Development of diagnostic model through Analysis of Nystagmus in Patients with Dizziness

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Development of diagnostic model through Analysis of Nystagmus in Patients with Dizziness

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ABSTRACT

Development of Diagnostic Model through Analysis of Nystagmus in Patients with Dizziness

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Purpose

We assessed whether the interpreting and analysis of video nystagmus using our coordinate extraction algorithm and machine learning could screen the vertigo patients.

Methods

We analyzed 1064 of video nystagmus recorded from 842 patients in our clinical data warehouse. All videos are reviewed and annotated with the diagnosis by two otologic experts. We used our nystagmus analysis algorithm and extracted coordinates from each nystagmus in the video. The nystagmus is classified following sets; 1) normal, 2) acute vestibular syndrome (AVS), 3) posterior canal benign paroxysmal positional vertigo (BPPV), 4) geotropic horizontal canal BPPV, 5) apogeotropic horizontal canal BPPV, and 6) anterior canal BPPV. The distributions from all coordinate sets were analyzed using machine learning, including logistic regression (LR), decision tree, bagging, boosting, random forest (RF), and deep neural network (DNN) to assess positive prediction value and prediction accuracy.

Results

The mean age of 842 patients was 57.8±14.6, and the male/female ratio was 314:528. The LR model for prediction as normal or disease showed 72.3% of accuracy. The RF and DNN models for classification as each nystagmus showed high accuracy (98.2%, 97.4%). However, when analyzing the type of disease, the accuracy of all models was low.

Conclusions

The deep learning model for the diagnosis of dizziness showed excellent

performance in our study. As our machine-learning model has high accuracy, it has broad clinical applicability to screening patients with vertigo even in primary care clinical practice.

Keywords: Sound localization, Spatial hearing, questionnaire, psychometric, validation

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I. INTRODUCTION

Dizziness affects about 15% to 20% of adults per year in large population studies. Peripheral vertigo accounts for about a quarter of dizziness complaints and has 5% of 12-month prevalence and 1.4% of annual incidence. It is more common in women than in men.

Taking a systematic history and performing physical examination including nystagmus tests are essential to diagnosis dizziness. When the clinician meets dizziness patients, they should ask the patients carefully about dizziness and distinguish the dizziness symptom: 1) vertigo, 2) disequilibrium, 3) light-headedness, and 4) presyncope. Among the many diseases that can lead to dizziness, Benign paroxysmal peripheral vertigo (BPPV), vestibular neuritis, vestibular migraine, and Meniere's disease are common causes of vertigo, and they could be diagnosed through history and characteristic their nystagmus in most cases.

However, it is difficult to identify the characteristic nystagmus and diagnose dizziness for a general clinician who is not well trained in dizziness disease. In one report, 65% of dizziness patients were performed unnecessary tests including computed tomography (CT) and magnetic resonance imaging (MRI) in the emergency room; even they showed critical nystagmus to diagnose BPPV. It is known that asking questions about dizziness and completing focused physical examination tests is more accurate than performing CT or MRI. Thus, inadequate testing and interventions for dizziness patients can lead to wasted overall medical expenses and inconvenience to patients.

In recent years, deep learning methods have been used in medical sciences. They can help clinicians diagnose abnormal lesions in radiologic or pathological images, and their accuracy is quite high, at 98 to 99%. Using deep learning in medical science still has many limitations. It can even help clinicians who are not experts in a specific field to make decisions similar to experts.

We focused on the advantages of deep learning and assessed that the deep learning methods could automatically analyze the nystagmus to help clinicians diagnose dizziness. The nystagmus analysis should be performed through the nystagmus videos and needs several steps, including detecting and tracking the eyeball in the nystagmus videos. Several groups reported the mathematical methods to analyze the nystagmus videos. However, the mathematical techniques have some distance from the clinical way.

Therefore, we assess how well the deep learning method analyzes the nystagmus and helps the clinicians diagnose dizziness disease, especially in the clinical way.

II. MATERIALS AND METHODS

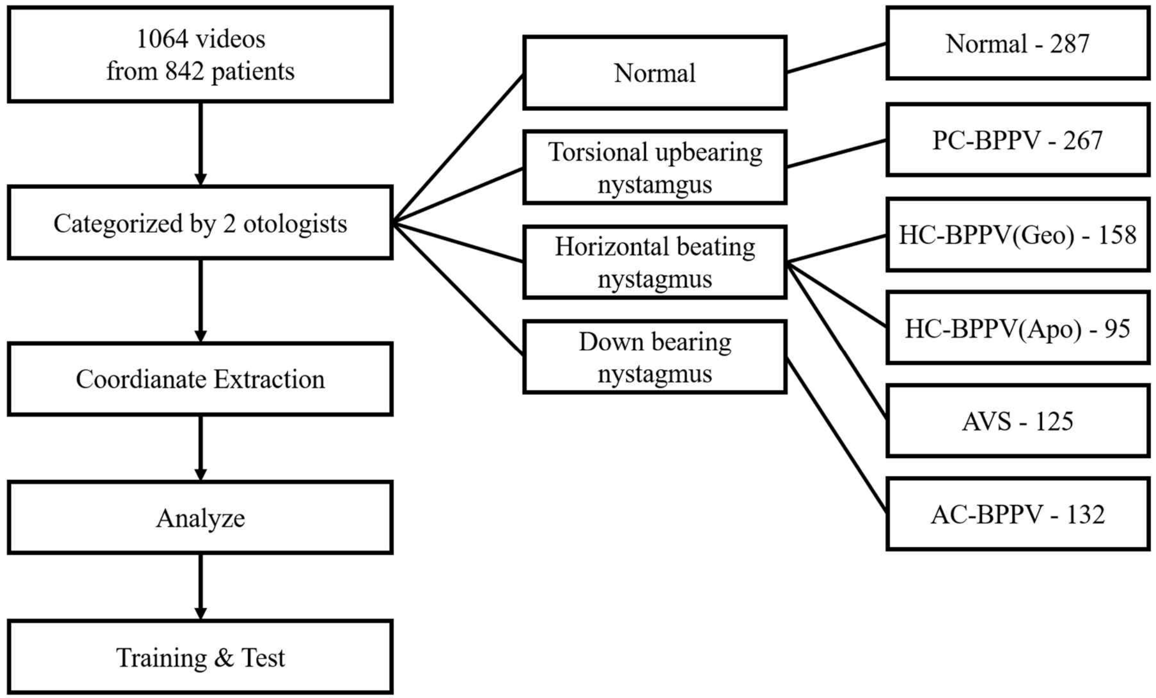
1. Data Collection

I performed a retrospective study in the dizziness clinic of a single tertial referral hospital. We reviewed 1064 videos from 842 patients in our data warehouse. The videos were collected from patients who visited our hospital and were performed serial tests for checking nystagmus. We used the video Frenzel goggle (SLMED, Seoul, Korea) when we assessed nystagmus. All patients were performed following serial tests using the video Frenzel goggle system to evaluate the pathological nystagmus; spontaneous nystagmus, gaze nystagmus, Dix-Hallpike test, Supine head roll test, and head-shaking test.

Two different otologists each reviewed all 1064 videos and checked each other. They were labeled as following categories; 1) normal, 2) posterior canal benign paroxysmal positional vertigo (PC-BPPV), 3) geotropic horizontal canal benign paroxysmal positional vertigo [HC-BPPV(Geo)], 4) apogeotropic horizontal canal benign paroxysmal positional vertigo [HC-BPPV(Apo)], 5) anterior canal horizontal canal benign paroxysmal positional vertigo (AC-BPPV) and 6) Acute vestibular syndrome (AVS). (Figure 1)

All labels were applied following the type of nystagmus that showed from positional tests. The Institutional Review Board of our institute approved this study in the following announcement with Helsinki's Declaration (CR319082).

Figure 1. Schematic diagram of study flows.



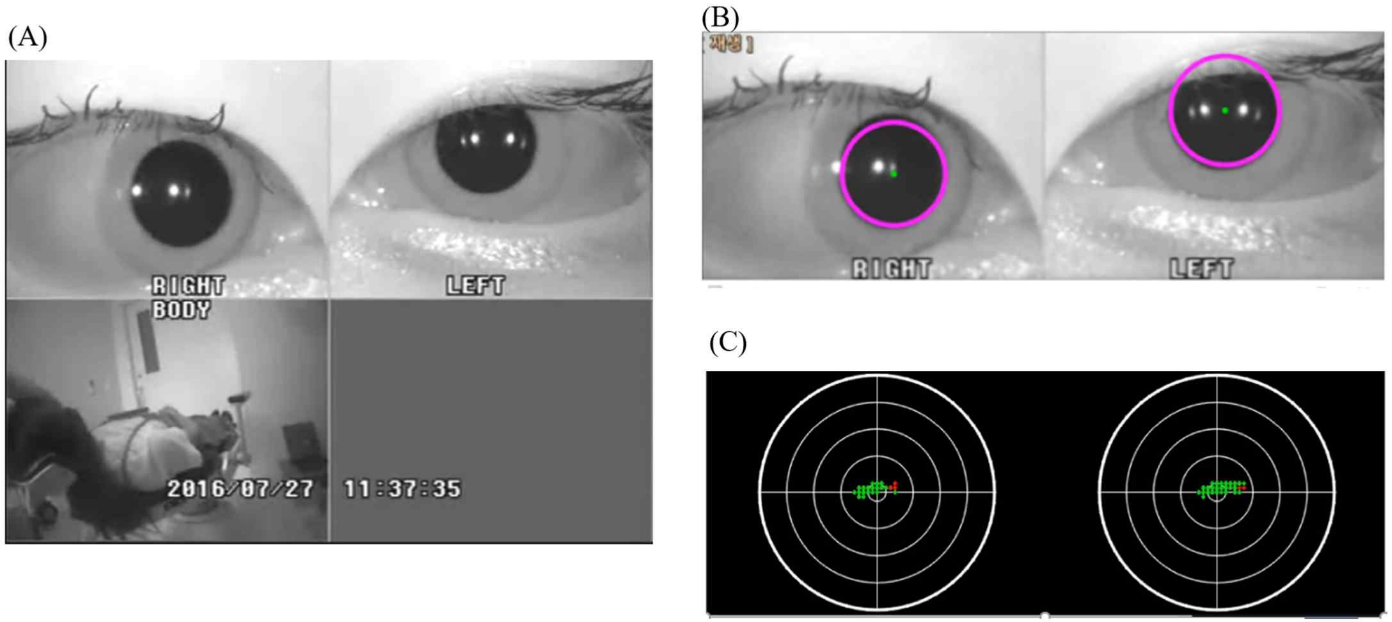
2. Eyeball detection and tracking algorithm

We used an algorithm that detects and tracks pupils in videos developed in the Biomedical engineering laboratory at Yonsei University. The algorithm was designed to be optimized for analyzing our nystagmus videos. All nystagmus videos produced by our video Frenzel goggle system were based on NIR-CCD and sized 640 x 480 with 30 frames/sec. (Figure 2A) For eyeball detection, the regions of interest (ROI) were pupils. The algorithm includes the processes of thresholding, morphology operation, and residual noise filtering stages.

The thresholding technique in our algorithm is global thresholding with a single threshold value. Because our nystagmus videos were based on NIR-CCD in the dark, the dark condition can suppress the environmental noise factors. The erosion and dilation technique was used for the morphology operation in our algorithm. The morphology operation used in our algorithm allows detection of the pupil by removing sclera from the eyeball in the videos and differentiating between the thresholds of iris and pupil. After thresholding and morphological transformation, the component-connected labeling (CCL) was applied for residual noise filtering. The principle of CCL is based on grouping the adjacent pixels into the same ROI and pixels in other ROI into different labels. Through the CCL, we can obtain a smooth boundary of the pupil that minimizes the noise from the pupil's adjacency structure, including eyelids or eyelashes. (Figure 2B)

After image processing, coordinate extraction from the pupil was performed. Following the pupil detection and tracking algorithm described above, the coordinates were extracted using the center of the pupil as a target. For the coordinates, the left eye and the right eye were separately extracted, and the left-bottom of each eye in the videos was used as a reference. (Figure 2C) Our algorithm can track and accumulate the 30 coordinated per second, following the nystagmus videos as 30 frames/sec. The algorithm was developed, and the stability of the algorithm was verified by Professor Key's laboratory of Biomedical Engineering in the Department of Biomedical Engineering, Yonsei University.

Figure 2. The algorithm for pupil detection and tracking. (A) A example nystagmus video clip sized 640 x 480 with 30 frames/sec. (B) Detection of pupil through the algorithm. (C) Accumulating coordinated from center of pupils.



3. Coordinate extraction from nystagmus videos

We extracted the coordinates from 1064 nystagmus videos obtained from 842 patients using the algorithm mentioned above. All 1064 videos consist of more than 10 seconds where nystagmus was observed. Using our algorithm, we can get more than 300 accumulated coordinates from each video. The accumulated coordinates refer to the position where the center pupil has moved during the video playback time. We can infer the vector and the speed at which the pupil moves in the nystagmus. The extracted coordinates were categorized according to the diagnosis of disease labeled on the video by two otologists as described above.

4. Data preprocessing

Since the accumulated coordinates are made by the tracking nystagmus, a continuous eyeball movement, the coordinate set must be made continuous. However, there were cases with outliers in separate locations. (Figure 3A) Most outliers were produced when performing a positional test while wearing our video Frenzel goggle, the goggle was suddenly moved, or the patient moved his eye voluntarily in the dark field wearing the goggle.

We decided on a uniform method to remove outliers from the accumulated coordinates as conventional methods. The outlier is defined as coordinates at more than 1.5 times of interquartile ranges (IQRs) below the first quartile or above the third quartile. After removing the outliers, we were able to obtain more refined data. (Figure 3B, Figure 4) Machine learning was performed using positional information when the nystagmus was shown and representative values reflecting the distribution of coordinates as data including mean, median, mode, range, IQR, minimum, maximum, variance, standard deviation, and correlation coefficient.

Figure 3. An example of outlier detection and removal. All outliers were removed collectively as the the outlier is defined as coordinates that are at more than 1.5 times of interquartile ranges (IQRs) below the first quartile or above the third quartile. We simulated outlier removal rules by randomly picking about 100 coordinates. (A) An example of simulating outlier removal. (B) Sample data before the outliers were removed. (C) Sample data after the outliers were removed.

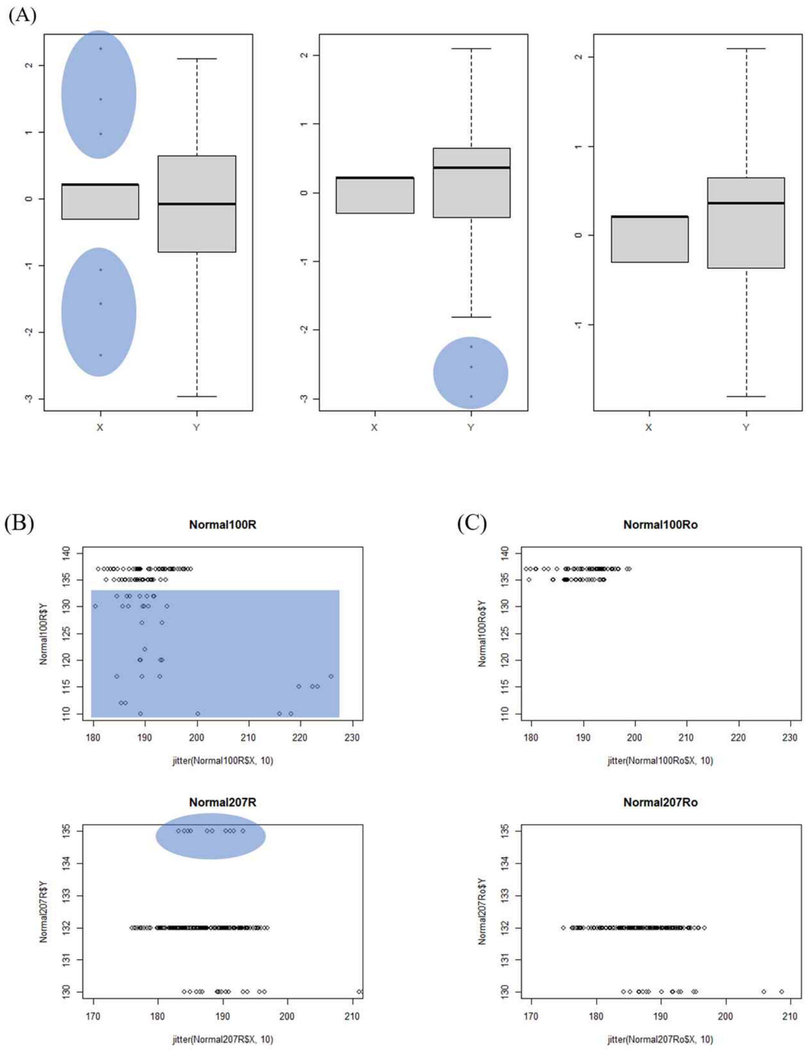
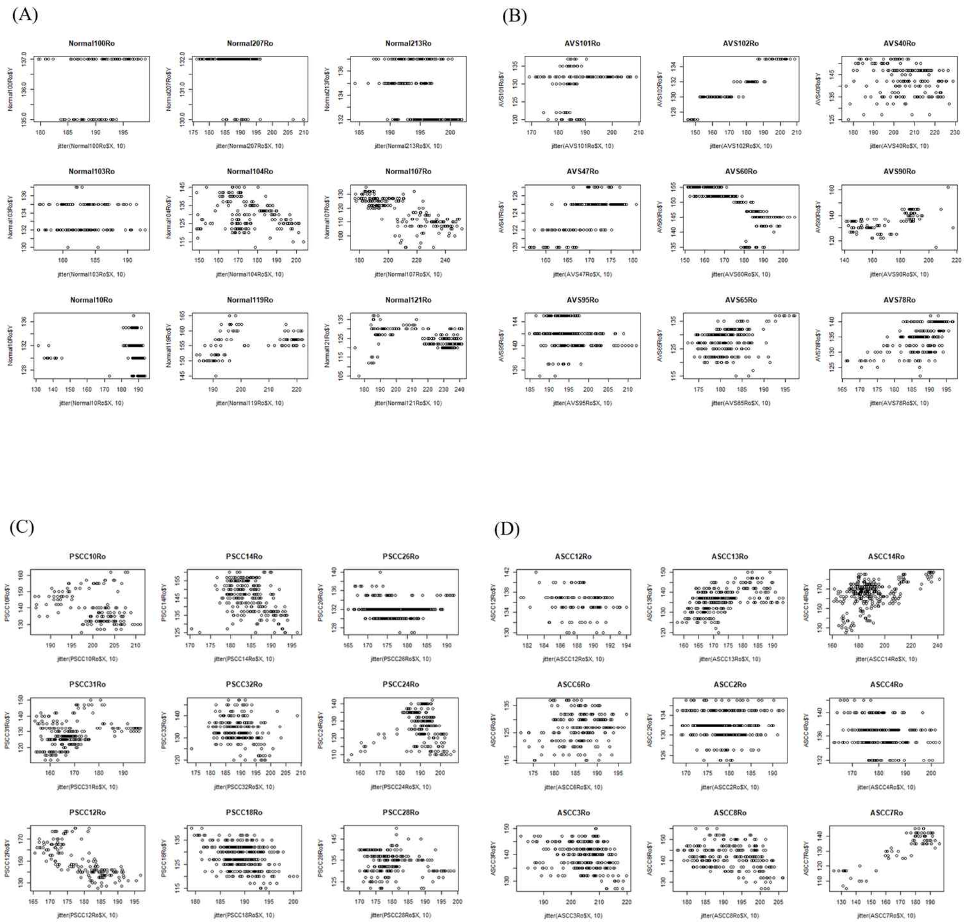


Figure 4. Examples of coordinates of each type of nystagmus. There are (A) normal, (B) horizontal beating nystagmus, (C) torsional upbeating nystagmus, and (D) down beating nystagmus. Outliers of each coordinate were removed, and duplicated coordinates are displayed using the jitter option.



5. Statistical analysis

We performed machine learning models of logistic regression (LR), decision tree, bagging, boosting, random forest, and deep neural network (DNN). All datasets were randomly divided by 7:3 to training data and validation data. The performance ability of machine learning was evaluated through the accuracy and positive predictive value (PPV), and the formula is as follows.

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

$$Positive \quad predictive \quad value = \frac{TP}{TP + FP}$$

(TP = true positive, TN = true negative, FP = false positive, FN = false negative)

The area under the curve (AUC) of the receiver operating characteristic (ROC) was calculated to measure the performance ability in each model's proper cutoff values. All statistical analysis was performed using R software (v. 4.0.0) and Rstudio 1.2.5 for Windows with the packages of rpart, adabag, randomForest, and neuralnet.

III. RESULTS

1. Clinical characteristics of dizziness patient

Among the total 842 patients, the mean age was 57.8 years and ranged from 19 to 84 years, with 314 males and 528 females. 232 of 842 (27.6%) showed no nystagmus during the serial tests, which mean normal, 206 (24.5%) were PC-BPPV, 122 (14.5%) were HC-BPPV(Geo), 73 were HC-BPPV(Apo), 102 (12.1%) were AC-BPPV, and 117 (13.9%) were AVS. (Table 1)

Among the total 1064 nystagmus from 842 patients, 287 videos showed no nystagmus as normal, 267 showed torsional upbeating nystagmus during Dix-hallpike test (DHT) as PC-BPPV, 158 showed geotropic direction-changing positional nystagmus (DCPN) in supine head roll test (SRT) as HC-BPPV(Geo), 95 were showed apogeotropic DCPN in SRT as HC-BPPV(Apo), 132 showed down beating nystagmus in DHT as AC-BPPV and 125 showed the characteristic nystagmus of AVS. (Figure 1)

Table 1. Clinical characteristics of dizziness patients

	Total (n=842)
Age (days, mean±SD)	57.8± 14.6
Sex (Male : Female)	314 : 528
Diagnosis	
Normal	232 (27.6%)
PC-BPPV	206 (24.5%)
HC-BPPV(Geo)	122 (14.5%)
HC-BPPV(Apo)	73 (8.7%)
AC-BPPV	102 (12.1%)
AVS	117 (13.9%)

2. The performance of machine learning models

The LR model was fitted by dividing into two groups, normal and abnormal, using representative values reflecting the distribution of coordinates. After fitting the LR model, model selection was performed according to stepwise selection. We selected the model with the smallest Akaike information criterion (AIC) value as the most suitable model. Following our model, the PPV was 72.3%, accuracy was 82.3% AUC was 72.3%. (Figure 5A)

We performed further machine learning models categorized by type of nystagmus, including decision tree, Bagging, Adaboost, random forest, and DNN model. Among them, 2 of the best performing models for differential diagnosis of dizziness were the DNN model with 98.6% of PPV, 97.4% accuracy and 99.1% of AUC, and a random forest model with 99.8% of PPV, 98.2% of accuracy, and 98.7% of AUC. (Table 2) However, the decision tree, the Bagging model and the Adaboot model showed low performance. We could observe the a few of top important variables used to fit both the Bagging model and the Adaboost model through the importance plots. (Figure 5B to 5E) However, they could not explain why the variables are important to fit both models.

When we divided by the type of disease of dizziness, the best performance model of the decision tree model showed the lowest performance with 61.3% of PPV, 63.7% of accuracy, and 60.1% of AUC.

Figure 5. The results of Machine learning models. (A) ROC curves of logistic regression model with 72.3% of AUC. (B) Decision tree model when nystagmus videos were categorized by type of disease, with 60.1% of AUC. (C) The importance plot indicates what variable were considered in the (C) Bagging model and the (D) Adaboost model. (E) The random forest model can show how many decision trees were needed to fit a model with good performance.

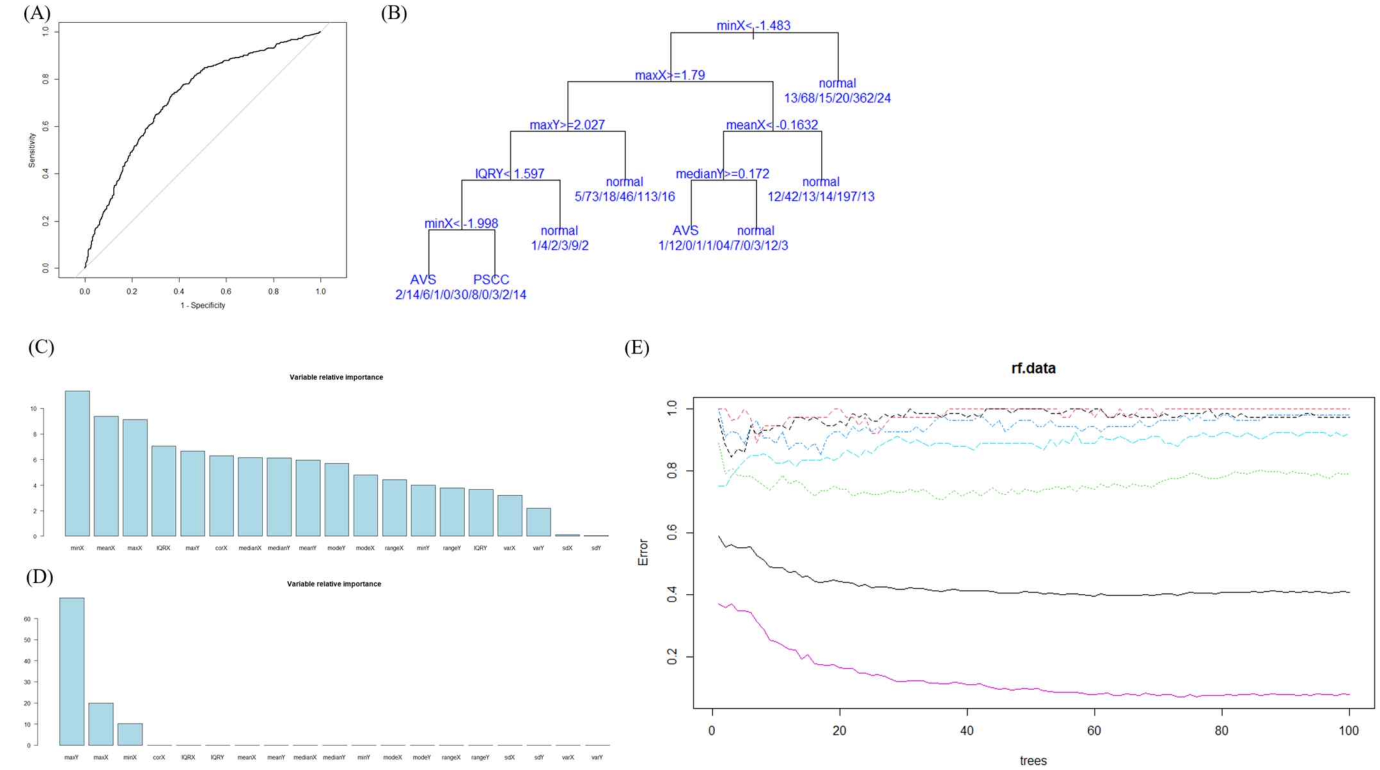


Table 2. The performance abilities of machine learning models.

	Decision Tree	**Bagging**	**AdaBoosting**	**Random Forest**	**DNN**
Positive predictive Value	62.0%	82.7%	20.3%	**99.8%**	**98.6%**
Accuracy	61.4%	83.4%	19.8%	**98.2%**	**97.4%**
AUC	63.5%	81.5%	18.5%	**98.7%**	**99.1%**

Bagging = Bootstrap aggrrgating, AdaBoosting = Adaptive boosting, DNN = Deep neural network, AUC = Area under the curve

IV. DISCUSSION

Our deep learning model to identify the type of nystagmus and differential diagnoses dizziness shows high PPV, accuracy, and AUC, although it differs depending on the type model. Physiologically, many factors, including the vestibule, brain stem, cerebellum, and proprioception, work in combination to maintain balance. The vestibulo-ocular reflex, one of the essential principles that make humans keep balanced, works a key role in diagnosing dizziness. Nystagmus occurs even if a problem occurs in any part from the vestibular organ labyrinth, through the vestibular nerve and the vestibular nucleus of the brain stem, to the vestibular area of the cerebral cortex. Most peripheral vertigo and be diagnosed from history and characteristic pattern nystagmus. Therefore, using our model can help clinicians identify characteristic nystagmus and diagnose dizziness.

Studies to extract and analyze nystagmus as a mathematical method have been carried out for a long time. Those studies had a technique of analyzing nystagmus by converting it into electrical signals (electronystagmography, ENG) or by converting nystagmus into video as it is (videonystagmography, VNG). To analyze nystagmus, the number of video frames needed to be sufficient to track the rapid movement of the eyeball well. In the case of ENG, the nystagmus can analyze by the continuous gathering of electrical signals of contraction and relaxation from the extraocular muscles. However, in VNG, it was necessary to acquire a video with enough frames per second to catch the rapid movement of the eyeball. Wierts et al. analyzed the saccade movement, the fastest movement of eye movement, and reported that 50Hz video was sufficient.

In addition to the method of acquiring nystagmus, there was another issue with the eye movement itself. Since the eyeball movement was not 2-dimensional but 3-dimensional, techniques are required to accurately detect torsional nystagmus in addition to horizontal and vertical nystagmus. Some groups analyzed the movement of the eyeball using a three-dimensional axis, and another group examined some ROI of the anatomical structures of the eyeball. Pupil and iris are common anatomical landmarks to measure the eyeball movements. In the case of the iris, there was a method of detecting the ROI of the iris and analyzing according to nystagmus and a way of detecting the iris and analyzing by the polar transformation. However, these methods were tracking and analyzing the nystagmus indirectly. We thought that detecting the pupil and tracking it without any processing reflect the eyeball movement directly. Moreover, the detection and tracking of the pupil are easier than iris as well. The method that detecting and tracking the center of the pupil and building up coordinates is the most direct way to track the eyeball movements as nystagmus.

Since machine learning was applied to medicine, some reports utilized machine learning to diagnose dizziness. Lim et al. analyzed nystagmus of BPPV patients and reported about 78 to 91% accuracy using their deep-learning models. Since they analyzed the only nystagmus obtained from BPPV patients, they analyzed using classification by type of nystagmus, not by disease classification. The accuracy for torsional nystagmus was lowest at 78%, which was a limitation of their study. Dong et al. proposed a dynamic, uncertain causality graph for differential diagnosis of BPPV. The mathematical method showed good performance, but there were limitations in that it was limited to BPPV and not clinical. Punuganti et al. reported automatic detection of quick phase of nystagmus. However, it was a method of analyzing the slope of the graph obtained from ENG, not directly analyzing nystagmus.

We detected and tracked the center of the pupil in the nystagmus videos to obtain data by accumulating coordinates, and analyzed it, which is the closest to the clinical method of diagnosing dizziness according to the characteristics of nystagmus. Our machine learning model distinguished the types of nystagmus (horizontal, torsional, down beating nystagmus). However, it could not categorize the same types of horizontal beating nystagmus into AVS, HC-BPPV(Geo), and HC-BPPV(Apo). Typically, AVS shows horizontal beating nystagmus with constant amplitude and velocity. However, HC-BPPV(Geo) has a characteristic that the horizontal nystagmus with acceleration and deceleration phase appears less than 1 minute after latency for several seconds in SRT. In the case of HC-BPPV(Geo), the horizontal nystagmus is shown as well. However, it appears upon performing the SRT without latency and lasts over 1 minute. It means that simple accumulation and analysis of coordinated of nystagmus cannot be used to distinguish in detail the characteristics of nystagmus having the same vector and amplitude. Therefore, to analyze this, it is considered that further studies should be performed with additional information such as the relationship between the speed and position coordinates of nystagmus accumulating over time, or the nystagmus was showed in which positional tests.

V. CONCLUSION

Our deep learning model of random forest and DNN were the best-performing model with high PPV and accuracy enough to distinguish the nystagmus shown in patients with dizziness. Our deep learning model using coordinates extracted from the pupil in the nystagmus video could categorize the type of nystagmus. Additional studies are needed to analyze with information, including when the nystagmus showed during serial positional tests. We hope that our model can be used in general practice to screen dizziness patients and reduce wasted overall medical expenses and unnecessary inconvenience to patients.

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ABSTRACT IN KOREAN (국문요약)

어지럼증 환자의 안진 영상 분석을 통한 진단 모델 개빨

< 지도교수 서영준 >

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성 명 공 태 훈

목적: 어지럼증 환자에서 진단에 사용되는 안진은 잘 훈련된 전문의사에 의해서만 수행되므로 일차 진료의에게는 어려운 일이다. 안진 영성 분석과 딥러닝 방법을 결합하여 안진 영상에서 어지럼증을 진단하기 한 능력을 평가하고자 한다.

대상 및 방법: 842명의 피험자에게서 추출한 1064개의 안진영상을 확보하여 이비인후과의 이과 전문의사에 의해 영상을 진단명 및 안진의 유형에 따라 분류하였다. 영상 전처리 알고리즘, 안구 감지 및 트랙킹 알고리즘, 좌표 추출 알고리즘을 결합한 일련의 알고리즘을 이용하여 안구의 위치과 움직임을 추적하고 이를 좌표로 누적한 데이터를 얻었다. 형성된 데이터를 머신러닝 모델에 적합하여 각 머신러닝 모델의 성능을 평가하였다. 머신러닝에 사용된 방법은 로짓모형, 나무모형, 배깅, 부스팅, 랜덤

포레스트, 딥 신경망 모형이다.

결과: 안진 영상을 안진의 종류별로 분류하여 딥러닝 모델이 적합하였을 때 신경망 모형 및 랜덤 포레스트 모형에서 97.4%에서 98.2%로 높은 성능이 관찰되었으며 안진영상을 어지럼증 질환의 종류별로 분류하였을때는 높은 성능을 보이지 않았다.

결론: 안진 영상 분석 알고리즘과 여기서 추출된 좌표 데이터들을 머신러닝을 활용하여 안진의 종류별로 질환을 스크리닝 할 수 있는 높은 성능을 보이는 모델을 적합할 수 있었다. 향후 일차의료에서 어지럼증 환자에서 관찰되는 안진을 스크리닝하고 어지럼증을 조기에 진단하며, 이는 어지럼증 관련 총 의료지 지출 감소와 불필요한 불편을 줄일 수 있다.

핵심되는 말: 안진, 현훈, 어지럼증, 머신러닝, 진단

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