CEO Clinical and Experimental Otorhinolaryngology Vol. 13, No. 4: 326-339, November 2020 https://doi.org/10.21053/ceo.2020.00654
pISSN 1976-8710 eISSN 2005-0720

Review

Recent Advances in the Application of Artificial Intelligence in Otorhinolaryngology-Head and Neck Surgery

Bayu Adhi Tama[1,*] · Do Hyun Kim[2,*] · Gyuwon Kim[1] · Soo Whan Kim[2] · Seungchul Lee[1,3]

[1]Department of Mechanical Engineering, Pohang University of Science and Technology, Pohang; [2]Department of Otolaryngology-Head and Neck Surgery, Seoul St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Seoul; [3]Graduate School of Artificial Intelligence, Pohang University of Science and Technology, Pohang, Korea

This study presents an up-to-date survey of the use of artificial intelligence (AI) in the field of otorhinolaryngology, considering opportunities, research challenges, and research directions. We searched PubMed, the Cochrane Central Register of Controlled Trials, Embase, and the Web of Science. We initially retrieved 458 articles. The exclusion of non-English publications and duplicates yielded a total of 90 remaining studies. These 90 studies were divided into those analyzing medical images, voice, medical devices, and clinical diagnoses and treatments. Most studies (42.2%, 38/90) used AI for image-based analysis, followed by clinical diagnoses and treatments (24 studies). Each of the remaining two subcategories included 14 studies. Machine learning and deep learning have been extensively applied in the field of otorhinolaryngology. However, the performance of AI models varies and research challenges remain.

Keywords. *Artificial Intelligence; Machine Learning; Deep Learning; Otorhinolaryngology*

INTRODUCTION

Artificial intelligence (AI) refers to the ability of machines to mimic human intelligence without explicit programming; AI can solve tasks that require complex decision-making [1,2]. Recent advances in computing power and big data handling have encouraged the use of AI to aid or substitute for conventional approaches. The results of AI applications are promising, and have attracted the attention of researchers and practitioners. In 2015, some AI applications began to outperform human intelligence: ResNet performed better than humans in the ImageNet Large Scale Visual Recognition Competition 2015 [3], and AlphaGo became the first computer Go program to beat a professional Go player in October 2015 [4]. Such technical advances have promising implications for medical applications, particularly because the amount of medical data is doubling every 73 days in 2020 [5]. As such, it is expected that AI will revolutionize healthcare because of its ability to handle data at a massive scale. Currently, AI-based medical platforms support diagnosis, treatment, and prognostic assessments at many healthcare facilities worldwide. The applications of AI include drug development, patient monitoring, and personalized treatment. For example, IBM Watson is a pioneering AI-based medical technology platform used by over 230 organizations worldwide. IBM Watson has consistently outperformed humans in several case studies. In 2016, IBM Watson diagnosed a rare form of leukemia by referring to a dataset of 20 million oncology records [6]. It is clear that the use of AI will fundamentally revolutionize medicine. Frost and Sullivan (a research company) forecast that AI will boost medical outcomes by 30%–40% and reduce treatment costs by up to

• Received April 16, 2020
Revised May 24, 2020
Accepted June 9, 2020

• Corresponding author: **Soo Whan Kim**
Department of Otolaryngology-Head and Neck Surgery, Seoul St. Mary's Hospital, College of Medicine, The Catholic University of Korea, 222 Banpo-daero, Seocho-gu, Seoul 06591, Korea
Tel: +82-2-2258-6214, Fax: +82-2-535-1354
E-mail: kshent@catholic.ac.kr

• Co-Corresponding author: **Seungchul Lee**
Department of Mechanical Engineering, Pohang University of Science and Technology, 223 5th Engineering Building, 77 Cheongam-ro, Pohang 37673, Korea
Tel: +82-54-279-2181, Fax: +82-54-279-5997
E-mail: seunglee@postech.ac.kr

*The first two authors contributed equally to this article.

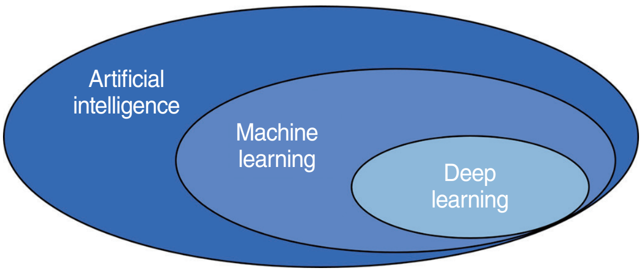

Fig. 1. Flowchart of the literature search and study selection.

50%. The AI healthcare market is expected to attain a value of USD 31.3 billion by 2025 [7].

Otorhinolaryngologists use many instruments to examine patients. Since the early 1990s, AI has been increasingly used to analyze radiological and pathological images, audiometric data, and cochlear implant (CI). Performance [8-10]. As various methods of AI analysis have been developed and refined, the practical scope of AI in the otorhinolaryngological field has been broadened (e.g., virtual reality technology [11-13]). Therefore, it is essential for otorhinolaryngologists to understand the capabilities and limitations of AI. In addition, a data-driven approach to healthcare requires clinicians to ask the right questions and to fit well into interdisciplinary teams [8].

Herein, we review the basics of AI, its current status, and future opportunities for AI in the field of otorhinolaryngology. We seek to answer two questions: "Which areas of otorhinolaryngology have benefited most from AI?" and " What does the future hold?"

MACHINE LEARNING AND DEEP LEARNING

AI has fascinated medical researchers and practitioners since the advent of machine learning (ML) and deep learning (DL) (two forms of AI) in 1990 and 2010, respectively. A flowchart of the literature search and study selection is presented in Fig. 1. Importantly, AI, ML, and DL overlap (Fig. 2). There is no single definition of AI; its purpose is to automate tasks that generally require the application of human intelligence [14]. Such tasks include object detection and recognition, visual understanding, and decision-making. Generally, AI incorporates both ML and DL, as well as many other techniques that are difficult to map onto recognized learning paradigms. ML is a data-driven technique that blends computer science with statistics, optimization, and probability [15]. An ML algorithm requires (1) input data, (2) examples of correct predictions, and (3) a means of validating algorithm performance. ML uses input data to build a model (i.e., a pattern) that allows humans to draw inferences [16,17]. DL is a subfield of ML, in which tens or hundreds of representative layers are learned with the aid of neural networks. A neural network is a learning structure that features several neurons; when combined with an activation function, a neural network delivers non-linear predictions. Unlike traditional ML algorithms, which typically only extract features, DL processes raw data to define the representations required for classification [18]. DL has been incorporated in many AI applications, including those for medical purposes [19]. The applications of DL thus far include image classification, speech recognition, autonomous driving, and text-to-speech conversion; in these domains, the performance of DL is at least as good as that of humans. Given the significant roles played by ML and DL in the medical field, clinicians must understand both the advantages and limitations of data-driven analytical tools.

HIGHLIGHTS

- Ninety studies that implemented artificial intelligence (AI) in otorhinolaryngology were reviewed and classified.
- The studies were divided into four subcategories.
- Research challenges regarding future applications of AI in otorhinolaryngology are discussed.

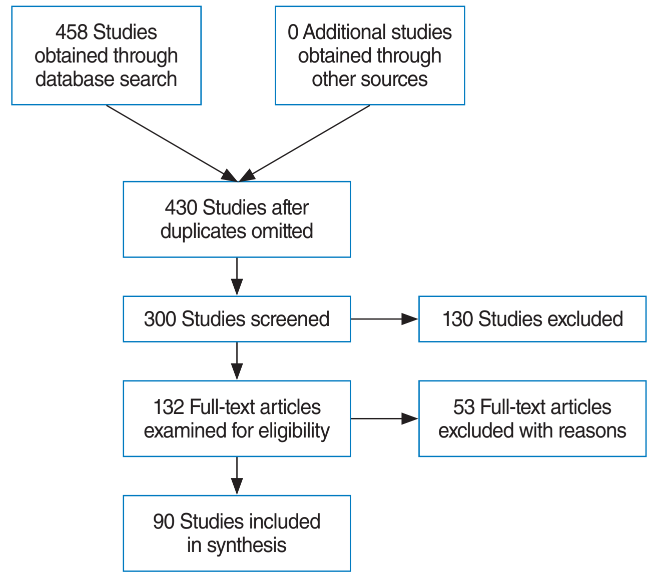

Fig. 2. Interconnections between artificial intelligence, machine learning, and deep learning.

AI IN THE FIELD OF OTORHINOLARYNGOLOGY

AI aids medical image-based analysis

Medical imaging yields a visual representation of an internal bodily region to facilitate analysis and treatment. Ear, nose, and throat-related diseases are imaged in various manners. Table 1 summarizes the 38 studies that used AI to assist medical image-

Table 1. AI techniques used for medical image-based analysis

Study	Analysis modality	Objective	AI technique	Validation method	No. of samples in the training dataset	No. of samples in the testing dataset	Best result	
							Accuracy (%)/AUC	Sensitivity (%)/specificity (%)
[20]	CT	Anterior ethmoidal artery anatomy	CNN: Inception-V3	Hold-out	675 Images from 388 patients	197 Images	82.7/0.86	-
[21]	CT	Osteomeatal complex occlusion	CNN: Inception-V3	-	1.28 Million images from 239 patients	-	85.0/0.87	-
[22]	CT	Chronic otitis media diagnosis	CNN: Inception-V3	Hold-out	975 Images	172 Images	-/0.92	83.3/91.4
[23]	DECT	HNSCC lymph nodes	RF, GBM	Hold-out	Training and testing set are randomly chosen with a ratio 70:30 from a total of 412 lymph nodes from 50 patients.		90.0/0.96	89.0/91.0
[24]	microCT	Intratemporal facial nerve anatomy	PCA+SSM	-	40 Cadaveric specimens from 21 donors	-	-	-
[25]	CT	Extranodal extension of HNSCC	CNN	Hold out	2,875 Lymph nodes	200 Lymph nodes	83.1/0.84	71.0/85.0
[26]	CT	Prediction of overall survival of head and neck cancer	NN, DT, boosting, Bayesian, bagging, RF, MARS, SVM, k-NN, GLM, PLSR	10-CV	101 Head and neck cancer patients, 440 radiomic features		-/0.67	-
[27]	DECT	Benign parotid tumors classification	RF	Hold-out	882 Images from 42 patients	Two-thirds of the samples	92.0/0.97	86.0/100
[28]	fMRI	Predicting the language outcomes following cochlear implantation	SVM	LOOCV	22 Training samples, including 15 labeled samples and 7 unlabeled samples		81.3/0.97	77.8/85.7
[29]	fMRI	Auditory perception	SVM	10-CV	42 Images from 6 participants		47.0/-	-
[30]	MRI	Relationship between tinnitus and thicknesses of internal auditory canal and nerves	ELM	Repeated hold-out	46 Images from 23 healthy subjects and 23 patients. Test was repeated 10 times for three training ratios, i.e., 50%, 60%, and 70%.		94.0/-	-
[31]	MRI	Prediction of treatment outcomes of sinonasal squamous cell carcinomas	SVM	9-CV	36 Lesions from 36 patients		92.0/-	100/82.0
[32]	Neuroimaging biomarkers	Tinnitus	SVM	5-CV	102 Images from 46 patients and 56 healthy subjects		80.0/0.86	-
[33]	MRI	Differentiate sinonasal squamous cell carcinoma from inverted papilloma	SVM	LOOCV	22 Patients with inverted papilloma and 24 patients with SCC		89.1/-	91.7/86.4
[34]	MRI	Speech improvement for CI candidates	SVM	LOOCV	37 Images from 37 children with hearing loss and 40 images from 40 children with normal hearing		84.0/0.84	80.0/88.0
[35]	Endoscopic images	Laryngeal soft tissue	Weighted voting (UNet+ErfNet)	Hold-out	200 Images	100 Images	84.7/-	-
[36]	Laryngoscope images	laryngeal neoplasms	CNN	Hold-out	14,340 Images from 5,250 patients	5,093 Images from 2,271 patients	96.24/-	92.8/98.9
[37]	Laryngoscope images	Laryngeal cancer	CNN	Hold-out	13,721 Images	1,176 Images	86.7/0.92	73.1/92.2
[38]	Laryngoscope images	Oropharyngeal cariconoma	Naive Bayes	Hold-out	4 Patients with oropharyngeal cariconoma and 1 healthy subject	16 Patients with oropharyngeal cariconoma and 9 healthy subjects	65.9/-	66.8/64.9
[39]	Otoscopic images	Otologic diseases	CNN	Hold-out	734 Images; 80% of the images were used for the training and 20% were used for validation.		84.4/-	-

(*Continued to the next page*)

Table 1. Continued

Study	Analysis modality	Objective	AI technique	Validation method	No. of samples in the training dataset	No. of samples in the testing dataset	Best result: Accuracy (%)/AUC	Best result: Sensitivity (%)/specificity (%)
[40]	Otoscopic images	Otitis media	MJSR	Hold-out	1,230 Images; 80% of the images were used for the training and 20% were used for validation.		91.41/-	89.48/93.33
[41]	Otoscopic images	Otoscopic diagnosis	AutoML	Hold-out	1,277 Images	89 Images	88.7/-	86.1/-
[42]	Digitized images	H&E-stained tissue of oral cavity squamous cell carcinoma	LDA, QDA, RF, SVM	Hold-out	50 Images	65 Images	88.0/0.87	78.0/93.0
[43]	PESI-MS	Intraoperative specimens of HNSCC	LR	LOOCV	114 Non-cancerous specimens and 141 cancerous specimens		95.35/-	-
[44]	Biopsy specimen	Frozen section of oral cavity cancer	SVM	LOOCV	176 Specimen pairs from 27 subjects		-/0.94	100/88.78
[45]	HSI	Head and neck cancer classification	CNN	LOOCV	88 Samples from 50 patients		80.0/-	81.0/78.0
[46]	HSI	Head and neck cancer classification	CNN	LOOCV	12 Tumor-bearing samples for 12 mice		91.36/-	86.05/93.36
[47]	HSI	Oral cancer	SVM, LDA, QDA, RF, RUSBoost	10-CV	10 Images from 10 mice		79.0/0.86	79.0/79.0
[48]	HSI	Head and neck cancer classification	LDA, QDA, ensemble LDA, SVM, RF	Repeated hold-out	20 Specimens from 20 patients	16 Specimens from 16 patients	94.0/0.97	95.0/90.0
[49]	HSI	Tissue surface shape reconstruction	SSRNet	5-CV	200 SL images		96.81/-	92.5/-
[50]	HSI	Tumor margin of HNSCC	CNN	5-CV	395 Surgical specimens		98.0/0.99	-
[51]	HSI	Tumor margin of HNSCC	LDA	10-CV	16 Surgical specimens		90.0/-	89.0/91.0
[52]	HSI	Optical biopsy of head and neck cancer	CNN	LOOCV	21 Surgical gross-tissue specimens		81.0/0.82	81.0/80.0
[53]	SRS	Frozen section of laryngeal squamous cell carcinoma	CNN	5-CV	18,750 Images from 45 patients		100/-	-
[54]	HSI	Cancer margins of *ex-vivo* human surgical specimens	CNN	Hold-out	11 Surgical specimens	9 Surgical specimens	81.0/0.86	84.0/77.0
[55]	USG	Genetic risk stratification of thyroid nodules	AutoML	Hold-out	556 Images from 21 patients	127 Images	77.4/-	45.0/97.0
[56]	CT	Concha bullosa on coronal sinus classification	CNN: Inception-V3	Hold-out	347 Images (163 concha bullosa images and 184 normal images)	100 Images (50 concha bullosa images and 50 normal images)	81.0/0.93	-
[57]	Panoramic radiography	Maxillary sinusitis diagnosis	AlexNet CNN	Hold-out	400 Healthy images and 400 inflamed maxillary sinuses images	60 Healthy and 60 inflamed maxillary sinuses images	87.5/0.875	86.7/88.3

AI, artificial intelligence; AUC, area under the receiver operating characteristic curve; CT, computed tomography; CNN, convolutional neural network; DECT, dual-energy computed tomography; HN-SCC, head and neck squamous cell carcinoma; RF, random forest; GBM, gradient boosting machine; PCA, principle component analysis; SSM, statistical shape model; NN, neural network; DT, decision tree; MARS, multi adaptive regression splines; SVM, support vector machine; k-NN, k-nearest neighbor; GLM, generalized linear model; PLSR, partial least squares and principal component regression; CV, cross-validation; fMRI, functional magnetic resonance imaging; LOOCV, leave-one-out cross-validation; ELM, extreme learning machine; CI, cochlear implant; MJSR, multitask joint sparse representation; LDA, linear discriminant analysis; QDA, quadratic discriminant analysis; PESI-MS, probe electrospray ionization mass spectrometry; LR, logistic regression; HSI, hyperspectral imaging; SSRNet, super-spectral-resolution network; SRS, stimulated Raman scattering; USG, ultrasonography.

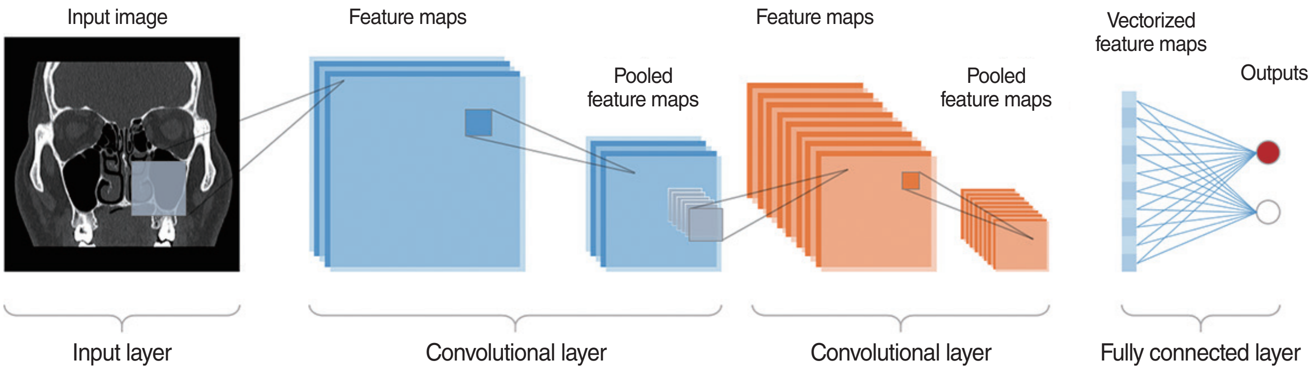

Fig. 3. Artificial intelligence (AI) techniques used for medical image-based analysis.

Table 2. AI techniques used for voice-based analysis

Study	Analysis modality	Objective	AI technique	Validation method	No. of samples in the training dataset	No. of samples in the testing dataset	Best result
[58]	CI	Noise reduction	NC+DDAE	Hold-out	120 Utterances	200 Utterances	Accuracy: 99.5%
[59]	CI	Segregated speech from background noise	DNN	Hold-out	560×50 Mixtures for each noise type and SNR	160 Noise segments from original unperturbed noise	Hit ratio: 84%; false alarm: 7%
[60]	CI	Improved pitch perception	ANN	Hold-out	1,500 Pitch pairs	10% of the training material	Accuracy: 95%
[61]	CI	Predicted speech recognition and QoL outcomes	k-NN, DT	10-CV	A total of 29 patients, including 48% unilateral CI users and 51% bimodal CI users		Accuracy: 81%
[62]	CI	Noise reduction	DDAE	Hold-out	12,600 Utterances	900 Noisy utterances	Accuracy: 36.2%
[63]	CI	Improved speech intelligibility in unknown noisy environments	DNN	Hold-out	640,000 Mixtures of sentences and noises	-	Accuracy: 90.4%
[64]	CI	Modeling electrode-to-nerve interface	ANN	Hold-out	360 Sets of fiber activation patterns per electrode	40 Sets of fiber activation patterns per electrode	-
[65]	CI	Provided digital signal processing plug-in for CI	WNN	Hold-out	120 Consonants and vowels, sampled at 16 kHz; half of data was used as training set and the rest was used as testing set.		SNR: 2.496; MSE: 0.086; LLR: 2.323
[66]	CI	Assessed disyllabic speech test performance in CI	k-NN	-	60 Patients	-	Accuracy: 90.83%
[67]	Acoustic signals	Voice disorders detection	CNN	10-CV	451 Images from 10 health adults and 70 adults with voice disorders		Accuracy: 90%
[68]	Dysphonic symptoms	Voice disorders detection	ANN	Repeated hold-out	100 Cases of neoplasm, 508 cases of benign phonotraumatic, 153 cases of vocal palsy		Accuracy: 83%
[69]	Pathological voice	Voice disorders detection	DNN, SVM, GMM	5-CV	60 Normal voice samples and 402 pathological voice samples		Accuracy: 94.26%
[70]	Acoustic signal	Hot potato voice detection	SVM	Hold-out	2,200 Synthetic voice samples	12 HPV samples from real patients	Accuracy: 88.3%
[71]	SEMG signals	Voice restoration for laryngectomy patients	XGBoost	Hold-out	75 Utterances using 7 SEMG sensors	-	Accuracy: 86.4%

AI, artificial intelligence; CI, cochlear implant; NC, noise classifier; DDAE, deep denoising autoencoder; DNN, deep neural network; SNR, signal-to-noise ratio; ANN, artificial neural network; QoL, quality of life; k-NN, k-nearest neighbors; DT, decision tree; CV, cross-validation; WNN, wavelet neural network; MSE, mean square error; LLR, log-likelihood ratio; CNN, convolutional neural network; GMM, Gaussian mixture model; SVM, support vector machine; HPV, human papillomavirus; SEMG, surface electromyographic.

based analysis in clinical otorhinolaryngology. Nine studies (23.7%) addressed hyperspectral imaging, nine studies (23.7%) analyzed computed tomography, six studies (15.8%) applied AI to magnetic resonance imaging, and one study (2.63%) analyzed panoramic radiography. Laryngoscopic and otoscopic imaging were addressed in three studies each (7.89% each). The remaining seven studies (18.39%) used AI to aid in the analysis of neuroimaging biomarker levels, biopsy specimens, simulated Raman scattering data, ultrasonography and mass spectrometry data, and digitized images. Nearly all AI algorithms comprised convolutional neural networks. Fig. 3 presents a schematic diagram of the application of convolutional neural networks in medical image-based analysis; the remaining algorithms consisted of support vector machines and random forests.

AI aids voice-based analysis

The subfield of voice-based analysis within otorhinolaryngology seeks to improve speech, to detect voice disorders, and to reduce the noise experienced by patients with (CIs; Table 2 lists the 14 studies that used AI for speech-based analyses. Nine (64.29%) sought to improve speech intelligibility or reduce noise for patients with CIs. Two (14.29%) used acoustic signals to detect voice disorders [67] and "hot potato voice" [70]. In other studies, AI was used for symptoms, voice pathologies, or electromyographic signals as a way to detect voice disorders [68,69], or to restore the voice of a patient who had undergone total laryngectomy [71]. Neural networks were favored, followed by k-nearest neighbor methods, support vector machines, and other widely known classifiers (e.g., decision trees and XGBoost). Fig. 4 presents a schematic diagram of the application of convolutional neural networks in medical voice-based analysis.

AI analysis of biosignals detected from medical devices

Medical device-based analyses seek to predict the responses to clinical treatments in order to guide physicians who may wish to choose alternative or more aggressive therapies. AI has been used to assist polysomnography, to explore gene expression profiles, to interpret cellular cartographs, and to evaluate the outputs of non-contact devices. These studies are summarized in Table 3. Of these 14 studies, most (50%, seven studies) focused on analyses of gene expression data. Three studies (21.43%) used AI to examine polysomnography data in an effort to score sleep stages [72,73] or to identify long-term cardiovascular disease [74]. Most algorithms employed ensemble learning (random forests, Gentle Boost, XGBoost, and a general linear model+support vector machine ensemble); this approach was followed by neural network-based algorithms (convolutional neural networks, autoencoders, and shallow artificial neural networks). Fig. 5 presents a schematic diagram of the application of the autoencoder and the support vector machine in the analysis of gene expression data.

AI for clinical diagnoses and treatments

Clinical diagnoses and treatments consider only symptoms, medical records, and other clinical documentation. We retrieved 24 relevant studies (Table 4). Of the ML algorithms, most used logistic regression for classification, followed by random forests and support vector machines. Notably, many studies used hold-outs to validate new methods. Fig. 6 presents a schematic diagram of the process cycle of utilizing AI for clinical diagnoses and treatments.

DISCUSSION

We systematically analyzed reports describing the integration of AI in the field of otorhinolaryngology, with an emphasis on how AI may best be implemented in various subfields. Various AI techniques and validation methods have found favor. As described above, advances in 2015 underscored that AI would play a major role in future medicine. Here, we reviewed post-2015 AI applications in the field of otorhinolaryngology. Before 2015, most AI-based technologies focused on CIs [10,75-86]. However, AI applications have expanded greatly in recent years. In terms of image-based analysis, images yielded by rigid endoscopes, laryngoscopes, stroboscopes, computed tomography, magnetic resonance imaging, and multispectral narrow-band imaging [38], as

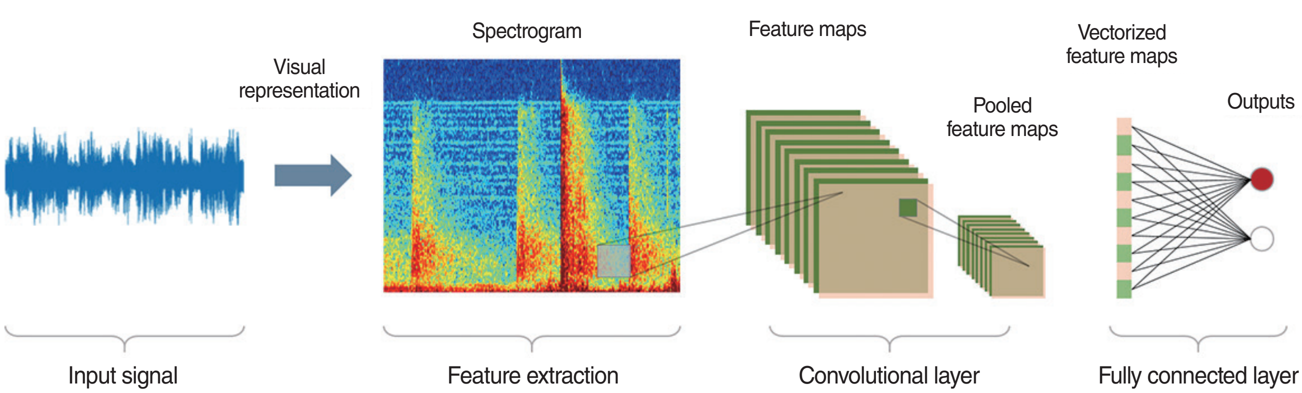

Fig. 4. Artificial intelligence (AI) techniques used for voice-based analysis.

Table 3. AI analysis of biosignals detected from medical device

Study	Analysis modality	Objective	AI technique	Validation method	No. of samples in the training dataset	No. of samples in the testing dataset	Best result
[73]	EEG signal of PSG	Sleep stage scoring	CNN	5-CV	294 Sleep studies; 122 composed the training set, 20 composed the validation set, and 152 were used in the testing set.		Accuracy: 81.81%; F_1 score: 81.50%; Cohen's Kappa: 72.76%
[72]	EEG, EMG, EOG signals of PSG	Sleep stage scoring	CNN	Hold-out	42,560 Hours of PSG data from 5,213 patients	580 PSGs	Accuracy: 86%; F_1 score: 81.0%; Cohen's Kappa: 82.0%
[74]	Sleep heart rate variability in PSG	Long-term cardiovascular outcome prediction	XGBoost	5-CV	1,252 Patients with cardio vascular disease and 859 patients with non-cardio vascular disease		Accuracy: 75.3%
[87]	Sleep breathing sound using an air-conduction microphone	AHI prediction	Gaussian process, SVM, RF, LiR	10-CV	116 Patients with OSA		CC: 0.83; LMAE: 9.54 events/hr; RMSE: 13.72 events/hr
[88]	Gene signature	Thyroid cancer lymph node metastasis and recurrence rediction	LDA	6-CV	363 Samples	72 Samples	AUC: 0.86; sensitivity: 86%; specificity: 62%; PPV: 93%; NPV: 42%
[89]	Gene expression profile	Response prediction to chemotherapy in patient with HNSCC	SVM	LOOCV	16 TPF-sensitive patients and 13 non-TPF-sensitive patients		Sensitivity: 88.3%; specificity: 88.9%
[90]	Mucus cytokines	SNOT-22 scores prediction of CRS patients	RF, LiR	-	147 Patients with 65 patients with postoperative follow-up		R^2: 0.398
[91]	Cellular cartography	Single-cell resolution mapping of the organ of Corti	Gentle boost, RF, CNN	Hold-out	20,416 Samples	19,594 Samples	Recall: 99.3%; precision: 99.3%; F_1: 93.3%
[92]	RNA sequencing, miRNA sequencing, methylation data	HNSCC progress prediction	Autoencoder and SVM	2×5-CV	360 Samples from TCGA		C-index: 0.73; Brier score: 0.22
[93]	DNA repair defect	HNSCC progress prediction	CART	10×5-CV	180 HPV-negative HNSCC patients		AUC: 1.0
[94]	PESI-MS	Identified TGF-β signaling in HNSCC	LDA	LOOCV	A total of 240 and 90 mass spectra from TGF-β-unstimulated and stimulated HNSCC cells, respectively		Accuracy: 98.79%
[95]	Next generation sequencing of RNA	Classified the risk of malignancy in cytologically indeterminate thyroid nodules	Ensemble of elastic net GLM and SVM	40×5-CV	A total of 10,196 genes, among which are 1,115 core genes		Sensitivity: 91%; specificity: 68%
[96]	Gene expression profile	HPV-positive oropharyngeal squamous cell carcinoma detection	LR	500-CV	146 Genes from patients with node-negative disease and node-positive disease		AUC: 0.93
[97]	miRNA expression profile	Sensorineural hearing loss prediction	DF, DJ, LR, NN	LOOCV	16 Patients were included.		Accuracy: 100%

AI, artificial intelligence; EEG, electroencephalogram; PSG, polysomnography; CNN, convolutional neural network; CV, cross-validation; EMG, electromyography; EOG, electrooculogram; AHI, apnea-hypopnea index; SVM, support vector machine; RF, random forest; LiR, linear regression; OSA, obstructive sleep apnea; CC, correlation coefficient; LMAE, least mean absolute error; RMSE, root mean squared error; LDA, linear discriminant analysis; AUC, area under the receiver operating characteristic curve; PPV, positive predictive value; NPV, negative predictive value; HNSCC, head and neck squamous cell carcinoma; LOOCV, leave-one-out cross validation; TPF, docetaxel, cisplatin, and 5-fluorouracil; SNOT-22, 22-item sinonasal outcome test; CRS, chronic rhinosinusitis; miRNA, microRNA; TCGA, the cancer genome atlas; CART, classification and regression trees; HPV, human papillomavirus; PESI-MS, probe electrospray ionization mass spectrometry; TGF-β, transforming growth factor beta; GLM, generalized linear model; LR, logistic regression; DF, decision forest; DJ, decision jungle; NN, neural network.

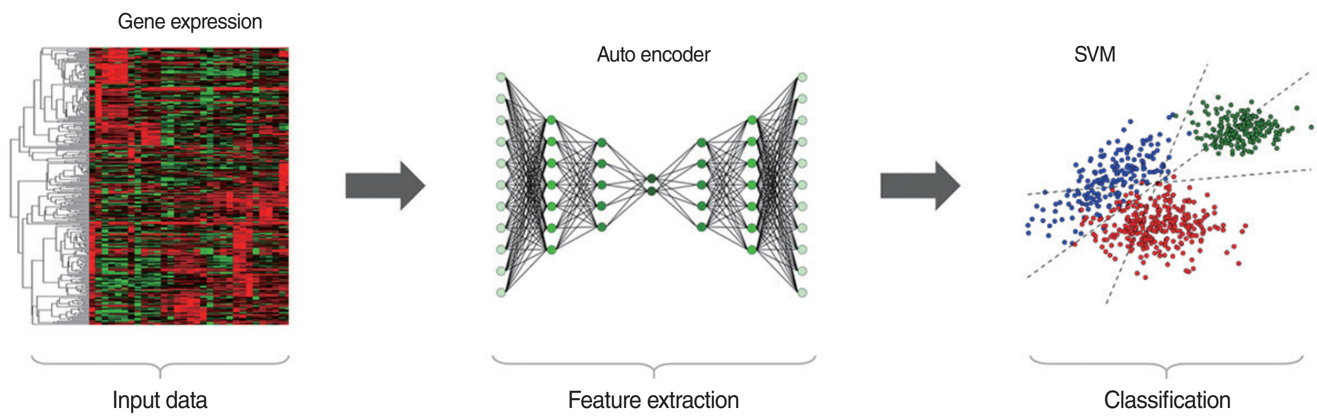

Fig. 5. Artificial intelligence (AI) analyses of biosignals detected from medical devices. SVM, support vector machine.

Table 4. AI techniques used for clinical diagnoses and treatments

Study	Analysis modality	Objective	AI technique	Validation method	No. of samples in the training dataset	No. of samples in the testing dataset	Best result
[98]	Hearing aids	Hearing gain prediction	CRDN	Hold-out	2,182 Patients that were diagnosed with hearing loss; the percentages of randomly sampled training, validation, and test sets were 40%, 30%, and 30%, respectively.		MAPE: 9.2%
[99]	Hearing aids	Predicted CI outcomes	RF	LOOCV	121 Postlingually deaf adults with CI		MAE: 6.1; Pearson's correlation coefficient: 0.96
[100]	Clinical data	SSHL prediction	DBN, LR, SVM, MLP	4-CV	1,220 Unilateral SSHL patients		Accuracy: 77.58%; AUC: 0.84
[101]	Clinical data including demographics and risk factors	Determined the risk of head and neck cancer	LR	Hold-out	1,005 Patients, containing 932 patients with no cancer outcome and 73 patients with cancer outcome	235 Patients, containing 212 patients with no cancer outcome and 23 patients with cancer outcome	AUC: 0.79
[102]	Clinical data including symptom	Peritonsillar abscess diagnosis prediction	NN	Hold-out	641 Patients	275 Patients	Accuracy: 72.3%; sensitivity: 6.0%; specificity: 50%
[103]	Vestibular test batteries	Vestibular function assessment	DT, RF, LR, AdaBoost, SVM	Hold-out	5,774 Individuals	100 Individuals	Accuracy: 93.4%
[104]	Speakers and microphones within existing smartphones	Middle ear fluid detection	LR	LOOCV	98 Patient ears		AUC: 0.9; sensitivity: 84.6%; specificity: 81.9%
[105]	Cancer data survival	5-Year survival patients with oral cavity squamous cell carcinoma	DF, DJ, LR, NN	Hold-out	26,452 Patients	6,613 Patients	AUC: 0.8; accuracy: 71%; precision: 71%; recall: 68%
[106]	Histological data	Occult lymph node metastases identification in clinically oral cavity squamous cell	RF, SVM, LR, C5.0	Hold-out	56 Patients	112 Patients	AUC: 0.89; accuracy: 88.0%; NPV: >95%
[107]	Clinicopathologic data	Head and neck free tissue transfer surgical complications prediction	GBDT	Hold-out	291 Patients	73 Patients	Specificity: 62.0%; sensitivity: 60.0%; F1: 60.0%

(*Continued to the next page*)

Table 4. Continued

Study	Analysis modality	Objective	AI technique	Validation method	No. of samples in the training dataset	No. of samples in the testing dataset	Best result
[108]	Clinicopathologic data	Delayed adjuvant radiation prediction	RF	Hold-out	61,258 Patients	15,315 Patients	Accuracy: 64.4%; precision: 58.5%
[109]	Clinicopathologic data	Occult nodal metastasis prediction in oral cavity squamous cell carcinoma	LR, RF, SVM, GBM	Hold-out	1,570 Patients	391 Patients	AUC: 0.71; sensitivity: 75.3%; specificity: 49.2%
[110]	Dataset of the center of pressure sway during foam posturography	Peripheral vestibular dysfunction prediction	GBDT, bagging, LR	CV	75 Patients with vestibular dysfunction and 163 healthy controls		AUC: 0.9; recall: 0.84
[111]	TEOAE signals	Meniere's disease hearing outcome prediction	SVM	5-CV	30 Unilateral patients		Accuracy: 82.7%
[112]	Semantic and syntactic patterns in clinical documentation	Vestibular diagnoses	NLP+Naïve Bayes	10-CV	866 Physician-generated histories from vestibular patients		Sensitivity: 93.4%; specificity: 98.2%; AUC: 1.0
[113]	Endoscopic imaging	Nasal polyps diagnosis	ResNet50, Xception, and Inception V3	Hold-out	23,048 Patches (167 patients) as training set, 1,577 patches (12 patients) as internal validation set, and 1,964 patches (16 patients) as external test set		Inception V3: AUC: 0.974
[114]	Intradermal skin tests	Allergic rhinitis diagnosis	Associative classifier	10-CV	872 Patients with allergic symptoms		Accuracy: 88.31%
[115]	Clinical data	Identified phenotype and mucosal eosinophilia endotype subgroups of patients with medical refractory CRS	Cluster analysis	-	46 Patients with CRS without nasal polyps and 67 patients with nasal polyps		-
[116]	Clinical data	Prognostic information of patient with CRS	Discriminant analysis	-	690 Patients		-
[117]	Clinical data	Identified phenotypic subgroups of CRS patients	Discriminant analysis	-	382 Patients		-
[118]	Clinical data	Characterization of distinguishing clinical features between subgroups of patients with CRS	Cluster analysis	-	97 Surgical patients with CRS		-
[119]	Clinical data	Identified features of CRS without nasal polyposis	Cluster analysis	-	145 Patients of CRS without nasal polyposis		-
[120]	Clinical data	Identified inflammatory endotypes of CRS	Cluster analysis	-	682 Cases (65% with CRS without nasal polyps)		-
[121]	Clinical data	Identified features of CRS with nasal polyps	Cluster analysis	-	375 Patients		-

AI, artificial intelligence; CRDN, cascade recurring deep network; MAPE, mean absolute percentage error; RF, random forest; LOOCV, leave-one-out cross validation; CI, cochlear implant; MAE, mean absolute error; SSHL, sudden sensorineural hearing loss; DBN, deep belief network; LR, logistic regression; SVM, support vector machine; MLP, multilayer perceptron; CV, cross-validation; AUC, area under the receiver operating characteristic curve; NN, neural network; DT, decision tree; DF, decision forest; DJ, decision jungle; NPV, negative predictive value; GBDT, gradient boosted decision trees; GBM, gradient boosting machine; TEOAE, transient-evoked otoacoustic emission; NLP, natural language processing; CRS, chronic rhinosinusitis.

well as hyperspectral imaging [45-52,54], are now interpreted by AI. In voice-based analysis, AI is used to evaluate pathological voice conditions associated with vocal fold disorders, to analyze and decode phonation itself [67], to improve speech perception in noisy conditions, and to improve the hearing of patients with CIs. In medical device-based analyses, AI is used to evaluate tissue and blood test results, as well as the outcomes of otorhinolaryngology-specific tests (e.g., polysomnography) [72,73,122] and audiometry [123,124]. AI has also been used to support clinical diagnoses and treatments, decision-making, the

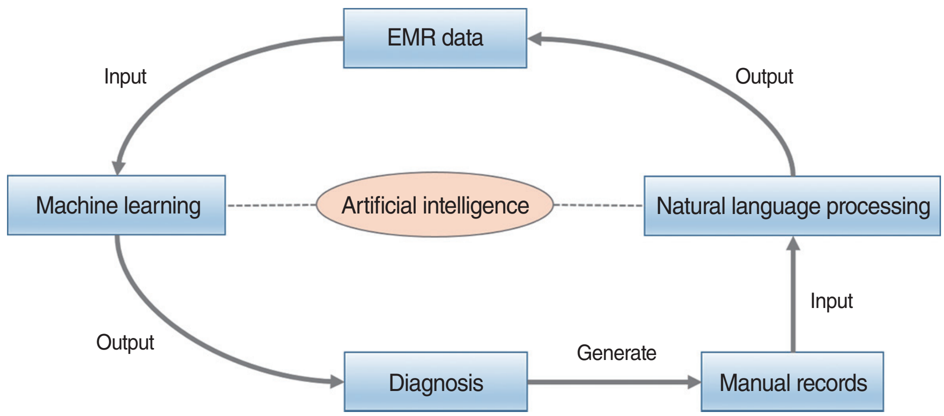

Fig. 6. Artificial intelligence (AI) techniques used for clinical diagnoses and treatments. EMR, electronic medical record.

prediction of prognoses [98-100,125,126], disease profiling, the construction of mass spectral databases [43,127-129], the identification or prediction of disease progress [101,105,107-110,130], and the confirmation of diagnoses and the utility of treatments [102-104,112,131].

Although many algorithms have been applied, some are not consistently reliable, and certain challenges remain. AI will presumably become embedded in all tools used for diagnosis, treatment selection, and outcome predictions; thus, AI will be used to analyze images, voices, and clinical records. These are the goals of most studies, but again, the results have been variable and are thus difficult to compare. The limitations include: (1) small training datasets and differences in the sizes of the training and test datasets; (2) differences in validation techniques (notably, some studies have not included data validation); and (3) the use of different performance measures during either classification (e.g., accuracy, sensitivity, specificity, F1, or area under the receiver operating characteristic curve) or regression (e.g., root mean square error, least mean absolute error, R-squared, or log-likelihood ratio).

ML algorithms always require large, labeled training datasets. The lack of such data was often a major limitation of the studies that we reviewed. AI-based predictions in the field of otorhinolaryngology must be rigorously validated. Often, as in the broader medical field, an element of uncertainty compromises an otherwise ideal predictive method, and other research disparities were also apparent in the studies that we reviewed. Recent promising advances in AI include the ensemble learning model, which is more intuitive and interpretable than other models; this model facilitates bias-free AI-based decision-making. The algorithm incorporates a concept of "fairness," considers ethical and legal issues, and respects privacy during data mining tasks. In summary, although otorhinolaryngology-related AI applications were divided into four categories in the present study, the practical use of a particular AI method depends on the circumstances. AI will be helpful for use in real-world clinical treatment involving complex datasets with heterogeneous variables.

CONCLUSION

We have described several techniques and applications for AI; notably, AI can overcome existing technical limitations in otorhinolaryngology and aid in clinical decision-making. Otorhinolaryngologists have interpreted instrument-derived data for decades, and many algorithms have been developed and applied. However, the use of AI will refine these algorithms, and big health data and information from complex heterogeneous datasets will become available to clinicians, thereby opening new diagnostic, treatment, and research frontiers.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

ACKNOWLEDGMENTS

This research was supported by the Basic Science Research Program through an NRF grant funded by the Korean government (MSIT) (No. 2020R1A2C1009744), the Bio Medical Technology Development Program of the NRF funded by the Ministry of Science ICT (No. 2018M3A9E8020856), and the Po-Ca Networking Group funded by the Postech-Catholic Biomedical Engineering Institute (PCBMI) (No. 5-2020-B0001-00046).

ORCID

Bayu Adhi Tama https://orcid.org/0000-0002-1821-6438
Do Hyun Kim https://orcid.org/0000-0002-9248-5572
Gyuwon Kim https://orcid.org/0000-0002-7259-099X
Soo Whan Kim https://orcid.org/0000-0002-6917-5998
Seungchul Lee https://orcid.org/0000-0002-1034-1410

AUTHOR CONTRIBUTIONS

Conceptualization: DHK, SWK, SL. Data curation: BAT, DHK, GK. Formal analysis: BAT, DHK, GK. Funding acquisition: DHK, SL. Methodology: BAT, DHK, GK. Project administration: DHK, SWK, SL. Visualization: BAT, DHK, GK. Writing–original draft: BAT, DHK. Writing–review & editing: all authors.

REFERENCES

1. Pomerol JC. Artificial intelligence and human decision making. Eur J Oper Res. 1997 May;99(1):3-25.
2. Simon HA. The sciences of the artificial. Cambridge (MA): MIT Press; 2019.
3. He K, Zhang X, Ren S, Sun J, editors. Deep residual learning for image recognition. Proceedings of the IEEE Conference on Computer Vision and Pattern Recognition; 2016.
4. Silver D, Hassabis D. Alphago: mastering the ancient game of go with machine learning [Internet]. Google AI Blog; 2016 [cited 2020 Aug 1]. Available from: https://ai.googleblog.com/2016/01/alphago-mastering-ancient-game-of-go.html.
5. Densen P. Challenges and opportunities facing medical education. Trans Am Clin Climatol Assoc. 2011;122:48-58.
6. Monegain B. IBM Watson pinpoints rare form of leukemia after doctors misdiagnosed patient [Internet]. Healthcare IT News; 2016 [cited 2020 Aug 1]. Available from: https://www.healthcareitnews.com/news/ibm-watson-pinpoints-rare-form-leukemia-after-doctors-misdiagnosed-patient.
7. Grand View Research. Artificial intelligence in healthcare market size, share & trends analysis by component (hardware, software, services), by application, by region, competitive insights, and segment forecasts, 2019-2025 [Internet]. San Francisco, CA: Grand View Research; 2019 [cited 2020 Aug 1]. Available from: https://www.grandviewresearch.com/industry-analysis/artificial-intelligence-ai-healthcare-market.
8. Crowson MG, Ranisau J, Eskander A, Babier A, Xu B, Kahmke RR, et al. A contemporary review of machine learning in otolaryngology-head and neck surgery. Laryngoscope. 2020 Jan;130(1):45-51.
9. Freeman DT. Computer recognition of brain stem auditory evoked potential wave V by a neural network. Proc Annu Symp Comput Appl Med Care. 1991:305-9.
10. Zadak J, Unbehauen R. An application of mapping neural networks and a digital signal processor for cochlear neuroprostheses. Biol Cybern. 1993;68(6):545-52.
11. Kim DH, Kim Y, Park JS, Kim SW. Virtual reality simulators for endoscopic sinus and skull base surgery: the present and future. Clin Exp Otorhinolaryngol. 2019 Feb;12(1):12-7.
12. Park JH, Jeon HJ, Lim EC, Koo JW, Lee HJ, Kim HJ, et al. Feasibility of eye tracking assisted vestibular rehabilitation strategy using immersive virtual reality. Clin Exp Otorhinolaryngol. 2019 Nov; 12(4):376-84.
13. Song JJ. Virtual reality for vestibular rehabilitation. Clin Exp Otorhinolaryngol. 2019 Nov;12(4):329-30.
14. Chollet F, Allaire JJ. Deep learning with R. Shelter Island (NY): Manning Publications; 2018.
15. Mohri M, Rostamizadeh A, Talwalkar A. Foundations of machine learning. Cambridge (MA): MIT Press; 2012.
16. Flach P. Machine learning: the art and science of algorithms that make sense of data. Cambridge: Cambridge University Press; 2012.
17. James G, Witten D, Hastie T, Tibshirani R. An introduction to statistical learning. Berlin: Springer; 2013.
18. LeCun Y, Bengio Y, Hinton G. Deep learning. Nature. 2015 May; 521(7553):436-44.
19. Tama BA, Rhee KH. Tree-based classifier ensembles for early detection method of diabetes: an exploratory study. Artif Intell Rev. 2019;51:355-70.
20. Huang J, Habib AR, Mendis D, Chong J, Smith M, Duvnjak M, et al. An artificial intelligence algorithm that differentiates anterior ethmoidal artery location on sinus computed tomography scans. J Laryngol Otol. 2020 Jan;134(1):52-5.
21. Chowdhury NI, Smith TL, Chandra RK, Turner JH. Automated classification of osteomeatal complex inflammation on computed tomography using convolutional neural networks. Int Forum Allergy Rhinol. 2019 Jan;9(1):46-52.
22. Wang YM, Li Y, Cheng YS, He ZY, Yang JM, Xu JH, et al. Deep learning in automated region proposal and diagnosis of chronic otitis media based on computed tomography. Ear Hear. 2020 May/Jun; 41(3):669-77.
23. Seidler M, Forghani B, Reinhold C, Perez-Lara A, Romero-Sanchez G, Muthukrishnan N, et al. Dual-energy CT texture analysis with machine learning for the evaluation and characterization of cervical lymphadenopathy. Comput Struct Biotechnol J. 2019 Jul;17: 1009-15.
24. Hudson TJ, Gare B, Allen DG, Ladak HM, Agrawal SK. Intrinsic measures and shape analysis of the intratemporal facial nerve. Otol Neurotol. 2020 Mar;41(3):e378-86.
25. Kann BH, Hicks DF, Payabvash S, Mahajan A, Du J, Gupta V, et al. Multi-institutional validation of deep learning for pretreatment identification of extranodal extension in head and neck squamous cell carcinoma. J Clin Oncol. 2020 Apr;38(12):1304-11.
26. Parmar C, Grossmann P, Rietveld D, Rietbergen MM, Lambin P, Aerts HJ. Radiomic machine-learning classifiers for prognostic biomarkers of head and neck cancer. Front Oncol. 2015 Dec;5:272.
27. Al Ajmi E, Forghani B, Reinhold C, Bayat M, Forghani R. Spectral multi-energy CT texture analysis with machine learning for tissue classification: an investigation using classification of benign parotid tumours as a testing paradigm. Eur Radiol. 2018 Jun;28(6):2604-11.
28. Tan L, Holland SK, Deshpande AK, Chen Y, Choo DI, Lu LJ. A semi-supervised support vector machine model for predicting the language outcomes following cochlear implantation based on pre-implant brain fMRI imaging. Brain Behav. 2015 Oct;5(12):e00391.
29. Zhang F, Wang JP, Kim J, Parrish T, Wong PC. Decoding multiple sound categories in the human temporal cortex using high resolution fMRI. PLoS One. 2015 Feb;10(2):e0117303.
30. Ergen B, Baykara M, Polat C. Determination of the relationship between internal auditory canal nerves and tinnitus based on the findings of brain magnetic resonance imaging. Biomed Signal Process Control. 2018 Feb;40:214-9.
31. Fujima N, Shimizu Y, Yoshida D, Kano S, Mizumachi T, Homma A, et al. Machine-learning-based prediction of treatment outcomes using MR imaging-derived quantitative tumor information in patients with sinonasal squamous cell carcinomas: a preliminary study. Cancers (Basel). 2019 Jun;11(6):800.
32. Liu Y, Niu H, Zhu J, Zhao P, Yin H, Ding H, et al. Morphological neuroimaging biomarkers for tinnitus: evidence obtained by applying machine learning. Neural Plast. 2019 Dec;2019:1712342.
33. Ramkumar S, Ranjbar S, Ning S, Lal D, Zwart CM, Wood CP, et al. MRI-based texture analysis to differentiate sinonasal squamous cell carcinoma from inverted papilloma. AJNR Am J Neuroradiol. 2017 May;38(5):1019-25.
34. Feng G, Ingvalson EM, Grieco-Calub TM, Roberts MY, Ryan ME, Birmingham P, et al. Neural preservation underlies speech improvement from auditory deprivation in young cochlear implant recipients. Proc Natl Acad Sci U S A. 2018 Jan;115(5):E1022-31.

35. Laves MH, Bicker J, Kahrs LA, Ortmaier T. A dataset of laryngeal endoscopic images with comparative study on convolution neural network-based semantic segmentation. Int J Comput Assist Radiol Surg. 2019 Mar;14(3):483-92.
36. Ren J, Jing X, Wang J, Ren X, Xu Y, Yang Q, et al. Automatic recognition of laryngoscopic images using a deep-learning technique. Laryngoscope. 2020 Feb 18 [Epub]. https://doi.org/10.1002/lary.28539.
37. Xiong H, Lin P, Yu JG, Ye J, Xiao L, Tao Y, et al. Computer-aided diagnosis of laryngeal cancer via deep learning based on laryngoscopic images. EBioMedicine. 2019 Oct;48:92-9.
38. Mascharak S, Baird BJ, Holsinger FC. Detecting oropharyngeal carcinoma using multispectral, narrow-band imaging and machine learning. Laryngoscope. 2018 Nov;128(11):2514-20.
39. Livingstone D, Talai AS, Chau J, Forkert ND. Building an otoscopic screening prototype tool using deep learning. J Otolaryngol Head Neck Surg. 2019 Nov;48(1):66.
40. Tran TT, Fang TY, Pham VT, Lin C, Wang PC, Lo MT. Development of an automatic diagnostic algorithm for pediatric otitis media. Otol Neurotol. 2018 Sep;39(8):1060-5.
41. Livingstone D, Chau J. Otoscopic diagnosis using computer vision: an automated machine learning approach. Laryngoscope. 2020 Jun;130(6):1408-13.
42. Lu C, Lewis JS Jr, Dupont WD, Plummer WD Jr, Janowczyk A, Madabhushi A. An oral cavity squamous cell carcinoma quantitative histomorphometric-based image classifier of nuclear morphology can risk stratify patients for disease-specific survival. Mod Pathol. 2017 Dec;30(12):1655-65.
43. Ashizawa K, Yoshimura K, Johno H, Inoue T, Katoh R, Funayama S, et al. Construction of mass spectra database and diagnosis algorithm for head and neck squamous cell carcinoma. Oral Oncol. 2017 Dec;75:111-9.
44. Grillone GA, Wang Z, Krisciunas GP, Tsai AC, Kannabiran VR, Pistey RW, et al. The color of cancer: margin guidance for oral cancer resection using elastic scattering spectroscopy. Laryngoscope. 2017 Sep;127 Suppl 4(Suppl 4):S1-9.
45. Halicek M, Lu G, Little JV, Wang X, Patel M, Griffith CC, et al. Deep convolutional neural networks for classifying head and neck cancer using hyperspectral imaging. J Biomed Opt. 2017 Jun;22(6):60503.
46. Ma L, Lu G, Wang D, Wang X, Chen ZG, Muller S, et al. Deep learning based classification for head and neck cancer detection with hyperspectral imaging in an animal model. Proc SPIE Int Soc Opt Eng. 2017 Feb;10137:101372G.
47. Lu G, Wang D, Qin X, Muller S, Wang X, Chen AY, et al. Detection and delineation of squamous neoplasia with hyperspectral imaging in a mouse model of tongue carcinogenesis. J Biophotonics. 2018 Mar;11(3):e201700078.
48. Lu G, Little JV, Wang X, Zhang H, Patel MR, Griffith CC, et al. Detection of head and neck cancer in surgical specimens using quantitative hyperspectral imaging. Clin Cancer Res. 2017 Sep;23(18):5426-36.
49. Lin J, Clancy NT, Qi J, Hu Y, Tatla T, Stoyanov D, et al. Dual-modality endoscopic probe for tissue surface shape reconstruction and hyperspectral imaging enabled by deep neural networks. Med Image Anal. 2018 Aug;48:162-76.
50. Halicek M, Dormer JD, Little JV, Chen AY, Myers L, Sumer BD, et al. Hyperspectral imaging of head and neck squamous cell carcinoma for cancer margin detection in surgical specimens from 102 patients using deep learning. Cancers (Basel). 2019 Sep;11(9):1367.
51. Fei B, Lu G, Wang X, Zhang H, Little JV, Patel MR, et al. Label-free reflectance hyperspectral imaging for tumor margin assessment: a pilot study on surgical specimens of cancer patients. J Biomed Opt. 2017 Aug;22(8):1-7.
52. Halicek M, Little JV, Wang X, Chen AY, Fei B. Optical biopsy of head and neck cancer using hyperspectral imaging and convolutional neural networks. J Biomed Opt. 2019 Mar;24(3):1-9.
53. Zhang L, Wu Y, Zheng B, Su L, Chen Y, Ma S, et al. Rapid histology of laryngeal squamous cell carcinoma with deep-learning based stimulated Raman scattering microscopy. Theranostics. 2019 Apr;9(9):2541-54.
54. Halicek M, Little JV, Wang X, Patel M, Griffith CC, Chen AY, et al. Tumor margin classification of head and neck cancer using hyperspectral imaging and convolutional neural networks. Proc SPIE Int Soc Opt Eng. 2018 Feb;10576:1057605.
55. Daniels K, Gummadi S, Zhu Z, Wang S, Patel J, Swendseid B, et al. Machine learning by ultrasonography for genetic risk stratification of thyroid nodules. JAMA Otolaryngol Head Neck Surg. 2019 Oct;146(1):1-6.
56. Parmar P, Habib AR, Mendis D, Daniel A, Duvnjak M, Ho J, et al. An artificial intelligence algorithm that identifies middle turbinate pneumatisation (concha bullosa) on sinus computed tomography scans. J Laryngol Otol. 2020 Apr;134(4):328-31.
57. Murata M, Ariji Y, Ohashi Y, Kawai T, Fukuda M, Funakoshi T, et al. Deep-learning classification using convolutional neural network for evaluation of maxillary sinusitis on panoramic radiography. Oral Radiol. 2019 Sep;35(3):301-7.
58. Lai YH, Tsao Y, Lu X, Chen F, Su YT, Chen KC, et al. Deep learning-based noise reduction approach to improve speech intelligibility for cochlear implant recipients. Ear Hear. 2018 Jul/Aug;39(4):795-809.
59. Healy EW, Yoho SE, Chen J, Wang Y, Wang D. An algorithm to increase speech intelligibility for hearing-impaired listeners in novel segments of the same noise type. J Acoust Soc Am. 2015 Sep;138(3):1660-9.
60. Erfanian Saeedi N, Blamey PJ, Burkitt AN, Grayden DB. An integrated model of pitch perception incorporating place and temporal pitch codes with application to cochlear implant research. Hear Res. 2017 Feb;344:135-47.
61. Guerra-Jimenez G, Ramos De Miguel A, Falcon Gonzalez JC, Borkoski Barreiro SA, Perez Plasencia D, Ramos Macias A. Cochlear implant evaluation: prognosis estimation by data mining system. J Int Adv Otol. 2016 Apr;12(1):1-7.
62. Lai YH, Chen F, Wang SS, Lu X, Tsao Y, Lee CH. A deep denoising autoencoder approach to improving the intelligibility of vocoded speech in cochlear implant simulation. IEEE Trans Biomed Eng. 2017 Jul;64(7):1568-78.
63. Chen J, Wang Y, Yoho SE, Wang D, Healy EW. Large-scale training to increase speech intelligibility for hearing-impaired listeners in novel noises. J Acoust Soc Am. 2016 May;139(5):2604.
64. Gao X, Grayden DB, McDonnell MD. Modeling electrode place discrimination in cochlear implant stimulation. IEEE Trans Biomed Eng. 2017 Sep;64(9):2219-29.
65. Hajiaghababa F, Marateb HR, Kermani S. The design and validation of a hybrid digital-signal-processing plug-in for traditional cochlear implant speech processors. Comput Methods Programs Biomed. 2018 Jun;159:103-9.
66. Ramos-Miguel A, Perez-Zaballos T, Perez D, Falconb JC, Ramosb A. Use of data mining to predict significant factors and benefits of bilateral cochlear implantation. Eur Arch Otorhinolaryngol. 2015 Nov;272(11):3157-62.
67. Powell ME, Rodriguez Cancio M, Young D, Nock W, Abdelmessih B, Zeller A, et al. Decoding phonation with artificial intelligence (DeP AI): proof of concept. Laryngoscope Investig Otolaryngol. 2019 Mar;4(3):328-34.
68. Tsui SY, Tsao Y, Lin CW, Fang SH, Lin FC, Wang CT. Demographic and symptomatic features of voice disorders and their potential application in classification using machine learning algorithms. Folia Phoniatr Logop. 2018;70(3-4):174-82.

69. Fang SH, Tsao Y, Hsiao MJ, Chen JY, Lai YH, Lin FC, et al. Detection of pathological voice using cepstrum vectors: a deep learning approach. J Voice. 2019 Sep;33(5):634-41.
70. Fujimura S, Kojima T, Okanoue Y, Shoji K, Inoue M, Hori R. Discrimination of "hot potato voice" caused by upper airway obstruction utilizing a support vector machine. Laryngoscope. 2019 Jun; 129(6):1301-7.
71. Rameau A. Pilot study for a novel and personalized voice restoration device for patients with laryngectomy. Head Neck. 2020 May; 42(5):839-45.
72. Zhang L, Fabbri D, Upender R, Kent D. Automated sleep stage scoring of the Sleep Heart Health Study using deep neural networks. Sleep. 2019 Oct;42(11):zsz159.
73. Zhang X, Xu M, Li Y, Su M, Xu Z, Wang C, et al. Automated multimodel deep neural network for sleep stage scoring with unfiltered clinical data. Sleep Breath. 2020 Jun;24(2):581-90.
74. Zhang L, Wu H, Zhang X, Wei X, Hou F, Ma Y. Sleep heart rate variability assists the automatic prediction of long-term cardiovascular outcomes. Sleep Med. 2020 Mar;67:217-24.
75. Yao J, Zhang YT. The application of bionic wavelet transform to speech signal processing in cochlear implants using neural network simulations. IEEE Trans Biomed Eng. 2002 Nov;49(11):1299-309.
76. Nemati P, Imani M, Farahmandghavi F, Mirzadeh H, Marzban-Rad E, Nasrabadi AM. Artificial neural networks for bilateral prediction of formulation parameters and drug release profiles from cochlear implant coatings fabricated as porous monolithic devices based on silicone rubber. J Pharm Pharmacol. 2014 May;66(5):624-38.
77. Middlebrooks JC, Bierer JA. Auditory cortical images of cochlear-implant stimuli: coding of stimulus channel and current level. J Neurophysiol. 2002 Jan;87(1):493-507.
78. Charasse B, Thai-Van H, Chanal JM, Berger-Vachon C, Collet L. Automatic analysis of auditory nerve electrically evoked compound action potential with an artificial neural network. Artif Intell Med. 2004 Jul;31(3):221-9.
79. Botros A, van Dijk B, Killian M. AutoNR: an automated system that measures ECAP thresholds with the Nucleus Freedom cochlear implant via machine intelligence. Artif Intell Med. 2007 May; 40(1):15-28.
80. van Dijk B, Botros AM, Battmer RD, Begall K, Dillier N, Hey M, et al. Clinical results of AutoNRT, a completely automatic ECAP recording system for cochlear implants. Ear Hear. 2007 Aug;28(4): 558-70.
81. Gartner L, Lenarz T, Joseph G, Buchner A. Clinical use of a system for the automated recording and analysis of electrically evoked compound action potentials (ECAPs) in cochlear implant patients. Acta Otolaryngol. 2010 Jun;130(6):724-32.
82. Nemati P, Imani M, Farahmandghavi F, Mirzadeh H, Marzban-Rad E, Nasrabadi AM. Dexamethasone-releasing cochlear implant coatings: application of artificial neural networks for modelling of formulation parameters and drug release profile. J Pharm Pharmacol. 2013 Aug;65(8):1145-57.
83. Zhang J, Wei W, Ding J, Roland JT Jr, Manolidis S, Simaan N. Inroads toward robot-assisted cochlear implant surgery using steerable electrode arrays. Otol Neurotol. 2010 Oct;31(8):1199-206.
84. Chang CH, Anderson GT, Loizou PC. A neural network model for optimizing vowel recognition by cochlear implant listeners. IEEE Trans Neural Syst Rehabil Eng. 2001 Mar;9(1):42-8.
85. Castaneda-Villa N, James CJ. Objective source selection in blind source separation of AEPs in children with cochlear implants. Conf Proc IEEE Eng Med Biol Soc. 2007;2007:6224-7.
86. Desmond JM, Collins LM, Throckmorton CS. Using channel-specific statistical models to detect reverberation in cochlear implant stimuli. J Acoust Soc Am. 2013 Aug;134(2):1112-20.
87. Kim JW, Kim T, Shin J, Lee K, Choi S, Cho SW. Prediction of apnea-hypopnea index using sound data collected by a noncontact device. Otolaryngol Head Neck Surg. 2020 Mar;162(3):392-9.
88. Ruiz EM, Niu T, Zerfaoui M, Kunnimalaiyaan M, Friedlander PL, Abdel-Mageed AB, et al. A novel gene panel for prediction of lymph-node metastasis and recurrence in patients with thyroid cancer. Surgery. 2020 Jan;167(1):73-9.
89. Zhong Q, Fang J, Huang Z, Yang Y, Lian M, Liu H, et al. A response prediction model for taxane, cisplatin, and 5-fluorouracil chemotherapy in hypopharyngeal carcinoma. Sci Rep. 2018 Aug;8(1): 12675.
90. Chowdhury NI, Li P, Chandra RK, Turner JH. Baseline mucus cytokines predict 22-item Sino-Nasal Outcome Test results after endoscopic sinus surgery. Int Forum Allergy Rhinol. 2020 Jan;10(1): 15-22.
91. Urata S, Iida T, Yamamoto M, Mizushima Y, Fujimoto C, Matsumoto Y, et al. Cellular cartography of the organ of Corti based on optical tissue clearing and machine learning. Elife. 2019 Jan;8:e40946.
92. Zhao Z, Li Y, Wu Y, Chen R. Deep learning-based model for predicting progression in patients with head and neck squamous cell carcinoma. Cancer Biomark. 2020;27(1):19-28.
93. Essers PBM, van der Heijden M, Verhagen CV, Ploeg EM, de Roest RH, Leemans CR, et al. Drug sensitivity prediction models reveal a link between DNA repair defects and poor prognosis in HNSCC. Cancer Res. 2019 Nov;79(21):5597-611.
94. Ishii H, Saitoh M, Sakamoto K, Sakamoto K, Saigusa D, Kasai H, et al. Lipidome-based rapid diagnosis with machine learning for detection of TGF-β signalling activated area in head and neck cancer. Br J Cancer. 2020 Mar;122(7):995-1004.
95. Patel KN, Angell TE, Babiarz J, Barth NM, Blevins T, Duh QY, et al. Performance of a genomic sequencing classifier for the preoperative diagnosis of cytologically indeterminate thyroid nodules. JAMA Surg. 2018 Sep;153(9):817-24.
96. Stepp WH, Farquhar D, Sheth S, Mazul A, Mamdani M, Hackman TG, et al. RNA oncoimmune phenotyping of HPV-positive p16-positive oropharyngeal squamous cell carcinomas by nodal status. Version 2. JAMA Otolaryngol Head Neck Surg. 2018 Nov;144(11): 967-75.
97. Shew M, New J, Wichova H, Koestler DC, Staecker H. Using machine learning to predict sensorineural hearing loss based on perilymph micro RNA expression profile. Sci Rep. 2019 Mar;9(1):3393.
98. Nam Y, Choo OS, Lee YR, Choung YH, Shin H. Cascade recurring deep networks for audible range prediction. BMC Med Inform Decis Mak. 2017 May;17(Suppl 1):56.
99. Kim H, Kang WS, Park HJ, Lee JY, Park JW, Kim Y, et al. Cochlear implantation in postlingually deaf adults is time-sensitive towards positive outcome: prediction using advanced machine learning techniques. Sci Rep. 2018 Dec;8(1):18004.
100. Bing D, Ying J, Miao J, Lan L, Wang D, Zhao L, et al. Predicting the hearing outcome in sudden sensorineural hearing loss via machine learning models. Clin Otolaryngol. 2018 Jun;43(3):868-74.
101. Lau K, Wilkinson J, Moorthy R. A web-based prediction score for head and neck cancer referrals. Clin Otolaryngol. 2018 Mar;43(4): 1043-9.
102. Wilson MB, Ali SA, Kovatch KJ, Smith JD, Hoff PT. Machine learning diagnosis of peritonsillar abscess. Otolaryngol Head Neck Surg. 2019 Nov;161(5):796-9.
103. Priesol AJ, Cao M, Brodley CE, Lewis RF. Clinical vestibular testing assessed with machine-learning algorithms. JAMA Otolaryngol Head Neck Surg. 2015 Apr;141(4):364-72.
104. Chan J, Raju S, Nandakumar R, Bly R, Gollakota S. Detecting middle ear fluid using smartphones. Sci Transl Med. 2019 May;11(492): eaav1102.
105. Karadaghy OA, Shew M, New J, Bur AM. Development and assessment of a machine learning model to help predict survival among

patients with oral squamous cell carcinoma. JAMA Otolaryngol Head Neck Surg. 2019 May;145(12):1115-20.
106. Mermod M, Jourdan EF, Gupta R, Bongiovanni M, Tolstonog G, Simon C, et al. Development and validation of a multivariable prediction model for the identification of occult lymph node metastasis in oral squamous cell carcinoma. Head Neck. 2020 Aug;42(8):1811-20.
107. Formeister EJ, Baum R, Knott PD, Seth R, Ha P, Ryan W, et al. Machine learning for predicting complications in head and neck microvascular free tissue transfer. Laryngoscope. 2020 Jan 28 [Epub]. https://doi.org/10.1002/lary.28508.
108. Shew M, New J, Bur AM. Machine learning to predict delays in adjuvant radiation following surgery for head and neck cancer. Otolaryngol Head Neck Surg. 2019 Jun;160(6):1058-64.
109. Bur AM, Holcomb A, Goodwin S, Woodroof J, Karadaghy O, Shnayder Y, et al. Machine learning to predict occult nodal metastasis in early oral squamous cell carcinoma. Oral Oncol. 2019 May;92:20-5.
110. Kamogashira T, Fujimoto C, Kinoshita M, Kikkawa Y, Yamasoba T, Iwasaki S. Prediction of vestibular dysfunction by applying machine learning algorithms to postural instability. Front Neurol. 2020 Feb;11:7.
111. Liu YW, Kao SL, Wu HT, Liu TC, Fang TY, Wang PC. Transient-evoked otoacoustic emission signals predicting outcomes of acute sensorineural hearing loss in patients with Meniere's disease. Acta Otolaryngol. 2020 Mar;140(3):230-5.
112. Luo J, Erbe C, Friedland DR. Unique clinical language patterns among expert vestibular providers can predict vestibular diagnoses. Otol Neurotol. 2018 Oct;39(9):1163-71.
113. Wu Q, Chen J, Deng H, Ren Y, Sun Y, Wang W, et al. Expert-level diagnosis of nasal polyps using deep learning on whole-slide imaging. J Allergy Clin Immunol. 2020 Feb;145(2):698-701.
114. Jabez Christopher J, Khanna Nehemiah H, Kannan A. A clinical decision support system for diagnosis of allergic rhinitis based on intradermal skin tests. Comput Biol Med. 2015 Oct;65:76-84.
115. Adnane C, Adouly T, Khallouk A, Rouadi S, Abada R, Roubal M, et al. Using preoperative unsupervised cluster analysis of chronic rhinosinusitis to inform patient decision and endoscopic sinus surgery outcome. Eur Arch Otorhinolaryngol. 2017 Feb;274(2):879-85.
116. Soler ZM, Hyer JM, Rudmik L, Ramakrishnan V, Smith TL, Schlosser RJ. Cluster analysis and prediction of treatment outcomes for chronic rhinosinusitis. J Allergy Clin Immunol. 2016 Apr;137(4):1054-62.
117. Soler ZM, Hyer JM, Ramakrishnan V, Smith TL, Mace J, Rudmik L, et al. Identification of chronic rhinosinusitis phenotypes using cluster analysis. Int Forum Allergy Rhinol. 2015 May;5(5):399-407.
118. Divekar R, Patel N, Jin J, Hagan J, Rank M, Lal D, et al. Symptom-based clustering in chronic rhinosinusitis relates to history of aspirin sensitivity and postsurgical outcomes. J Allergy Clin Immunol Pract. 2015 Nov-Dec;3(6):934-40.
119. Lal D, Hopkins C, Divekar RD. SNOT-22-based clusters in chronic rhinosinusitis without nasal polyposis exhibit distinct endotypic and prognostic differences. Int Forum Allergy Rhinol. 2018 Jul;8(7):797-805.
120. Tomassen P, Vandeplas G, Van Zele T, Cardell LO, Arebro J, Olze H, et al. Inflammatory endotypes of chronic rhinosinusitis based on cluster analysis of biomarkers. J Allergy Clin Immunol. 2016 May;137(5):1449-56.
121. Kim JW, Huh G, Rhee CS, Lee CH, Lee J, Chung JH, et al. Unsupervised cluster analysis of chronic rhinosinusitis with nasal polyp using routinely available clinical markers and its implication in treatment outcomes. Int Forum Allergy Rhinol. 2019 Jan;9(1):79-86.
122. Goldstein CA, Berry RB, Kent DT, Kristo DA, Seixas AA, Redline S, et al. Artificial intelligence in sleep medicine: background and implications for clinicians. J Clin Sleep Med. 2020 Apr;16(4):609-18.
123. Weininger O, Warnecke A, Lesinski-Schiedat A, Lenarz T, Stolle S. Computational analysis based on audioprofiles: a new possibility for patient stratification in office-based otology. Audiol Res. 2019 Nov;9(2):230.
124. Barbour DL, Howard RT, Song XD, Metzger N, Sukesan KA, DiLorenzo JC, et al. Online machine learning audiometry. Ear Hear. 2019 Jul/Aug;40(4):918-26.
125. Wu YH, Ho HC, Hsiao SH, Brummet RB, Chipara O. Predicting three-month and 12-month post-fitting real-world hearing-aid outcome using pre-fitting acceptable noise level (ANL). Int J Audiol. 2016;55(5):285-94.
126. Bramhall NF, McMillan GP, Kujawa SG, Konrad-Martin D. Use of non-invasive measures to predict cochlear synapse counts. Hear Res. 2018 Dec;370:113-9.
127. Rasku J, Pyykko I, Levo H, Kentala E, Manchaiah V. Disease profiling for computerized peer support of Meniere's disease. JMIR Rehabil Assist Technol. 2015 Sep;2(2):e9.
128. Morse JC, Shilts MH, Ely KA, Li P, Sheng Q, Huang LC, et al. Patterns of olfactory dysfunction in chronic rhinosinusitis identified by hierarchical cluster analysis and machine learning algorithms. Int Forum Allergy Rhinol. 2019 Mar;9(3):255-64.
129. Quon H, Hui X, Cheng Z, Robertson S, Peng L, Bowers M, et al. Quantitative evaluation of head and neck cancer treatment-related dysphagia in the development of a personalized treatment deintensification paradigm. Int J Radiat Oncol Biol Phys. 2017 Dec;99(5):1271-8.
130. Jochems A, Leijenaar RT, Bogowicz M, Hoebers FJ, Wesseling F, Huang SH, et al. Combining deep learning and radiomics to predict HPV status in oropharyngeal squamous cell carcinoma. Radiat Oncol. 2018 Apr;127:S504-5.
131. Bao T, Klatt BN, Whitney SL, Sienko KH, Wiens J. Automatically evaluating balance: a machine learning approach. IEEE Trans Neural Syst Rehabil Eng. 2019 Feb;27(2):179-86.