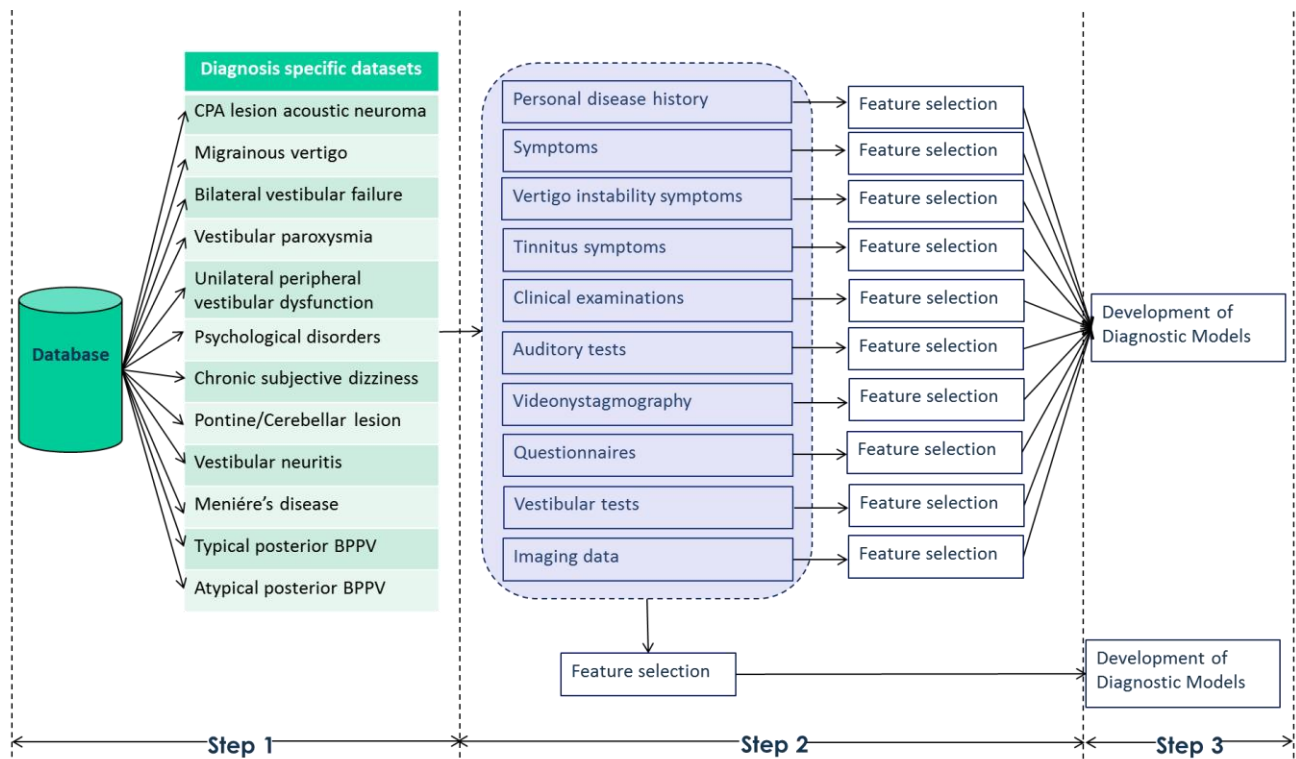


Figure 1: The building blocks of the methodology for developing the diagnostic models. The two data mining frameworks that were used are also shown. In the first, feature selection is applied to each different source of features and then the results are summarized in order to train the classification algorithms for balance disorders.

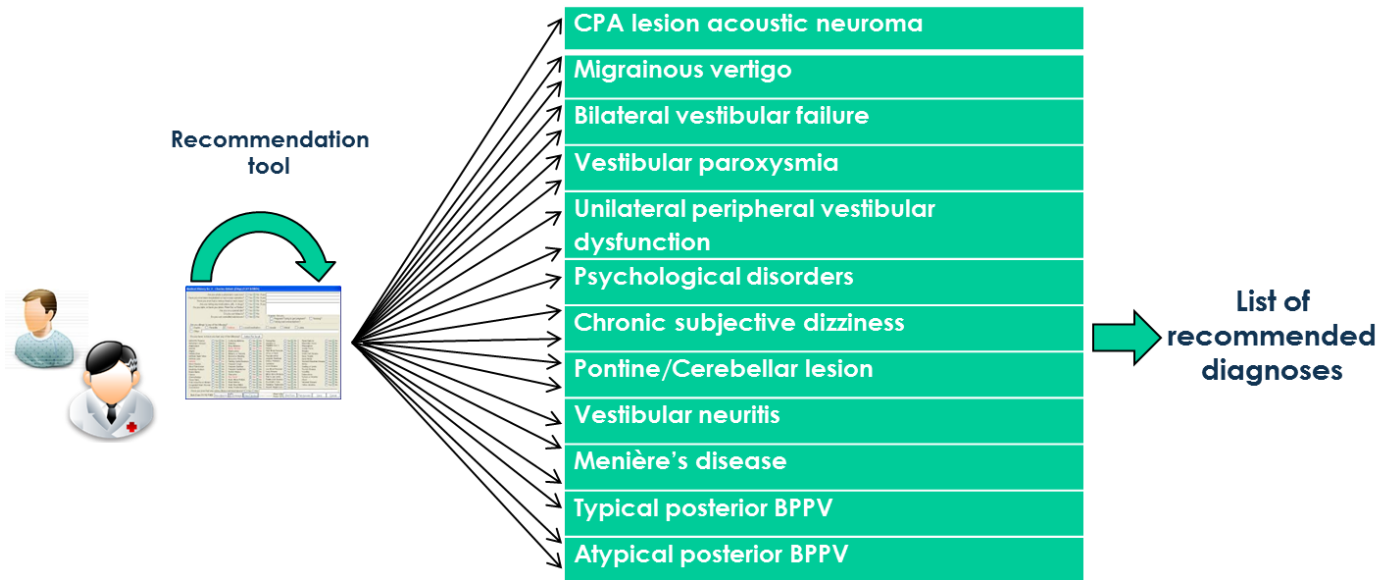


Figure 2: The interaction between the recommendation tool, which utilizes the features encountered in the paths of the decision trees, and the diagnostic decision support system, which is composed by the 12 different decision trees, one for each diagnosis as shown above. The outcome is the list of the recommended diagnosis.

TABLE I: DIAGNOSES CONSIDERED IN THE EMBALANCE DSS AND THE CORRESPONDING NUMBER OF CASES

A/A	Diagnosis	# of cases
1	Unilateral Peripheral Dysfunction/Failure	134
2	Psychological Disorders	40
3	Bilateral Vestibular failure/dysfunction	23
4	Cerebellar/Pontine lesion	43
5	CPA Acoustic neuroma	34
6	Chronic Subjective Dizziness Persistent Postural-Perceptual Dizziness (PPPD)	35
7	Vestibular Neuritis	89
8	Menière's disease	127
9	Migrainous vertigo (Vestibular Migraine)	222
10	Vestibular Paroxysmia	30
11	Typical Posterior Benign Paroxysmal Positional Vertigo (Typical BPPV)	156
12	Possible Posterior Benign Paroxysmal Positional Vertigo (Atypical BPPV) ¹	52
	Total	985

¹ As possible BPPV cases were considered those cases with a consistent history but negative Dix Hallpike examination.

Table II: Results for the 12 different diagnoses in terms of sensitivity, specificity, positive predictive value, negative predictive value accuracy and features used for the GPs and the experts are presented. The first line in the reported results are the measurements for the GPs and the second line for the experts

	SE (%)	SP (%)	PPV (%)	NPV (%)	ACC (%)	Features for GPs	Features for Experts
Unilateral Peripheral Dysfunction/ Failure	58.2	60.4	59.5	59.1	59.3	[patient_sex] [patient_age] [patient_ability_to_work] [patient_smoking] [symptoms_fall] [symptoms_hearing_loss] [symptoms_hearing_loss_evolution] [vertigo_instability_symptoms] [vertigo_instability_symptom_duration_time_interval] [vertigo_symptom_type_bundle_name] [symptom_type_anxiety_and_or_depression] [symptom_type_difficulty_walking_in_darkness] [symptom_type_headache] [symptom_type_tinnitus] [vertigo_trigger_head_movement] [symptom_type_dizziness]	[vestibular_test_sinusoidal_rotation] [auditory_test_PTA_250_AC_right] [auditory_test_PTA_8000_AC_right] [auditory_test_PTA_250_AC_left] [auditory_test_PTA_500_AC_left] [auditory_test_hearing_right_manual] [auditory_test_hearing_left_manual] [caloric_observational_test_canal_paresis_category] [caloric_vng_canal_paresis_category] [questionnaire_dizziness_emotional_subscore] [vertigo_instability_symptom_symptom_type] [symptom_type_anxiety_and_or_depression] [symptom_type_drunk_feeling] [vertigo_trigger_head_movement] [vertigo_trigger_standing_up_rapid_ascents] [symptom_type_dizziness]
	76.1	74.6	75.0	75.8	75.4		
Psychological Disorders	75.0	85.0	83.3	77.3	80	[symptom_type_anxiety_and_or_depression] [symptom_type_visual_vertigo]	[symptom_type_anxiety_and_or_depression] [symptom_type_visual_vertigo]
	75.0	85.0	83.3	77.3	80		
Bilateral Vestibular Failure/ dysfunction	82.6	82.6	82.6	82.6	82.6	[vertigo_instability_symptom_symptom_type] [symptom_type_difficulty_walking_in_darkness] [symptom_type_difficulty_walking_on_uneven_surfaces] [symptom_type_oscillopsia]	[vertigo_instability_symptom_symptom_type] [symptom_type_difficulty_walking_in_darkness] [symptom_type_difficulty_walking_on_uneven_surfaces] [symptom_type_oscillopsia]
	82.6	82.6	82.6	82.6	82.6		
Cerebellar/ Pontine lesion	79.1	79.1	79.1	79.1	79.1	[patient_age] [patient_smoking] [clinical_examination_gaze_test] [clinical_examination_head_thrust] [clinical_examination_romberg] [clinical_examination_gait] [personaldisease_bundle_name] [vertigo_instability_symptom_symptom_type] [vertigo_instability_symptom_duration_time_interval] [vertigo_symptom_type_bundle_name] [symptom_type_drunk_feeling] [symptom_type_headache] [symptom_type_tinnitus] [symptom_type_visual_vertigo]	[clinical_examination_gaze_test] [clinical_examination_head_thrust] [clinical_examination_gait] [vestibular_test_sinusoidal_rotation] [vertigo_instability_symptom_symptom_type] [symptom_type_difficulty_walking_on_uneven_surfaces] [symptom_type_headache] [symptom_type_tinnitus]
	88.4	83.7	84.4	87.8	86.1		
CPA Acoustic neuroma	79.4	91.2	90	81.6	85.3	[clinical_examination_gaze_test] [clinical_examination_head_thrust] [symptoms_hearing_loss] [personaldisease_bundle_name] [tinnitus_symptom_tinnitus_symptom_type] [tinnitus_symptom_frequency] [vertigo_symptom_type_bundle_name] [symptom_type_cervicalgia] [symptom_type_headache] [symptom_type_hearing_loss] [symptom_type_lightheaded] [symptom_type_tinnitus] [vertigo_trigger_head_movement] [vertigo_trigger_rolling_over_in_bed]	[clinical_examination_gaze_test] [clinical_examination_head_thrust] [symptoms_hearing_loss] [personaldisease_bundle_name] [tinnitus_symptom_frequency] [imaging_imaging_result] [personaldisease_bundle_name] [tinnitus_symptom_frequency] [symptom_type_lightheaded] [symptom_type_tinnitus] [vertigo_trigger_head_movement]
	85.3	91.2	90.6	86.1	88.2		
Chronic Subjective Dizziness PPPD	77.1	68.6	71.1	75.0	72.9	[patient_sex] [patient_age] [clinical_examination_head_thrust] [clinical_examination_romberg] [clinical_examination_tandem_gait] [symptoms_hearing_loss] [tinnitus_symptom_tinnitus_symptom_type] [vertigo_instability_symptom_symptom_type] [vertigo_instability_symptom_duration_time_interval] [vertigo_symptom_type_bundle_name] [preceding_event_bundle_name] [symptom_type_headache] [symptom_type_muscle_weakness]	[patient_sex] [clinical_examination_romberg] [clinical_examination_tendency_to_fall] [caloric_vng_canal_paresis_category] [questionnaire_hospital_anxiety_subscore] [symptom_type_anxiety_and_or_depression] [symptom_type_headache] [symptom_type_tinnitus] [symptom_type_dizziness]
	77.1	71.4	73.0	75.8	74.3		

						[symptom_type_phonophobic] [symptom_type_dizziness]	
Vestibular Neuritis	69.7 73.0	74.2 79.8	72.9 78.3	71.0 74.7	71.9 76.4	[vertigo_instability_symptom_symptom_type] [vertigo_instability_symptom_duration_time_interval] [vertigo_instability_symptom_frequency] [vertigo_symptom_type_bundle_name] [preceding_event_bundle_name]	[caloric_vng_canal_paresis_category] [symptoms_hearing_loss] [vertigo_instability_symptom_symptom_type] [vertigo_instability_symptom_duration_time_interval] [vertigo_symptom_type_bundle_name] [vertigo_instability_symptom_frequency] [preceding_event_bundle_name]
Menière's disease	88.2 89.8	91.3 94.5	91.1 94.2	88.5 90.2	89.8 92.1	[symptoms_hearing_loss] [symptoms_hearing_loss_evolution] [vertigo_instability_symptom_duration_time_interval] [vertigo_symptom_type_bundle_name] [symptom_type_dizziness]	[auditory_test_PTA_250_AC_right] [auditory_test_PTA_500_AC_left] [symptoms_hearing_loss] [symptoms_hearing_loss_evolution] [vertigo_instability_symptom_duration_time_interval] [vertigo_symptom_type_bundle_name] [symptom_type_dizziness]
Migrainous vertigo	82.9 82.9	82.9 82.9	82.9 82.9	82.9 82.9	82.9 82.9	[clinical_examination_romberg] [symptoms_hearing_loss] [personaldisease_bundle_name] [tinnitus_symptom_frequency] [vertigo_instability_symptom_symptom_type] [vertigo_instability_symptom_duration_time_interval] [vertigo_symptom_type_bundle_name] [preceding_event_bundle_name] [symptom_type_anxiety_and_or_depression] [symptom_type_cervicalgia] [symptom_type_difficulty_walking_on_uneven_surfaces] [symptom_type_headache] [symptom_type_lightheaded] [symptom_type_phonophobic] [symptom_type_scotoma] [symptom_type_tinnitus] [vertigo_trigger_complex_visual_environments]	[clinical_examination_romberg] [symptoms_hearing_loss] [personaldisease_bundle_name] [tinnitus_symptom_frequency] [vertigo_instability_symptom_symptom_type] [vertigo_instability_symptom_duration_time_interval] [vertigo_symptom_type_bundle_name] [preceding_event_bundle_name] [symptom_type_anxiety_and_or_depression] [symptom_type_cervicalgia] [symptom_type_difficulty_walking_on_uneven_surfaces] [symptom_type_headache] [symptom_type_lightheaded] [symptom_type_phonophobic] [symptom_type_scotoma] [symptom_type_tinnitus] [vertigo_trigger_complex_visual_environments]
Vestibular Paroxysmia	60.0 80.0	76.7 86.7	72.0 85.7	65.7 81.3	68.3 83.3	[personaldisease_bundle_name] [vertigo_instability_symptom_symptom_type] [vertigo_instability_symptom_duration_time_interval] [vertigo_symptom_type_bundle_name]	caloric_vng_directional_preponderance_category] imaging_imaging_result] vertigo_instability_symptom_symptom_type] vertigo_instability_symptom_duration_time_interval] vertigo_symptom_type_bundle_name] preceding_event_bundle_name] symptom_type_hearing_loss] vertigo_trigger_standing_up_rapid_ascents]
Typical Posterior Benign Paroxysmal Positional Vertigo	86.5 86.5	87.8 89.1	87.7 88.8	86.7 86.9	87.2 87.8	[patient_sex] [clinical_examination_dix_hallpike] [personaldisease_bundle_name] [tinnitus_symptom_tinnitus_symptom_type] [vertigo_instability_symptom_symptom_type] [vertigo_instability_symptom_duration_time_interval] [vertigo_symptom_type_bundle_name] [symptom_type_hearing_loss] [symptom_type_motion_sickness] [symptom_type_tinnitus] [vertigo_trigger_head_movement]	[patient_sex] [clinical_examination_dix_hallpike] [vestibular_test_sinusoidal_rotation] [vestibular_test_smooth_pursuit] [caloric_vng_canal_paresis_category] [caloric_vng_directional_preponderance_category] [symptoms_hearing_loss] [symptoms_hearing_loss_evolution] [diagnosed_nystagmus_nystagmus_direction] [personaldisease_bundle_name] [vertigo_instability_symptom_duration_time_interval] [vertigo_symptom_type_bundle_name] [preceding_event_bundle_name] [nystagmus_type_bundle_name] [vertigo_trigger_bending_over] [symptom_type_dizziness]
Atypical posterior Benign Paroxysmal Positional Vertigo	82.7 82.7	82.7 82.7	82.7 82.7	82.7 82.7	82.7 82.7	[patient_sex] [clinical_examination_dix_hallpike] [vertigo_instability_symptom_symptom_type] [vertigo_instability_symptom_duration_time_interval] [vertigo_symptom_type_bundle_name] [vertigo_trigger_bending_over] [vertigo_trigger_rolling_over_in_bed]	[patient_sex] [clinical_examination_dix_hallpike] [vertigo_instability_symptom_symptom_type] [vertigo_instability_symptom_duration_time_interval] [vertigo_symptom_type_bundle_name] [vertigo_trigger_bending_over] [vertigo_trigger_rolling_over_in_bed]

Table III: Comparison of previous works for the diagnosis of balance disorders

Reference	Results (Accuracy %)				Method	# of features	# of classes	# of cases	Evaluation method
	Vestibular Schwannoma (CPA Acoustic neuroma)	Benign Paroxysmal Positional vertigo	Meniere's Disease	Vestibular Neuritis					
[9]	95.4% (128 cases)	99.5% (59 cases)	94.1% (243 cases)	99.5 (60 cases)	Decision trees (C4.5 and C5.0 algorithms)	123	6	564	10 fold cross validation
[10]	92% (130+1 cases)	88% (147+27 cases)	84% (313+37 cases)	95% (120+37 cases)	Artificial neural networks	38	6	815+116	10 fold cross validation, independent testing
[11]	98% (130 cases)	96% (146 cases)	94% (313 cases)	98% (120 cases)	Bayesian probabilistic models	40	6	815	10 fold cross validation
[12]	78.9% (131 cases)	64.9% (173 cases) 13.8% (80 new cases)	95.9% (350 cases) 78.9% (128 new cases)	80.5% (157 cases) 30% (20 new cases) 66.9-80.5	Expert knowledge, k-nearest neighbours, fitness values optimization	266	9	1030+253	10 fold cross validation, independent testing
[13]	1 vs 1 approach 95% (131 cases) 1 vs all 90.7%	1 vs 1 approach 79% (173 cases) 1 vs all 78.6%	1 vs 1 approach 93.1% (350 cases) 1 vs all 91.5%	1 vs 1 approach 88.2% (157 cases) 1 vs all 85.4%	k-nearest neighbours and support vector machines (1 vs 1 and 1 vs all)	94	9	1030	10 fold cross validation
[14]	-	91.7%	Overall 81.7-88.3%		Clinical knowledge modelled with Dynamic Uncertain Causality Graphs	249	18	60	60 cases for testing
This work	88.2% (34 cases)	82.7% (52 cases)- 87.8% (156 cases)	92.1% (127 cases)	76.4 (89 cases)	Wrapper based feature selection, Adaboost and decision trees (C4.5 algorithm)	350	12	985	10 fold cross validation

Mining Balance Disorders' data for the development of Diagnostic Decision Support Systems

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Abstract— In this work we present the methodology for the development of the EMBalance diagnostic Decision Support System (DSS) for balance disorders. Medical data from patients with balance disorders have been analysed using data mining techniques for the development of the diagnostic DSS. The proposed methodology uses various data, ranging from demographic characteristics to clinical examination, auditory and vestibular tests, in order to provide an accurate diagnosis. The system aims to provide decision support for general practitioners (GPs) and experts in the diagnosis of balance disorders as well as to provide recommendations for the appropriate information and data to be requested at each step of the diagnostic process. Detailed results are provided for the diagnosis of 12 balance disorders, both for GPs and experts. Overall, the reported accuracy ranges from 59.3 to 89.8% for GPs and from 74.3 to 92.1% for experts.

Index Terms—Balance disorders, data mining, decision support systems, vestibular system

I. INTRODUCTION

Human balance requires vision, joint and muscle proprioception and the vestibular system. The integration of the above input and motor output to the visionary and muscle systems are required in order to achieve balance. If one of the three above mentioned systems or their integration fails, this could lead to several different pathologies that can cause balance disorders. The reasons that can cause balance disorders can be many and different [1]. In approximately 5%, the causes are mainly neurological; in 5% are medical; in 15% are psychological; in more than 50% the causes are related to diseases of the inner ear while in the rest 25%, the causes are multiple. Balance disorders can lead to falls [2], which can subsequently lead to other complications

The diagnosis of balance disorders is challenging, sometimes even for the expert otolaryngologists or expert neurologists [3]. A systematic history taking, followed by appropriate clinical examinations chosen on a patient and symptom specific basis are the cornerstones of diagnosis and are tasks where a Decision Support System (DSS) could be of great help, facilitating the diagnostic process, especially for medical practitioners with less expertise in balance disorders such as GPs. Only a few DSS have been developed in the past regarding the diagnosis of vestibular disorders. Mira et. al. [4] proposed an automated diagnosis system, VERTIGO, which is based on rules. CAMISEL is another DSS [5], which is based on a two-step approach for reaching a diagnosis. In the first step, the system suggests a potential diagnosis based on initial evidence, while in the second step the system confirms or rejects the diagnosis, taking into account information from the patient's history and clinical examinations. Galactica is a machine learning approach [6, 7] which learns and develops diagnostic decision rules using data from 564 patients with vertigo, with as primary diagnoses Menière's disease, vestibular schwannoma, traumatic vertigo, sudden deafness, benign paroxysmal positional vertigo (BPPV) and vestibular neuritis. OtoNeurological Expert (ONE) [8,9] developed diagnostic rules using 815 neuro-otology patients, which included the same diagnosis as Galactica and subsequently tested for 1030 cases, including cases with benign recurrent vertigo, vestibulopathia and central lesion. The best total classification accuracies using the combined knowledge bases with machine learning knowledge and experts' knowledge, classified 82.5–84.7% of cases correctly within

the first and second diagnostic suggestion. NetSet has been developed using 815 patient cases with the same primary diagnoses [10]. NetSet showed a sensitivity, specificity, positive predictive value and total accuracy for all six diagnostic classes 85%, 83%, 96% and 95%, respectively.

Miettinen and Juhola [11], employed Bayesian probabilistic models for the diagnosis of six otoneurological diseases. Additional experiments with the ONE diagnostic system were also presented in [12,13], using different machine learning methods, such as the k-nearest neighbor method, the Naïve Bayes classifier and Support Vector Machines. Finally, Dong *et al.* [14] developed a diagnostic system, through dynamic uncertain causality graphs. The graphs were developed using medical knowledge and validated in 60 patient cases, resulting in an average accuracy ranging from 81.7 to 88.3%.

A newly developed diagnostic DSS is part of an integrated system, EMBalance (<http://www.embalance.eu/>), which is a system for the management of patients with balance disorders in terms of diagnosis, treatment and disease evolution. The EMBalance diagnostic platform goes beyond current state of the art in several directions. All previous works focus only on the development of data mining models for classifying patients in different diagnostic categories. The proposed methodology aims to provide a recommendation tool which is able to guide the GPs and experts in requesting the appropriate information for reaching the diagnosis. Another innovative feature of the proposed DSS is that due to the several data mining models developed for each one of the diagnoses, it can provide more than one diagnosis for each patient. An additional benefit of the EMBalance DSS is that while in previous systems, the patients' data used for training and testing the algorithms contained approximately 10-240 features, the EMBalance repository characterizes patients using approximately 350 features. This exhaustive patient characterization coupled with extensive experiments with feature selection algorithms enables the EMBalance DSS to identify the critical information needed for the diagnosis of the different pathologies. Finally, the proposed DSS has two different modules, one for expert use and the other for GP use, which utilize different features which are determined by the access that each of the two groups (GPs and

experts) has to specialized equipment and tests. Previous systems assumed only experts usage, judging on the features used by them for diagnosis.

II. MATERIALS AND METHODS

A. Dataset

Data from 985 patients were collected from the National Hospital of Neurology and Neurosurgery, Queen Square, UK, the 1st Otolaryngology University Clinic of Athens, Greece, the University of Antwerp, Belgium and the University Clinic of Freiburg, Germany. These data contained more than 350 features (variables), including epidemiological information, detailed medical history, disease related history, clinical findings and laboratory examination results (<http://www.embalance.eu/>). Furthermore, detailed information on different balance related types of symptoms together with symptom duration, symptom free intervals, association between symptoms and relevant triggers was collected, since these are important features for the diagnosis of vestibular disorders. It should be noted that in the GP case, only features corresponding to personal disease history, symptoms and clinical examinations were utilized, whereas in the expert case, all the above mentioned features were used. Diagnostic outcomes were classified into more than 100 diagnoses, using the standard ICD10 code, as well as additional, not as yet specified in the ICD code, diagnostic categories based on the Bárány Society proposed International Classification of Vestibular Disorders (see <http://www.jvr-web.org/Barany-feedback.html>). The study has been approved by the respective ethics committees of each Institute according to local/national regulations. Following numerous experiments and detailed analysis and collaboration with medical experts, 12 diagnostic categories shown in Table I, along with the corresponding recommendation for specific features are supported by the proposed DSS. Diagnostic categories with a very small number of patients (i.e. less than 20) were excluded because it was not feasible to be analysed. The proposed DSS is based on the above described dataset and provides diagnosis for 12 different diseases as they are described in Table I.

B. Methods

B1. Training

To develop the DSS for the diagnosis of 12 balance disorders, a three stage methodology was implemented which is shown in Fig. 1. In the first step, preprocessing of the dataset was performed; this included the removal of features with more than 50% missing values and the development of the datasets per class. Due to the large number of target classes (12), 12 different binary classification models have been developed instead of a 12-class classification model. A different dataset was thus prepared per diagnostic category; each dataset per class contained all records from the target class and randomly the same number of records from the rest of the database.

In the second step, feature selection was performed. Two different data mining frameworks have been tested for each diagnostic category (Fig. 1). In the first (upper part of Fig. 1), feature selection was applied separately in each category of features (Personal disease history, symptoms, vertigo-instability symptoms, tinnitus symptoms, clinical examinations, auditory tests, video-nystagmography, questionnaires, vestibular tests, imaging data) and selected features were collected at the end for the diagnostic process. In the second category (lower part of Fig. 1), feature selection was applied in all features from all categories and the optimal subset was used for the diagnostic process. Feature selection was applied on the training set of each diagnostic category (10 times since 10-fold cross validation was used). In our case, we employed feature subset selection methods, that consider the overall set of features collectively, compared to feature ranking methods that assess each feature independently. Further to that, feature subset selection methods can be classified into two categories: the filter [15], where the feature subset selection is independent of the training algorithm and removes irrelevant and high correlated features and the wrapper [16], where the feature subset selection is applied as a wrapper with the training algorithm and the optimal feature subset is identified based on its accuracy with the specific training algorithms.

Finally, in the third step, classification algorithms were applied. The reduced subset of features from the second step is used as input to predict the target class. The best results were obtained using the second data mining framework (overall feature subset selection in all available features) with the combination of wrapper feature

selection (second step) and decision trees enhanced with a boosting algorithm, Adaboost (third step). Wrapper feature selection performs an exhaustive search within the space of available features, targeting the optimization of the accuracy of the selected classification algorithm. Decision trees are one of the most common data mining techniques, employed in several different domains, including clinical applications [9]. A key element of the decision trees that makes their usage appealing in the medical domain is that they can be transformed to rules and provide transparency and interpretation in the decisions made (in contrast for example to neural networks or support vector machines). Given an initial dataset, with instances characterized by features, there are exponentially different decision trees that can be induced. For the development of diagnostic models for each of the diagnoses, decision trees were used as basic models, induced using the C4.5 algorithm. The C4.5 algorithm for decision tree induction creates a tree structure form with nodes, edges and leaves. The nodes correspond to features, the edges to different values or ranges of values of the features of the nodes and the leaves are the decisions of the tree.

In order to identify which feature to have in which node and in which values to divide this feature, the notion of information gain was considered. Details can be found in [17,18]. After the induction of the decision tree, the tree is pruned in order to avoid overfitting in leaves where only a small number of instances applies. Boosting is a procedure performed in an iterative manner and is used to change the distribution of the training instances so that the base classifier, in our case the decision tree induced using the C4.5 algorithm, focuses more on examples that are difficult to classify correctly. Boosting assigns weight to each training instance and then tunes the weight of all instances; instances easily classified receive a reduced weight, while instances not classified correctly receive an increased weight.

The assigned instance weights are then used in the sampling distribution in order to draw a set of bootstrap sample from the original dataset. A specific type of boosting is the algorithm Adaboost, which works as follows: Let $\{(x_j, y_j) | j = 1, 2 \dots N\}$ denote the set of N training instances, where x_j are the features characterizing record j and

y_j is the class. Adaboost assigns different weights in the base classifiers C_i , depending on the error rate of each classifier, given as:

$$\epsilon_i = \frac{1}{N} \left[\sum_{j=1}^N w_j I(C_i(x_j) \neq y_j) \right], \quad (1)$$

where $I(p) = 1$ if part p is true and 0 otherwise. i is the number of base of classifier. The weight of the C_i is given by:

$$a_i = \frac{1}{2} \ln \left(\frac{1-\epsilon_i}{\epsilon_i} \right), \quad (2)$$

which is used to define also the weight of the training instances as follows:

$$w_i^{(j+1)} = \frac{w_i^{(j)}}{Z_j} \times \begin{cases} e^{-a_j} & \text{if } C_j(x_i) = y_i \\ e^{a_j} & \text{if } C_j(x_i) \neq y_i \end{cases}, \quad (3)$$

where Z_j is the normalization factor that ensures that $\sum_i w_i^{(j+1)} = 1$. The weight equation (Eq. 3) increases the weight of the instances classified incorrectly and decreases the weight of those instances that are classified correctly. After the definition of the weights of the instances and of the base classifiers, the classification is performed according to the weight of each base classifier. In this way, base classifiers with low accuracy rate receive less weight and are used less in the classification.

It should be noted that several different combinations of classification schemes were tested prior to the resulting wrapper-decision trees and Adaboost approach. Besides wrapper, also filter based approaches were tested for feature selection. Due to the requirement of the collaborating clinicians and vestibular experts to provide the ability for interpretation for the decisions made, several classification methodologies were not selected (artificial neural networks, support vector machines, k-nearest neighbors) or due to their reduced reported results compared to decision trees and Adaboost (ripper algorithm [19], ridor algorithm [20], naïve Bayes algorithm). Moreover, instead of Adaboost, bagging and random forests were also tested. Additionally, due to the large number of classes, the 12 binary classification models approach was selected compared to the multiclass classification problem. An additional advantage to select binary diagnostic models was the nature of the vestibular diagnosis

problem; several subjects present with more than one pathology at the same time. A multiclass classification setting would not be able to address this requirement and assign two or more classes at the same time for a subject. The utilization of binary diagnostic models allows addressing this, by providing more than one diagnosis at the same time. For the C4.5 algorithm, the initial settings for pruning were set to 0.25 pruning factor and minimum instances per leaf to 5. The second value was tuned in each of the diagnostic categories. Adaboost was set to 10 different iterations and thus resulted in the generation of 10 decision trees per category.

B2. Testing

Fig. 2 shows the diagnostic (test) process which involves: (a) a recommendation tool that guides the GPs and experts in requesting the appropriate information (features), and (b) the diagnostic DSS, which has a different model/tree for each one of the 12 diagnoses. The recommendation system, based on the identified informative features for each diagnosis, recommends to the GP/Expert which parameter, clinical examination, and/or test to request in order to continue the diagnostic process. Specifically, the recommendation system proposes to the GP/Expert the feature identified in the respective path of the decision tree that is needed each time for the continuation of the tree parsing until the diagnosis is reached (Table I).

III. RESULTS

The 10-fold cross validation was used to evaluate the DSS. Sensitivity, specificity, positive predictive value, negative predictive value and accuracy were estimated for each diagnosis. Table II presents the results obtained for each different diagnosis considered, for both GPs and experts (since experts have access to specialized equipment and thus additional information compared to GPs). The first line of the results corresponds to the results obtained for the GPs, while the second line corresponds to the results for the experts. Also, the two columns, Features for GPs, Features for Experts, correspond to the resulting reduced subset of features identified for each diagnosis, for GPs and experts, respectively. This is due to the fact that GPs usually do not have access to the necessary equipment to perform specific tests (e.g. videonystagmography, auditory tests and vestibular tests).

For this reason, the first column (Features for GPs) contains only features made available to the GPs during the diagnostic process. The second column (Features for experts), contains additional features that can be acquired using sophisticated equipment, available only to expert settings. It should be noted that these two DSS modes were obtained and finalized after a series of experiments with different algorithms and different parameters. The reported results range in terms of all metrics in the different diagnoses taken into consideration, as well as, in terms of the features used. Overall, the metrics used for GPs are quite lower from the corresponding results of the experts. This is an expected finding, since the DSS developed for the experts, contains more sophisticated features (audiological and vestibular tests, imaging). When these test features are added, the corresponding metrics, as well as the diagnostic abilities, are improved in almost all cases.

The developed EMBalance DSS addresses the 4 most prevalent balance disorders (Migrainous vertigo, Typical Benign paroxysmal positional vertigo, Vestibular Neuritis and Menière's disease), as well as another 8 less prevalent (Possible Benign paroxysmal positional vertigo, Unilateral Peripheral Dysfunction/Failure, Psychological Disorders, Bilateral Vestibular failure/dysfunction, Cerebellar/Pontine lesion, CPA Acoustic neuroma, Chronic Subjective Dizziness Persistent Postural-Perceptual Dizziness, Vestibular Paroxysmia). For the 4 most prevalent diseases except Vestibular neuritis, quite high results have been reported, both for the GP and expert DSS modules. The best results were reported for Menière's disease, reaching an accuracy of 92.1% for the experts, while the lowest ones were reported for Unilateral Peripheral Dysfunction/Failure, with an accuracy of 59.3% for the GPs.

Based on the different number of records for each of the 12 classes, the classification framework used (feature subset selection, boosting, training of decision trees), required maximum 1 minute (in the case of Migrainous Vertigo, expert model). Regarding the testing time, decision trees are efficient classification structures and the testing time for a new record is negligible.

IV. DISCUSSION

The diagnosis of balance disorders is a difficult task, not only for the GPs but also for the experienced medical professionals which include otolaryngologists, audiovestibular physicians, neurologists, and audiologists. For those lacking the specialised medical training and the long clinical experience, the diagnostic process of vestibular disorders can be fraught with difficulties, and it may not be possible to gather all necessary information or to interpret such information meaningfully in order to conclude in the correct diagnosis. A DSS that would successfully address diagnosis of such disorders would address a significant public health need. The impact of this achievement includes better diagnostic outcomes and consequently improved quality of life for a large patient group, reduction of falls and fall related injuries, equity in health services access and cost reduction via referrals and follow up assessment decrease.

In this work we have presented the EMBalance diagnostic DSS for balance disorders, which includes one GP and one expert module, which reflect the availability of sophisticated tests and equipment in primary vs. secondary/tertiary clinical setups. According to Table II, for the unilateral peripheral dysfunction/failure, the diagnostic accuracy results for the GP mode are quite low. However, the diagnostic accuracy results are increased substantially in the expert module when the audiological test characteristics, which are very informative for unilateral diseases are added to the diagnostic process. Since audiological equipment is usually not available for the GPs, audiometry tests were not taken into consideration in this specific analysis for the GP DSS module. In the case of psychological disorders, the same simple models have been developed both for the GP and for the expert module, taking into consideration anxiety and/or depression validated questionnaire score levels and the existence or not of visual vertigo symptoms. For the Bilateral Vestibular failure/dysfunction case, the same models with quite accurate results have been developed for both GPs and experts, taking into consideration the same simple clinical history and examination features. In the Cerebellar/Pontine lesion case, the addition of vestibular tests improves the results from the GP to expert case, proving that vestibular tests are quite essential for this diagnosis. When considering the cerebellopontine angle (CPA) acoustic neuroma case, in the GP module, the

sensitivity obtained was quite low, which was increased substantially in the expert module, when the results of imaging tests are added. According to the medical expert module results, imaging and especially magnetic resonance imaging (MRI) is required to clearly identify a CPA acoustic neuroma. Nevertheless, in the GP module, results show that even with more easily acquired features, CPA lesions can be identified with satisfactory sensitivity. For Chronic Subjective Dizziness Persistent Postural-Perceptual Dizziness (PPPD), the results for GPs and experts are quite similar. Furthermore, the addition of the Videonystagmography (VNG) caloric test (canal paresis) category (a laboratory examination which is not available to the GPs) increases the accuracy for the identification of this diagnosis. In the vestibular neuritis case, the results are quite low in both modules. Still it can be seen that the addition of the VNG caloric test canal paresis category, improves the results for this diagnosis. In Menière's disease, quite high results are reported both for GPs and experts. Still, the addition of some auditory test results (low frequency 250-500 Hz hearing loss) increases the accuracy of the DSS for Menière's disease. Migrainous vertigo (vestibular migraine) is an important balance disorder, not addressed by most of the previous DSS in the literature [9-13]. For this diagnosis, the same model was developed and used for GP and expert DSS modules.

The diagnostic accuracy results for Vestibular paroxysmia are quite low in the case of the GPs, however those are substantially increased in the expert module, especially with the addition of the imaging results which are a key diagnostic feature for this disorder. Finally, the results for the posterior canal BPPV, both typical and atypical have been presented. The differentiation between typical and atypical BPPV depends on the existence or not of nystagmus in the Dix Hallpike examination. With a positive Dix Hallpike, i.e. typical posterior BPPV, the obtained results are quite satisfactory both for GPs and experts. In the case of the negative Dix Hallpike and the atypical posterior BPPV, the two modules report the same results.

Our work goes beyond the state of the art in many ways: A much more detailed feature vector has been formulated, accounting for more than 350 features including parameters regarding the medical history, symptoms, clinical examinations, audiological and imaging findings, questionnaire and, posturography results. In addition, an

advantage compared to the previously developed DSSs is that the EMBalance diagnostic DSS harnessed several different data mining models with a different model developed for each disease, which allowed the extraction of more than one diagnosis for each patient, since this is often required for patients with balance disorders. Through the decision tree based diagnostic DSSs, the medical professionals are thus able to obtain decision support in two tasks: (i) acquisition of patient's data, through the recommendation tool that has been developed based on the parsing of the decision trees, by requesting the specific features and in the correct order and, (ii) interpretations for the decisions made due to the decision tree based nature. More specifically, for each diagnosis made through the diagnostic decision support system, the corresponding rules that were applied for each patient case are presented to the medical expert.

Table III presents a summary of the current and of previous related works reported in the literature for the diagnosis of balance disorders including detailed accuracy for the common diagnosis (Benign Paroxysmal Positional Vertigo, Vestibular Neuritis and Menière's Disease) and high risk diagnosis (Vestibular Schwannoma-CPA acoustic neuroma). A direct comparison cannot be performed due to the different datasets and different methodologies (ranging from expert systems developed using expert knowledge [12] to more sophisticated modelling of knowledge with dynamic uncertain causality graphs [14], Bayesian networks analysis [11], artificial neural networks [10] etc.) that were employed by the different research groups. However, as it can be seen in Table III, the strength of the EMBalance DSS compared to DSSs presented in the literature include: (i) the number of different features used to inform the diagnostic process, allowing for a more detailed analysis of all available features and identification of the most informative ones per pathology. All previous works started their analysis from a smaller set, not taking into consideration several important features that the proposed DSS and analysis does. (ii) The number of different diagnostic classes considered. The proposed DSS can provide diagnosis for 12 different pathologies. All previous works reach up to 9 pathologies, limiting the exploitation of the DSS by a vestibular expert. An exception is the methodology presented in [14], which, however, was tested in a limited set of 60 patient cases, limiting its credibility in larger populations. Apart from the larger number of classes considered, the proposed DSS can provide simultaneously two or more diagnosis, which is typical for

several patients suffering from vestibular disorders. (iii) The comparable number of patient cases. As it is presented in Table III, the number of patient cases range from 60 to 1283; the 985 cases, using 10-fold cross validation used in our approach allows to consider the reported results credible and the DSS reliable. (iv) The availability of both GP and expert modules. This is an innovative point of the proposed DSS, compared to previous works that consider only usage by experts. In several healthcare systems, GPs are the first point of patient access for diagnosis; the GP mode of the proposed DSS allows GPs to perform the diagnostic process, helping them also during data acquisition.

In the future, the EMBalance DSS will be clinically evaluated in a multi-centre proof of concept clinical trial that will be conducted on a minimum of 200 prospective patients. Additionally, since in some of the diagnostic categories (Bilateral Vestibular failure/dysfunction, CPA Acoustic neuroma, Chronic Subjective Dizziness Persistent Postural-Perceptual Dizziness and Vestibular Paroxysmia), the number of available records was relatively small and the data highly skewed, in the future, when the EMBalance DB increase in terms of samples in these categories, retraining will be performed. Moreover, techniques for oversampling will be tested (e.g. Wilcoxon signed-rank, Friedman's, Iman-Davenport post hoc tests, Synthetic Minority Oversampling Technique) in order to address the relatively small number of records in the specific cases.

V. CONCLUSIONS

A methodology based on data mining techniques (feature selection, boosting algorithms, decision trees) has been employed for the development of a recommendation tool and a diagnostic DSS for 12 balance disorders, to assist GPs and experts, firstly in requesting the necessary information from the patients to reach a potential diagnosis and secondly to support the diagnosis of balance disorders. The reported results in most of the cases are satisfactory and the features used for each diagnosis are in line with clinical knowledge and guidelines. An increase in overall accuracy is presented, from the GP to the expert module, which is attributed to the additional

and more sophisticated features used by the experts. Further application of the diagnostic DSSs in real clinical settings could reveal the potential of the proposed approach.

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Figures and Tables

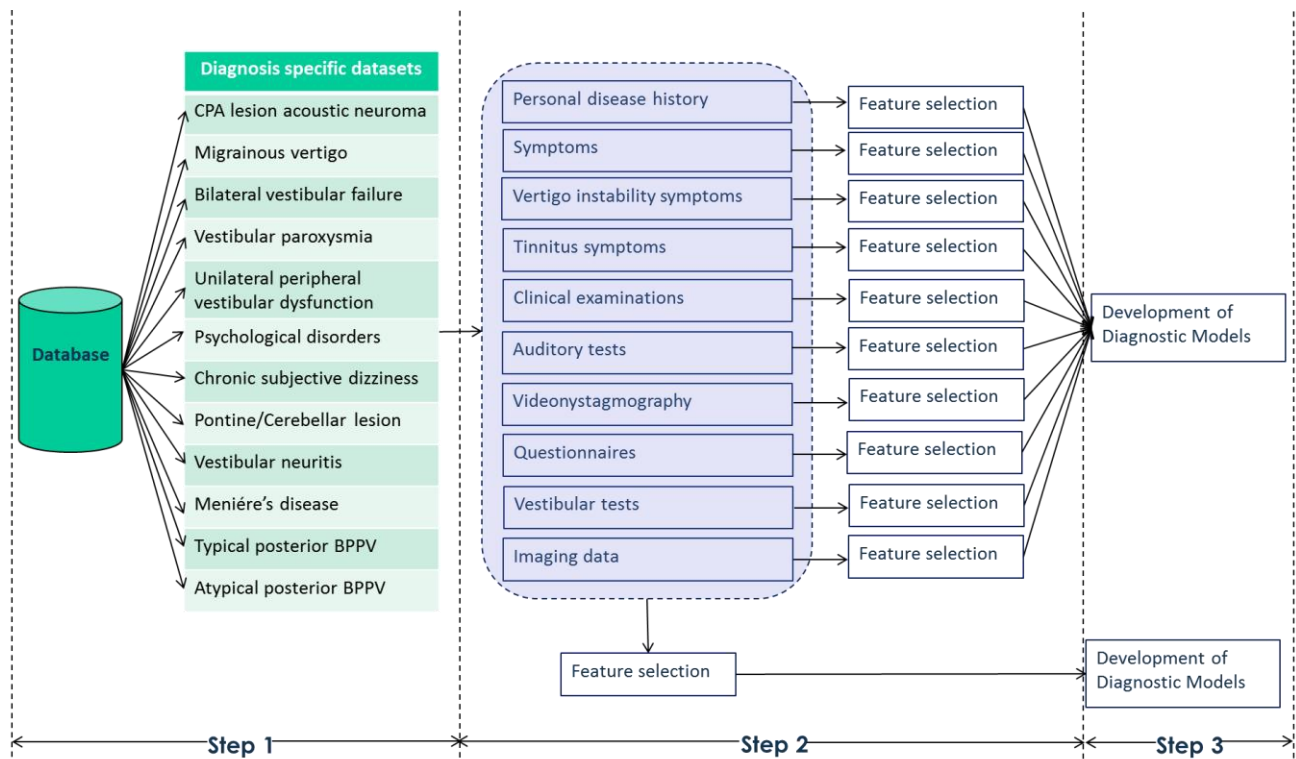


Figure 1: The building blocks of the methodology for developing the diagnostic models. The two data mining frameworks that were used are also shown. In the first, feature selection is applied to each different source of features and then the results are summarized in order to train the classification algorithms for balance disorders.

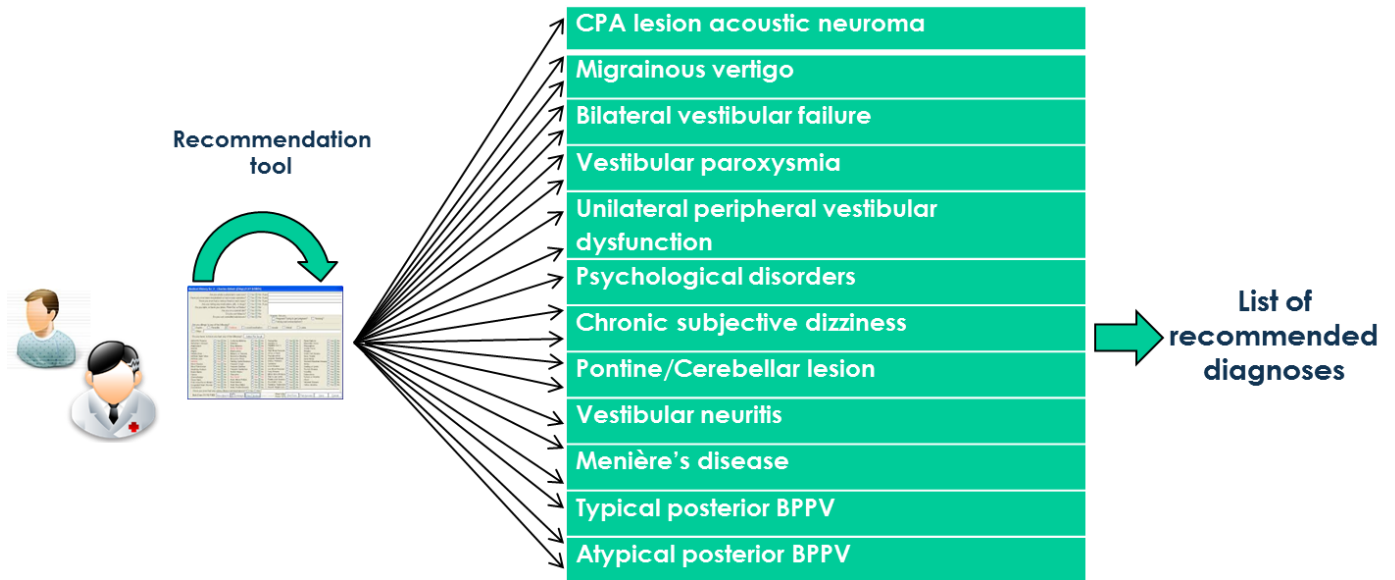


Figure 2: The interaction between the recommendation tool, which utilizes the features encountered in the paths of the decision trees, and the diagnostic decision support system, which is composed by the 12 different decision trees, one for each diagnosis as shown above. The outcome is the list of the recommended diagnosis.

TABLE I: DIAGNOSES CONSIDERED IN THE EMBALANCE DSS AND THE CORRESPONDING NUMBER OF CASES

A/A	Diagnosis	# of cases
1	Unilateral Peripheral Dysfunction/Failure	134
2	Psychological Disorders	40
3	Bilateral Vestibular failure/dysfunction	23
4	Cerebellar/Pontine lesion	43
5	CPA Acoustic neuroma	34
6	Chronic Subjective Dizziness Persistent Postural-Perceptual Dizziness (PPPD)	35
7	Vestibular Neuritis	89
8	Menière's disease	127
9	Migrainous vertigo (Vestibular Migraine)	222
10	Vestibular Paroxysmia	30
11	Typical Posterior Benign Paroxysmal Positional Vertigo (Typical BPPV)	156
12	Possible Posterior Benign Paroxysmal Positional Vertigo (Atypical BPPV) ¹	52
	Total	985

¹ As possible BPPV cases were considered those cases with a consistent history but negative Dix Hallpike examination.

Table II: Results for the 12 different diagnoses in terms of sensitivity, specificity, positive predictive value, negative predictive value accuracy and features used for the GPs and the experts are presented. The first line in the reported results are the measurements for the GPs and the second line for the experts

	SE (%)	SP (%)	PPV (%)	NPV (%)	ACC (%)	Features for GPs	Features for Experts
Unilateral Peripheral Dysfunction/ Failure	58.2	60.4	59.5	59.1	59.3	[patient_sex] [patient_age] [patient_ability_to_work] [patient_smoking] [symptoms_fall] [symptoms_hearing_loss] [symptoms_hearing_loss_evolution] [vertigo_instability_symptoms] [vertigo_instability_symptom_duration_time_interval] [vertigo_symptom_type_bundle_name] [symptom_type_anxiety_and_or_depression] [symptom_type_difficulty_walking_in_darkness] [symptom_type_headache] [symptom_type_tinnitus] [vertigo_trigger_head_movement] [symptom_type_dizziness]	[vestibular_test_sinusoidal_rotation] [auditory_test_PTA_250_AC_right] [auditory_test_PTA_8000_AC_right] [auditory_test_PTA_250_AC_left] [auditory_test_PTA_500_AC_left] [auditory_test_hearing_right_manual] [auditory_test_hearing_left_manual] [caloric_observational_test_canal_paresis_category] [caloric_vng_canal_paresis_category] [questionnaire_dizziness_emotional_subscore] [vertigo_instability_symptom_symptom_type] [symptom_type_anxiety_and_or_depression] [symptom_type_drunk_feeling] [vertigo_trigger_head_movement] [vertigo_trigger_standing_up_rapid_ascents] [symptom_type_dizziness]
	76.1	74.6	75.0	75.8	75.4		
Psychological Disorders	75.0	85.0	83.3	77.3	80	[symptom_type_anxiety_and_or_depression] [symptom_type_visual_vertigo]	[symptom_type_anxiety_and_or_depression] [symptom_type_visual_vertigo]
	75.0	85.0	83.3	77.3	80		
Bilateral Vestibular Failure/ dysfunction	82.6	82.6	82.6	82.6	82.6	[vertigo_instability_symptom_symptom_type] [symptom_type_difficulty_walking_in_darkness] [symptom_type_difficulty_walking_on_uneven_surfaces] [symptom_type_oscillopsia]	[vertigo_instability_symptom_symptom_type] [symptom_type_difficulty_walking_in_darkness] [symptom_type_difficulty_walking_on_uneven_surfaces] [symptom_type_oscillopsia]
	82.6	82.6	82.6	82.6	82.6		
Cerebellar/ Pontine lesion	79.1	79.1	79.1	79.1	79.1	[patient_age] [patient_smoking] [clinical_examination_gaze_test] [clinical_examination_head_thrust] [clinical_examination_romberg] [clinical_examination_gait] [personaldisease_bundle_name] [vertigo_instability_symptom_symptom_type] [vertigo_instability_symptom_duration_time_interval] [vertigo_symptom_type_bundle_name] [symptom_type_drunk_feeling] [symptom_type_headache] [symptom_type_tinnitus] [symptom_type_visual_vertigo]	[clinical_examination_gaze_test] [clinical_examination_head_thrust] [clinical_examination_gait] [vestibular_test_sinusoidal_rotation] [vertigo_instability_symptom_symptom_type] [symptom_type_difficulty_walking_on_uneven_surfaces] [symptom_type_headache] [symptom_type_tinnitus]
	88.4	83.7	84.4	87.8	86.1		
CPA Acoustic neuroma	79.4	91.2	90	81.6	85.3	[clinical_examination_gaze_test] [clinical_examination_head_thrust] [symptoms_hearing_loss] [personaldisease_bundle_name] [tinnitus_symptom_tinnitus_symptom_type] [tinnitus_symptom_frequency] [vertigo_symptom_type_bundle_name] [symptom_type_cervicalgia] [symptom_type_headache] [symptom_type_hearing_loss] [symptom_type_lightheaded] [symptom_type_tinnitus] [vertigo_trigger_head_movement] [vertigo_trigger_rolling_over_in_bed]	[clinical_examination_gaze_test] [clinical_examination_head_thrust] [symptoms_hearing_loss] [personaldisease_bundle_name] [tinnitus_symptom_frequency] [imaging_imaging_result] [personaldisease_bundle_name] [tinnitus_symptom_frequency] [symptom_type_lightheaded] [symptom_type_tinnitus] [vertigo_trigger_head_movement]
	85.3	91.2	90.6	86.1	88.2		
Chronic Subjective Dizziness PPPD	77.1	68.6	71.1	75.0	72.9	[patient_sex] [patient_age] [clinical_examination_head_thrust] [clinical_examination_romberg] [clinical_examination_tandem_gait] [symptoms_hearing_loss] [tinnitus_symptom_tinnitus_symptom_type] [vertigo_instability_symptom_symptom_type] [vertigo_instability_symptom_duration_time_interval] [vertigo_symptom_type_bundle_name] [preceding_event_bundle_name] [symptom_type_headache] [symptom_type_muscle_weakness]	[patient_sex] [clinical_examination_romberg] [clinical_examination_tendency_to_fall] [caloric_vng_canal_paresis_category] [questionnaire_hospital_anxiety_subscore] [symptom_type_anxiety_and_or_depression] [symptom_type_headache] [symptom_type_tinnitus] [symptom_type_dizziness]
	77.1	71.4	73.0	75.8	74.3		

						[symptom_type_phonophobic] [symptom_type_dizziness]	
Vestibular Neuritis	69.7 73.0	74.2 79.8	72.9 78.3	71.0 74.7	71.9 76.4	[vertigo_instability_symptom_symptom_type] [vertigo_instability_symptom_duration_time_interval] [vertigo_instability_symptom_frequency] [vertigo_symptom_type_bundle_name] [preceding_event_bundle_name]	[caloric_vng_canal_paresis_category] [symptoms_hearing_loss] [vertigo_instability_symptom_symptom_type] [vertigo_instability_symptom_duration_time_interval] [vertigo_symptom_type_bundle_name] [vertigo_instability_symptom_frequency] [preceding_event_bundle_name]
Menière's disease	88.2 89.8	91.3 94.5	91.1 94.2	88.5 90.2	89.8 92.1	[symptoms_hearing_loss] [symptoms_hearing_loss_evolution] [vertigo_instability_symptom_duration_time_interval] [vertigo_symptom_type_bundle_name] [symptom_type_dizziness]	[auditory_test_PTA_250_AC_right] [auditory_test_PTA_500_AC_left] [symptoms_hearing_loss] [symptoms_hearing_loss_evolution] [vertigo_instability_symptom_duration_time_interval] [vertigo_symptom_type_bundle_name] [symptom_type_dizziness]
Migrainous vertigo	82.9 82.9	82.9 82.9	82.9 82.9	82.9 82.9	82.9 82.9	[clinical_examination_romberg] [symptoms_hearing_loss] [personaldisease_bundle_name] [tinnitus_symptom_frequency] [vertigo_instability_symptom_symptom_type] [vertigo_instability_symptom_duration_time_interval] [vertigo_symptom_type_bundle_name] [preceding_event_bundle_name] [symptom_type_anxiety_and_or_depression] [symptom_type_cervicalgia] [symptom_type_difficulty_walking_on_uneven_surfaces] [symptom_type_headache] [symptom_type_lightheaded] [symptom_type_phonophobic] [symptom_type_scotoma] [symptom_type_tinnitus] [vertigo_trigger_complex_visual_environments]	[clinical_examination_romberg] [symptoms_hearing_loss] [personaldisease_bundle_name] [tinnitus_symptom_frequency] [vertigo_instability_symptom_symptom_type] [vertigo_instability_symptom_duration_time_interval] [vertigo_symptom_type_bundle_name] [preceding_event_bundle_name] [symptom_type_anxiety_and_or_depression] [symptom_type_cervicalgia] [symptom_type_difficulty_walking_on_uneven_surfaces] [symptom_type_headache] [symptom_type_lightheaded] [symptom_type_phonophobic] [symptom_type_scotoma] [symptom_type_tinnitus] [vertigo_trigger_complex_visual_environments]
Vestibular Paroxysmia	60.0 80.0	76.7 86.7	72.0 85.7	65.7 81.3	68.3 83.3	[personaldisease_bundle_name] [vertigo_instability_symptom_symptom_type] [vertigo_instability_symptom_duration_time_interval] [vertigo_symptom_type_bundle_name]	caloric_vng_directional_preponderance_category] imaging_imaging_result] vertigo_instability_symptom_symptom_type] vertigo_instability_symptom_duration_time_interval] vertigo_symptom_type_bundle_name] preceding_event_bundle_name] symptom_type_hearing_loss] vertigo_trigger_standing_up_rapid_ascents]
Typical Posterior Benign Paroxysmal Positional Vertigo	86.5 86.5	87.8 89.1	87.7 88.8	86.7 86.9	87.2 87.8	[patient_sex] [clinical_examination_dix_hallpike] [personaldisease_bundle_name] [tinnitus_symptom_tinnitus_symptom_type] [vertigo_instability_symptom_symptom_type] [vertigo_instability_symptom_duration_time_interval] [vertigo_symptom_type_bundle_name] [symptom_type_hearing_loss] [symptom_type_motion_sickness] [symptom_type_tinnitus] [vertigo_trigger_head_movement]	[patient_sex] [clinical_examination_dix_hallpike] [vestibular_test_sinusoidal_rotation] [vestibular_test_smooth_pursuit] [caloric_vng_canal_paresis_category] [caloric_vng_directional_preponderance_category] [symptoms_hearing_loss] [symptoms_hearing_loss_evolution] [diagnosed_nystagmus_nystagmus_direction] [personaldisease_bundle_name] [vertigo_instability_symptom_duration_time_interval] [vertigo_symptom_type_bundle_name] [preceding_event_bundle_name] [nystagmus_type_bundle_name] [vertigo_trigger_bending_over] [symptom_type_dizziness]
Atypical posterior Benign Paroxysmal Positional Vertigo	82.7 82.7	82.7 82.7	82.7 82.7	82.7 82.7	82.7 82.7	[patient_sex] [clinical_examination_dix_hallpike] [vertigo_instability_symptom_symptom_type] [vertigo_instability_symptom_duration_time_interval] [vertigo_symptom_type_bundle_name] [vertigo_trigger_bending_over] [vertigo_trigger_rolling_over_in_bed]	[patient_sex] [clinical_examination_dix_hallpike] [vertigo_instability_symptom_symptom_type] [vertigo_instability_symptom_duration_time_interval] [vertigo_symptom_type_bundle_name] [vertigo_trigger_bending_over] [vertigo_trigger_rolling_over_in_bed]

Table III: Comparison of previous works for the diagnosis of balance disorders

Reference	Results (Accuracy %)				Method	# of features	# of classes	# of cases	Evaluation method
	Vestibular Schwannoma (CPA Acoustic neuroma)	Benign Paroxysmal Positional vertigo	Meniere's Disease	Vestibular Neuritis					
[9]	95.4% (128 cases)	99.5% (59 cases)	94.1% (243 cases)	99.5 (60 cases)	Decision trees (C4.5 and C5.0 algorithms)	123	6	564	10 fold cross validation
[10]	92% (130+1 cases)	88% (147+27 cases)	84% (313+37 cases)	95% (120+37 cases)	Artificial neural networks	38	6	815+116	10 fold cross validation, independent testing
[11]	98% (130 cases)	96% (146 cases)	94% (313 cases)	98% (120 cases)	Bayesian probabilistic models	40	6	815	10 fold cross validation
[12]	78.9% (131 cases)	64.9% (173 cases) 13.8% (80 new cases)	95.9% (350 cases) 78.9% (128 new cases)	80.5% (157 cases) 30% (20 new cases) 66.9-80.5	Expert knowledge, k-nearest neighbours, fitness values optimization	266	9	1030+253	10 fold cross validation, independent testing
[13]	1 vs 1 approach 95% (131 cases) 1 vs all 90.7%	1 vs 1 approach 79% (173 cases) 1 vs all 78.6%	1 vs 1 approach 93.1% (350 cases) 1 vs all 91.5%	1 vs 1 approach 88.2% (157 cases) 1 vs all 85.4%	k-nearest neighbours and support vector machines (1 vs 1 and 1 vs all)	94	9	1030	10 fold cross validation
[14]	-	91.7%	Overall 81.7-88.3%		Clinical knowledge modelled with Dynamic Uncertain Causality Graphs	249	18	60	60 cases for testing
This work	88.2% (34 cases)	82.7% (52 cases)- 87.8% (156 cases)	92.1% (127 cases)	76.4 (89 cases)	Wrapper based feature selection, Adaboost and decision trees (C4.5 algorithm)	350	12	985	10 fold cross validation