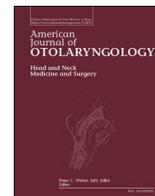




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Is it useful to use computerized tomography image-based artificial intelligence modelling in the differential diagnosis of chronic otitis media with and without cholesteatoma?

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ABSTRACT

Objective: Cholesteatoma is an aggressive form of chronic otitis media (COM). For this reason, it is important to distinguish between COM with and without cholesteatoma. In this study, the role of artificial intelligence modelling in differentiating COM with and without cholesteatoma on computed tomography images was evaluated.

Methods: The files of 200 patients who underwent mastoidectomy and/or tympanoplasty for COM in our clinic between January 2016 and January 2021 were retrospectively reviewed. According to the presence of cholesteatoma, the patients were divided into two groups as chronic otitis with cholesteatoma ($n = 100$) and chronic otitis without cholesteatoma ($n = 100$). The control group ($n = 100$) consisted of patients who did not have any previous ear disease and did not have any active complaints about the ear. Temporal bone computed tomography (CT) images of all patients were analyzed. The distinction between cholesteatoma and COM was evaluated by using 80% of the CT images obtained for the training of artificial intelligence modelling and the remaining 20% for testing purposes.

Results: The accuracy rate obtained in the hybrid model we used in our study was 95.4%. The proposed model correctly predicted 2952 out of 3093 CT images, while it predicted 141 incorrectly. It correctly predicted 936 (93.78%) of 998 images in the COM group with cholesteatoma, 835 (92.77%) of 900 images in the COM group without cholesteatoma, and 1181 (98.82%) of 1195 images in the normal group.

Conclusion: In our study, it has been shown that the differentiation of COM with and without cholesteatoma with artificial intelligence modelling can be made with highly accurate diagnosis rates by using CT images. With the deep learning modelling we proposed, the highest correct diagnosis rate in the literature was obtained. According to the results of our study, we think that with the use of artificial intelligence in practice, the diagnosis of cholesteatoma can be made earlier, it will help in the selection of the most appropriate treatment approach, and the complications can be reduced.

1. Introduction

Chronic otitis media (COM) is inflammation that causes changes such as long-term or permanent perforation, atelectasis, retraction, tympanosclerosis, and cholesteatoma in the middle ear and tympanic membrane [1]. It is divided into subgroups according to the factors playing a role in the etiology and histopathological features. Different degrees of

destruction are seen in the anatomical structures of the middle ear in these subgroups. However, larger and at least twice as many bone destructions are seen in cholesteatoma. Bone destruction is one of the features that make cholesteatoma dangerous. These destructions are an important process that causes the temporal bone and intracranial complications as well as conductive or sensorineural hearing loss [2,3]. In terms of possible complications that may develop, COM, and especially

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COM with cholesteatoma, should be diagnosed and treated as early as possible.

Cholesteatoma is suspected with audiological tests and imaging findings based on the patient's clinical and physical examination findings. Definitive diagnosis is based on surgical findings and histopathological examination. High-resolution computed tomography (HRCT) of the temporal bone is mostly used as an imaging examination in the diagnosis and preoperative planning of COM with and without suspected cholesteatoma [4]. Because of its excellent spatial resolution and ability to identify important anatomical structures, CT is considered the first choice for imaging the middle ear [5]. In temporal bone CT, the presence of bone erosions, aeration problems, and soft tissue density is evaluated. In COM, especially in the presence of cholesteatoma, erosion of adjacent bone structures may occur and surgical intervention may be indicated. However, it is not possible to distinguish cholesteatoma from granulation tissue, hypertrophic and fibrotic mucosa, scar changes, and mucus secretions with this method. Although the presence of cholesteatoma is frequently seen in the attic or sinus tympani region, all types of COM can be seen in different areas of the tympanic cavity, and CT is insufficient in differentiating COM subtypes [6]. In such cases, diffusion-weighted magnetic resonance imaging (DW-MRI), which does not require intravenous contrast material, is an excellent complement to CT for the diagnosis of cholesteatoma. MRI has a high resolution for soft tissue separation. Therefore, MRI is used in the differential diagnosis of soft tissue densities observed on CT. However, even in cases where both imaging tests are performed together, the diagnosis of cholesteatoma cannot be made preoperatively with 100% accuracy. This situation prompts researchers to search for different methods for preoperative diagnosis of cholesteatoma and surgical planning.

Artificial intelligence applications are applications that have increased in popularity in recent years and are used in the diagnosis of many diseases in medicine. In the literature, there are studies using artificial intelligence applications in the diagnosis of many diseases such as otitis media, head and neck squamous cell carcinoma, obstructive sleep apnea, otosclerosis [7–10]. It is aimed to increase the accuracy of preoperative diagnosis and to accelerate the diagnosis process of diseases with computer-aided systems. It is thought that it will be beneficial in minimizing individual errors and easing the workload of physicians by using artificial intelligence. We think that these artificial intelligence-based systems can help general practitioners in diagnosing suspected cholesteatoma in places where ENT and radiology specialists are not available.

In this study, we aimed to evaluate the usability of artificial intelligence modelling using computed tomography images in differentiating COM with and without cholesteatoma.

2. Materials and methods

The files of 200 patients who underwent mastoidectomy and/or tympanoplasty for chronic otitis media in our clinic between January 2016 and January 2021 were reviewed retrospectively. Local ethics committee approval was obtained for the study (approval date: 2021/08–20).

2.1. Creating groups

The patients included in the study were selected from patients who underwent mastoidectomy and/or tympanoplasty for chronic otitis media in our clinic between January 2016 and January 2021. Patients who had an ear operation for any reason, patients who did not have Temporal bone CT taken in our hospital, patients who did not have at least six months postoperative follow-up records, postoperative patients with disease recurrence at at least six months of follow-up and no discharge for at least six months, the middle ear mucosa is completely dry, only simple membrane perforation and completely normal CT patients with were not included in the study. The files of the patients who

were operated on according to these criteria were reviewed retrospectively. In total, the files of 352 patients were reviewed retrospectively. Considering the aforementioned exclusion criteria, the patients were divided into two groups as chronic otitis media with cholesteatoma and chronic otitis media without cholesteatoma, according to the presence of cholesteatoma during the operation. Then, considering the criteria mentioned in both groups, 100 patients were randomly selected from among themselves, and patient groups were formed. Afterward, preoperative computed tomography images of these patients were analyzed. “The control group (n= 100) was formed by using CT images of patients with otalgia etiology, temporomandibular joint disorder, and patients with sudden hearing loss and vertigo etiology who could not take MRI scanned and who reported as completely normal.”

2.2. CT imaging protocol

Axial and coronal reformatted images were obtained in all patients with a multidetector CT scanner (Revolution HD, GE Medical Systems, GE Healthcare, Milwaukee, WI) without intravenous contrast material administration. The temporal bone from the lower edge of the external auditory canal to the upper edge of the petrous bone was scanned. Images were acquired using the parameters 70–120 kVp tube voltage, 150 mA tube current, 0.625 mm section thickness, 25 cm field of view, 512 × 512 matrix size, 0.3 mm reconstruction interval, 0.848 pitch factor, exposure time 1,4 s.

2.3. Data set preparation

Bone window settings (window width; 3000 Hounsfield Units (HU), window level; 400–500 HU) were created in the axial and coronal planes of the CT image for each patient. Then, random 8–10 images were recorded in JPEG format containing the middle ear and mastoid bone using the same workstation (Enlil PACS Q/R server). A similar number of images were taken from each patient to create a more homogeneous data set. Images were prepared blindly by 2 otolaryngologists and 2 radiologists without knowing what their primary disease was. From the patients in our study groups; 998 CT images were evaluated in the COM group with cholesteatoma, 900 CT images in the COM group without cholesteatoma, and 1195 CT images in the control group (Fig. 1).

2.4. Deep models

The study consists of three stages. In the first stage, results were obtained using pre-trained Alexnet, Googlenet, and Densenet201 architectures. In the first step of the study, we obtained results with three deep learning architectures previously trained and accepted in the literature. While these models were being trained, 80% of the images in the data set were used for training, while 20% were used for testing. The first step of the study is given in Fig. 2.

In the first step of the study, results were obtained in three deep learning architectures. In the second step of the study, feature maps of the data in the data set were obtained using these three deep learning architectures [11,12]. These features are classified in machine learning classifiers. The aim here is to obtain more successful results than the models accepted in the literature. The second step of the study is given in Fig. 3.

In the third step of the study, that is, the proposed hybrid model, Alexnet, Googlenet, and Densenet201 architectures and the features obtained in the 2nd step were combined. These obtained features are classified in the SVM (Support Vector Machine) classifier. The aim here is to make use of the features of the 3 architectures and to minimize the error rate in the images to be classified [13]. As a result of this improvement, it is aimed to minimize the error to be made in the diagnosis process. The proposed hybrid model is presented in Fig. 4.

In the proposed model, it is aimed to diagnose temporal bone CT images with minimum error. Using temporal bone CT images, the

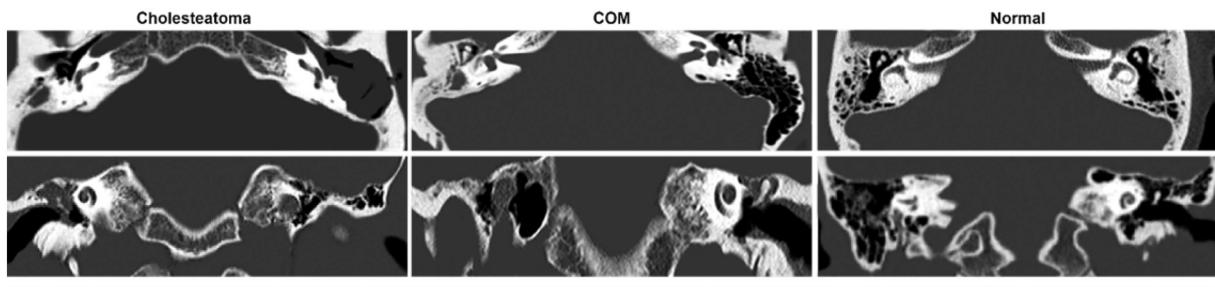


Fig. 1. Examples from the dataset.

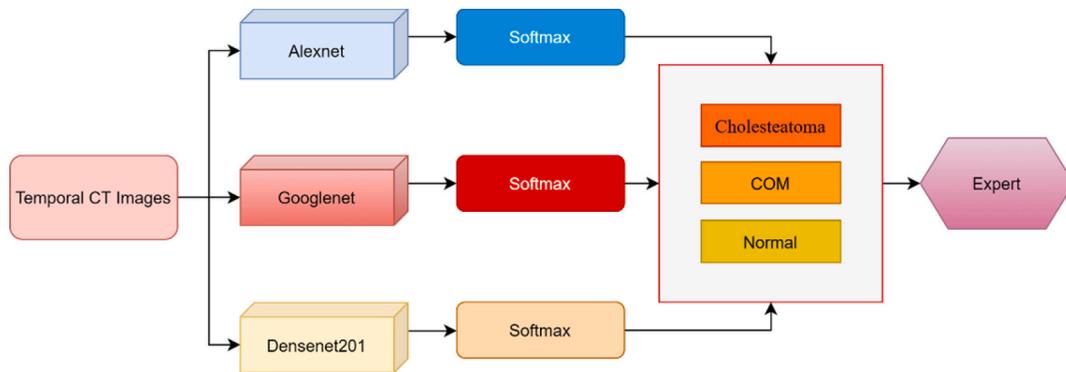


Fig. 2. Results with original architectures.

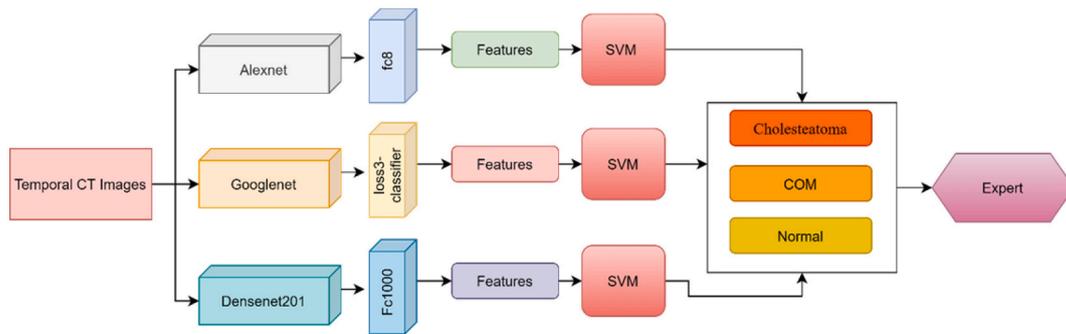


Fig. 3. Classification of features obtained with deep learning architectures in the Support Vector Machine (SVM) classifier.

proposed model divides the images into 3 classes: COM with cholesteatoma, COM without cholesteatoma, and normal.

All of the key performance measurement metrics accepted in machine learning models are calculated using Confusion Matrix [14]. Table 1 gives the confusion matrix.

3. Results

In our study, the diagnosis and classification of COM with cholesteatoma, COM without cholesteatoma, and normal group images were made using 3093 preoperative CT images of 300 patients, 100 from each group.

The results obtained in the pre-trained deep learning models are given in Table 2.

In the classification made using deep learning models, the highest accuracy rate was obtained in Alexnet architecture with 88.05%. Alexnet architecture correctly predicted 545 of the 619 test images and incorrectly predicted 74 of them. The most successful group was the COM group without cholesteatoma with an accuracy of 99.44%. The

accuracy value obtained in the Googlenet architecture is 84.65%. The Googlenet architecture predicted 524 of the 619 test images correctly, while it predicted 95 incorrectly. The accuracy value obtained in the Densenet201 architecture is 91.76%. Densenet201 architecture correctly predicted 568 out of a total of 619 test images, and incorrectly predicted 51.

With the deep learning architectures used in the second step of the study, the feature maps of the images in the data set were extracted and classified in the SVM classifier, which is one of the machine learning classifiers. The results obtained are given in Table 3.

As can be seen in Table 3, the highest accuracy rate was obtained by classifying the features obtained from the Densenet201 architecture in the SVM classifier. The accuracy value in this architecture was 92.4%. Densenet201 architecture correctly predicted 2858 of 3093 ear tomography images, while it predicted 235 images incorrectly. After Densenet201 architecture, the highest accuracy value was obtained in Alexnet architecture with 90%. On the other hand, Alexnet architecture correctly predicted 2847 out of 3093 CT images, while it predicted 246 images incorrectly. The accuracy value obtained in Googlenet, another

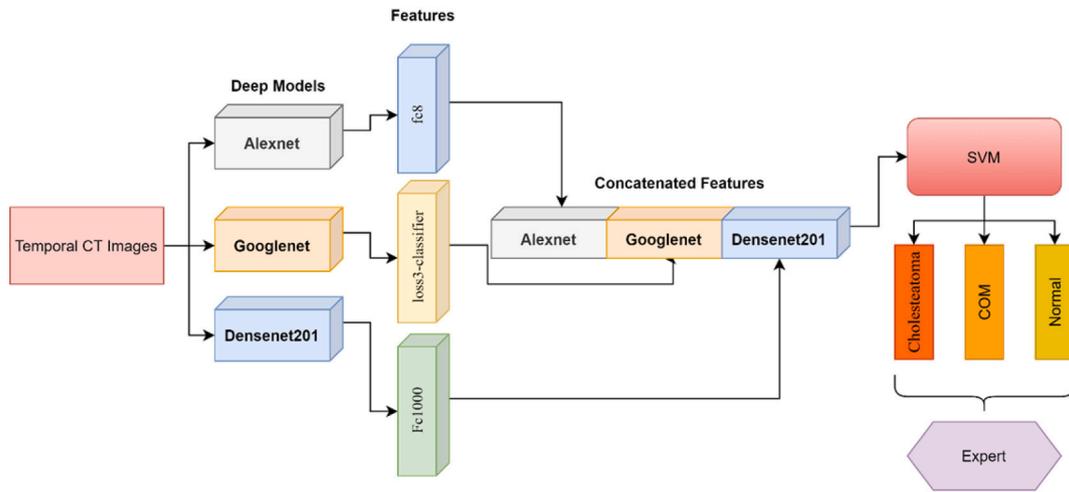


Fig. 4. Proposed approach.

Table 1
Confusion matrix.

	X	Y
X	TP	FP
Y	FN	TN

TP (True Positive): Correctly predicting X image as X,
 FP (False Positive): Incorrect prediction of X image as Y,
 FN (False Negative): Incorrect prediction of Y image as X,
 TN (True Negative): Correct prediction of Y image as Y.

architecture used in the study, was 88.3%. The Googlenet architecture correctly predicted 2732 of the 3093 CT images, and incorrectly predicted 361. The results we obtained in the second step of the study are more successful than the results obtained in the original architectures.

In the third step of the study, that is, in the proposed hybrid model,

deep learning architectures were used for feature extraction. Then, the features obtained in the 3 deep learning models were combined. Thanks to these combined features, it is aimed to increase the success rate of CT images in diagnosis. The confusion matrix obtained when these combined features are classified in the SVM classifier is given in Table 4.

The accuracy value obtained in the proposed hybrid model was 95.4%. The proposed model correctly predicted 2952 out of 3093 CT images, while it predicted 141 incorrectly. Among the methods used, the highest accuracy value was obtained in the proposed hybrid model. The proposed hybrid model correctly predicted 936 of 998 COM images with cholesteatoma, 835 of 900 COM images without cholesteatoma, and 1181 of 1195 normal images. Other performance criteria of the proposed model are given in Table 5.

The area under the curve AUC curves obtained in the proposed model is given in Fig. 5.

Table 2
Results from deep learning models.

		Alexnet	Googlenet	Densenet201
True Class	1	135	137	184
	2	47	52	12
	3	18	11	4
True Class	2	179	160	157
	3	1	1	2
	3	231	227	227
		1 2 3	1 2 3	1 2 3
		Predicted Class	Predicted Class	Predicted Class

1.COM with cholesteatoma, 2.COM without cholesteatoma, 3.Normal.

Table 3
Deep models + SVM.

		Alexnet + SVM (%92)	Googlenet + SVM (%88.3)	Densenet201 +SVM (%92.4)
True Class	1	891	845	903
	2	86	126	83
	3	21	27	12
True Class	2	801	752	798
	3	13	19	9
	3	1155	1135	1157
		1 2 3	1 2 3	1 2 3
		Predicted Class	Predicted Class	Predicted Class

1.COM with cholesteatoma, 2.COM without cholesteatoma, 3.Normal.

Table 4
Confusion matrix of the proposed approach.

		Proposed Approach + SVM (%95.4)		
True Class	1	936	55	7
	2	60	835	5
3	7	7	1181	
		1	2	3
		Predicted Class		

1.COM with cholesteatoma, 2.COM without cholesteatoma, 3.Normal.

Table 5
Performance metrics of the proposed approach.

	Accuracy	Sensitivity	Specificity
COM with cholesteatoma	93.78%	93.32%	97.03
COM without cholesteatoma	92.77%	93.08%	97.48
Normal	98.82%	98.99%	99.26%

4. Discussion

Chronic otitis media is one of the most important causes of preventable and treatable hearing loss, in which inflammation causes destruction in the middle ear bones. It can be divided into two as with cholesteatoma and without cholesteatoma. Cholesteatoma consists of keratinized squamous epithelium and can destroy middle ear structures [15]. Both COM with cholesteatoma and COM without cholesteatoma can cause ossicular chain damage. Destruction of bones is one of the most important processes of COM, and early diagnosis is important to prevent possible complications.

CT has a high sensitivity of up to 88% in detecting middle ear disease; however, the specificity of recognizing that these lesions are caused by cholesteatoma is lower [16].

A valuable complement to the information obtained in these situations where CT is insufficient is DW-MRI. With DW-MRI, scar tissue, inflamed granulation tissue and cholesteatoma can be differentiated from each other with high sensitivity (91%) and specificity (92%) (20). Thanks to its high sensitivity and specificity, DW-MRI is used in the investigation of recurrences of cholesteatoma tissue, especially in the postoperative period, and is seen as an alternative to second-look surgeries by many researchers. However, the inability of MRI to clearly visualize the bone tissue compared to CT and the lack of anatomical details cause the localization of the cholesteatoma to not be determined.

While COM can usually be treated conservatively, accurate preoperative diagnosis of both diseases is of high clinical importance, since cholesteatoma is treated surgically [17]. For this reason, researchers have turned to studies in order to differentiate COM with cholesteatoma and COM without cholesteatoma with higher success through imaging. In a study in the literature, it was suggested that the use of contrast-enhanced CT for the diagnosis of cholesteatoma was beneficial, while in another study. Profant et al. suggested non-echo planar DW-MRI as a valid method in the diagnosis and follow-up of cholesteatoma [18]. In another study, it was reported that Hounsfield Unit (HU) measurements on CT were significantly different between cholesteatoma and inflammatory tissue, and cholesteatoma could be diagnosed with this method [19]. With Radiomics analysis, a new method that has gained popularity recently, it has been possible to distinguish different tumor tissues in the body [20,21]. In a study using CT images, it was reported that COM with cholesteatoma and COM without cholesteatoma could be differentiated with 89% accuracy by radiomics analysis [22]. In another study, it was reported that CT and DW-MRI fusion images were useful for the diagnosis of cholesteatoma in patients with suspected cholesteatoma recurrences [23].

In our study, we aimed to differentiate COM with cholesteatoma and COM without cholesteatoma with a higher accuracy rate by using artificial intelligence models on CT images in the preoperative period. To our knowledge, the only study in the literature in which artificial intelligence was used on CT images to differentiate COM with cholesteatoma and COM without cholesteatoma was Wang et al. [24]. In this study, the correct prediction rates of artificial intelligence and specialist physicians were compared in COM with cholesteatoma, COM without cholesteatoma, and normal ear groups, and correct prediction rates were found higher in all groups in artificial intelligence. In this study, while the general accuracy of the artificial intelligence model is 76.7%, it is 73.8% for specialist doctors. It has been reported that artificial intelligence has a higher accuracy of 75% vs. 70% in the COM group, and 76% vs. 53% in the cholesteatoma group, compared to specialist doctors. In our study, the rate of correct prediction was found to be higher in all groups with 95.4%. The correct prediction rate was 92.77% in the COM group without cholesteatoma, 93.78% in the COM group with cholesteatoma, and 98.82% in the normal group. Wang et al. [24] showed higher accuracy in estimation compared to his study. Since we prefer a hybrid structure in our proposed model, the performance criteria of our model are higher. One of the main reasons for the high performance of our model is that we have benefited from the accumulation of three architectures. Later, the features we obtained with the three architectures were optimized and our model was aimed to run faster.

Three pre-trained models were used in the study. The first of these models is Alexnet. The Alexnet architecture, the first architecture used in the study, was the winner of the Imagenet ILSVRC competition held in

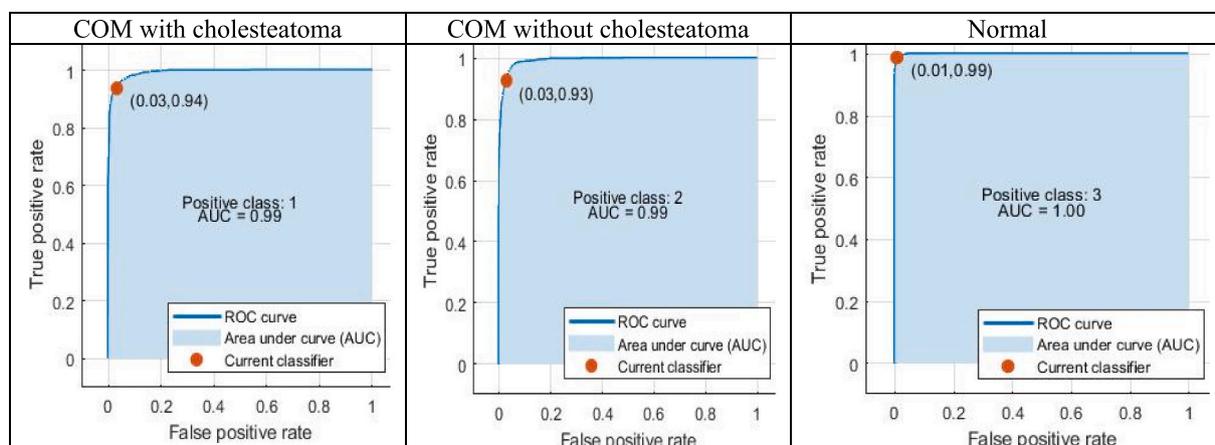


Fig. 5. In the proposed model, the AUC value of COM with cholesteatoma and COM without cholesteatoma is 0.99, while the AUC of the Normal class is 1.

2012. Alexnet architecture increased the classification accuracy from 74.3% to 83.6% in the ImageNet ILSVRC competition held in 2012. This model is a very deep and powerful model running on the GPU architecture [25].

The second model used in the study is Googlenet. The Googlenet architecture was the winner of the Imagenet ILSVRC competition in 2014 with an error rate of 6.66%. This model is one of the first architectures to move away from ordering layers in a sequential structure [26].

The third model used in the study is Densenet201. Huang et al. This architecture, proposed by, is logically similar to the Resnet architecture [27]. But the generated activation functions are simply put together rather than added to later layers. Therefore, in addition to activations from previous layers, the original data is retained in all types of layers.

With these results, it has been shown that using artificial intelligence modelling and CT images, it is possible to differentiate COM with cholesteatoma and COM without cholesteatoma with high success rates. However, there are some limitations to our study. The modelling in this study can only be used in primary cholesteatoma cases. Therefore, an evaluation cannot be made for recurrent cholesteatoma cases. One of the limitations of our study is the small number of patients. We think that by increasing the number of patients in the study groups, more CT cross-sections can be obtained, and artificial intelligence can be trained more, and higher accuracy rates can be obtained.

As a result, it has been shown that the diagnosis of cholesteatoma can be made earlier with the high accuracy rates obtained in this study. Thus, we think that aggressive complications such as ossicular chain destruction, facial paralysis, hearing loss, and intracranial events can be prevented. In addition, important contributions can be made in terms of both patient health and the health economy. In addition, we think that it will be possible to diagnose cholesteatoma more accurately and earlier, by minimizing the error rates of ENT and radiologists using artificial intelligence. In addition, all diagnoses made with this modelling are fully reproducible. In other words, high diagnostic consistency increases the use of modelling in the clinical setting. In addition, the fact that it does not require additional imaging examinations such as MRI in order to make a diagnosis will prevent cost and time loss. In addition, we intend to move our work to the next segment with the developing technology. In our next study, it is among our goals to strengthen our model with more patients, to create an internet-based system and to alleviate the workload of experts.

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Ethics approval

The protocol of this study was approved by the Firat University Ethics Committee, Turkey (approval nr. 2021/08-20).

Declaration of competing interest

The authors declare that there is no conflict of interest in the study.

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