Archives of Surgical Research | Review Article

Role of Artificial Intelligence in Management of Thyroid Nodule

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IMPORTANCE Prevalence of thyroid diseases is increasing globally. Detection of thyroid nodules using diagnostic imaging relies heavily on physicians' expertise. Development of artificial intelligence (AI) approaches has led to significant advancement in visual identification. Machine learning and radiomic are approaches of artificial intelligence that have the potential to improve clinical diagnosis. AI approaches can be used to detect biological anomalies, diagnose neoplasms, and predict response to therapy. However, diagnostic accuracy of these approaches is still a point of contention. Aim of this article is to give a general review of aspects, limits, and key challenges in use of artificial intelligence for thyroid imaging. Core principles and process parameters of learning algorithms, cavernous learning, and technological frontier as well as data processing criteria, distinction between AI approaches, and their constraints are discussed in this article.

KEYWORDS Artificial intelligence, thyroid nodule, imaging evaluation, radiomic, diagnosis.

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Review Article

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Role of medical imaging in healthcare has shifted from a screening tool to a significant contributor in early diagnosis and assessment of illness, patient management, and surveillance[1]. Medical imaging is a non-invasive, reproducible method of obtaining information about properties of human tissues[2]. In recent years, advancements in medical imaging focused on equipment modification (hardware) and analytical techniques. Primary application of medical imaging in clinical practice is qualitative evaluation of anatomical locations[3]. Furthermore, images characterized by a large amount of statistical information, and quantitative assessment create ability to detect possible links between statistical information included in digital photos and tissue pathology. Statistical method aims to extract details from images obtained through magnetic resonance imaging (MRI), computed tomography (CT), ultrasound imaging (US), and positron emission tomography (PET), which otherwise pose difficulty in quantifying health outcomes with naked eye observation[4].

Image characteristic analysis in medical imaging has become a topic of interest[5]. Attributes of imaging are evaluated in most studies with goal of detecting and diagnosing aberrant locations inside body tissues. Computer-aided detection (CAD) and computer-aided diagnosing (CADx) technologies are terms used to describe these operations. Doctors employ CAD assessment output in identifying lesions or making diagnoses with aim of boosting diagnostic performance and decreasing picture-processing duration[6].

Radiomics has emerged as a promising world of clinical study because of a more comprehensive development linked with statistical medical image analysis[7]. Radiomics tries to obtain relevant information regarding tissue damage and reaction through large set of numerical parameters of personalized medication[8]. Artificial intelligence (AI) technology is used to achieve partial or full automation of different aspects of medical image processing procedures. A complete understanding of its functioning principles is required to create effective forecasting analytics and customized treatments[9]. Goal of this article is to study benefits and drawbacks of many AI-based methodologies used to assess pathological status of thyroid[10].

RELATIONSHIP BETWEEN ARTIFICIAL INTELLIGENCE AND MEDICAL IMAGING

In 1950s artificial intelligence (AI) described an area of computer engineering which used statistical procedures requiring human cognitive processes to execute activities [11]. AI applications have had tremendous growth over the last decade because of advances in computer capacity and datasets accessibility. Artificial intelligence is used in healthcare to construct models that may increase diagnostic performance, prediction, and medical imaging interpretation[12]. In the subsequent sections, we will go through two separate machine learning (ML) approaches that are used for assessment of diagnostic imaging[13].

MACHINE LEARNING

Machine learning (ML), named by Arthur Samuel[14] is a type of artificial intelligence in which computers are trained to predict outcomes based on exposure to previous examples and observations. Machine learning algorithms are essential component of CAD systems and radiomics research. Unsupervised learning and supervised learning are types of machine learning. A tagged database or a set containing input information with matching output (labels) is required for reinforcement. Unsupervised machine learning works without labelling input sequence. This machine learning technique uses patterns and regularities in raw data to divide it into subgroups with similar attributes[15]. We concentrated on reinforcement methods in this review article because it is the most common strategy used to analyze medical images[16].

Output label can be used to differentiate benign and malignant tumors, categorize diseases, or study response to treatment, such as recurrence or longevity. Prediction model distinguish between two types of machine learning tasks: categorization and extrapolation. In classification techniques, a binary classifier is used to judge from a narrow and distinct set of options, such as determining benign and malignant tumors. Prediction model is used to estimate continuous output results, such as disease intensity evaluation. Machine learning algorithms are used in CAD systems for categorization. This technique is employed as a stage in radiomic assessment[17].

A guided machine-learning model has two main phases: training and implementation. Prediction model is trained by using sets of input photos and their corresponding labels. Qualified physicians draw region of interest (ROI) from source images either physically or semi-automatically. Subsequently, a series of feature representation is retrieved, such as morphological and grey threshold characteristics. Identification and evaluation of picture characteristics in ML algorithms is done manually by an experienced personal. It is a necessary step in determination of significant features linked to clinical outcome. Characteristics employed in design tools are used in diagnosing lesions[18]. These features are then fed to the machine-learning model.

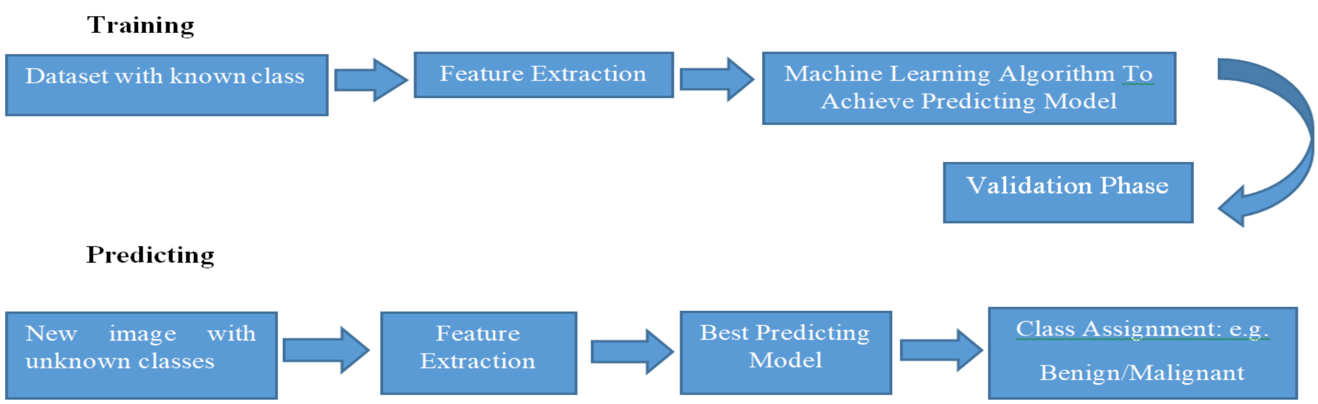

Figure 1. Schematic flowchart of the machine learning model implementation and application for medical image classification purpose.

Logistic regression analysis supports vector machine. Regression trees, and artificial neural are common examples of functionality supervised learning methods. Support vector machine (SVM) approach is extensively employed in biological binary classifier issues and it is an example of these functionality ML techniques. SVM is a classification method used to find maximum margin or higher dimensional space to optimize separation distance between two classifications. Minimization of boundary condition enhances distance between the two categories, classifier's generalization ability and matching efficiency.

This framework is then used to describe input values with undetermined label in the testing stage. It is worth noting that continuing to practice fully specifies classifier's conditional probability, but testing set is merely used to assess effectiveness of the algorithm. It can create a design that fits adequately once implemented to a new dataset.

Supervised learning should be vastly adequate. Testing set ought to be reasonably extensive to provide a consistent and trustworthy assessment of model's effectiveness. A k-fold cross-validation framework[19] is generally used because it's hard to fulfil requirements in medicine by simply partitioning existing evidence into training and testing sets. Database is partitioned into K equal-sized subgroups for K-fold testing data. Model trained on (k 1) observations with one subset is kept for testing. The process is rehashed k times among each fraction employed once as a testing dataset. Model's total effectiveness is then evaluated as standard result across K iterations. Forecasting is generated from minimal datasets. Machine learning algorithms are useful in clinical picture assessment. Furthermore, these approaches are frequently subjected to interpretation for obtaining information regarding a form of anticipation.

Description	Cohort	Method	Performance	Reference
Classification Benign/ Malignant Thyroid Nodules US	106 Patients	SVM	Accuracy 82% Sensitivity 91% Specificity78%	20
Classification Benign/ Malignant Thyroid Nodules US	286 Patients	SVM	Accuracy 75.9% Sensitivity 90.4% Specificity 58.8%	21
Classification Benign/ Malignant Thyroid Nodules US	826 Patients	SVM	Accuracy 83% Sensitivity 86.1% Specificity 82.7%	22
Classification Benign/ Malignant Thyroid Nodules US	50 Patients	SVM	Accuracy 84.6% Sensitivity 80% Specificity 88.1%	23
Classification Benign/ Malignant Thyroid Nodules US	118 Patients	SVM	Accuracy 98.3% Sensitivity N/A Specificity N/A	24

Table 1. Machine learning (ML) based studies.

Professionals should execute preliminary phase of the process, such as defining attributes to be retrieved from photos and selecting clinical objects of interest. Furthermore, all guided machine-learning approaches are influenced by imbalanced datasets. It occurs when prediction model precisely understands training dataset but fails to fit fresh data from validation dataset. Nevertheless, this problem can be mitigated by using a cross-validation setup and feature selection technique.

DEEP LEARNING

Deep learning (DL), named by Rina Dechter in 1986, is a new approach of machine learning (ML) established through growth of convolutional neural networks. DL is based on networks of computing elements, such as neural units stacked in levels, that retrieve greater features from input information. These frameworks automatically analyze exclusion characteristics from information, thereby, allowing to mimic complex non-linear relationships with enhanced precision. Unlike previous feature-based ML techniques, DL can accomplish diagnostic mechanization without need for human interaction. DL methods are used for detection and evaluation of tissue lesions, and investigation of pathogenicity. Amongst numerous DL architectures is LeCun's introduction of convolutional neural networks (CNNs)[25].

CNNs maintain spatial relations in 2D data and exceed alternative topologies in picture pattern classification which is commonly used in object recognition and computer vision. CNN's feed is organized in a grid layout and analyzed through convolution operation layers to maintain associations. Based on characteristics collected mechanically by convolution section, the layers are often linked intrinsically and it is considered multi-layer discernment classifier. The system is designed to spot similarities and responses to a set of labelled training data. Network weights is tweaked during learning until connections are detected by system to reflect decent training data. System uses additional data in testing set to create forecasts[26].

Convolution is a space-invariant continuous procedure on 2D grids analogous to filtering images. Filters are dragged across source images and results are multiplied by image pixel values. They are combined to measure value of extracted feature map's associated place. Figure 3a provides an illustration of Fourier procedure. CNN hyper parameters including quantity and quality of filtration are often not tuned during acquisition. Increasingly efficient networks raise danger of overloading with greater number of variables to tune which result from bigger filters [27].

Activated function is applied component by component to calculated combination of output, utilizing map as an input for next step of system. Rectified linear unit (ReLU) is amongst the most utilized kernel function and has shown to speed up learning process statistically[28]. Affirmative inputs are linear and map unmodified to the next level while lower values are blocked. ReLU can be stated mathematically (x) = max (0, x) (4) where x is a result gathered from last layer's activity[29].

Some clustering algorithms consider pooled procedures. This procedure takes tiny sections of input map in account and returns a single statistic. It lowers dimension of feature map and number of pixels to be analyzed in network's subsequent layers[30]. Neuron stimulation values indicate increasingly higher and significantly bigger fractal geometry in input as we travel further in the networks and demand lesser spatial resolution. A completely connected layer describes final component of CNN model, i.e., each neural component in current layer is linked to neural unit in next layer. The subset of features is compressed into a column vector and linked to one or even more fully associated levels. Features extracted from last fully linked layer represent an array of unnormalized probability. Soft-max function is defined as CNN's last convolution layer which convert values of k vector to a range of values (zero;1).

Neural units that make output layer of CNN represent chances for each category. Analysis of relevant literature points at a growing interest in using DL for medical image representation[31]. Simplified functionality ML algorithms, such as SVM methods, are easier to interpret and much more efficient for specified set of image elements. Set back in using DL is requirement of enormous datasets for training the model. Medical datasets in United States are scarce compared with standard datasets in other fields. Numerous investigations looked in pre-trained architecture constructed with ImageNet (a huge and labelled library of low-resolution color photographs) to meet information requirement[32]. Till date, there is no DL architecture on high-resolution medical images. Therefore, a large collection of medical images is required to improve performance.

Description	Cohort	Method	Performance	Reference
Malignancy risk thyroid nodules	757	CNN	Accuracy 85.1% Sensitivity 81.8% Specificity 86.1%	33
Classification Benign/ Malignant Thyroid Nodules US	1396	CNN	Accuracy 82% Sensitivity 85% Specificity 78%	34
Classification Benign/ Malignant Thyroid Nodules US	695	CNN	Accuracy 80.3% Sensitivity 80.6% Specificity 80.1%	35
Classification Benign/ Malignant Thyroid Nodules US	221	CNN	Accuracy 75% Sensitivity 84.9% Specificity 69%	36
Nodule detection predicted malignancy level stratification	1230	CNN	Accuracy N/A Sensitivity 87% Specificity 52%	37
Classification Benign/ Malignant Thyroid Nodules US	519	CNN	Accuracy 87.3% Sensitivity 90% Specificity 82%	38
Classification Benign/ Malignant Thyroid Nodules US	286	CNN	Accuracy 86% Sensitivity 91% Specificity 80%	21
Classification Benign/ Malignant Thyroid Nodules US	276	CNN	Accuracy 90.3% Sensitivity 90.5% Specificity 89.91%	39
Classification Benign/ Malignant Thyroid Nodules US	17627	CNN	Accuracy 86% Sensitivity 84% Specificity 87%	40
Classification Benign/ Malignant Thyroid Nodules US	592	CNN	Accuracy 96.3% Sensitivity 82.8% Specificity 99.3%	41
Classification Benign/ Malignant Thyroid Nodules US	4782	CNN	Accuracy 83% Sensitivity 82.4% Specificity 84.9%	42

Table 2. Deep learning (DL) studies.

RADIOMIC Radiomic is a new discipline that uses automatic extracting methods for extraction of huge numbers of measured values (200+) from medical imaging. Quantitative imaging is another term for radiomic and it can be applied to any medical image. It is used to treat tumor subareas, metastatic lesions and healthy cells[43].The term feature refers to descriptor of an image, such as parameters generated from grayscale intensity, shape of tumor or healthy tissue. Radiomic is based on machine diagnostic techniques albeit methodological approach and implementations are different. It is about extracting quantifiable features from medical pictures that are linked to biological objectives and clinical relevance. Radiomic uses digital information stored in images to create diagnosing, predicting, and prognosis methods that can help clinicians in judging and arranging more individualized treatment. Primary distinction between radiomic and CAD technologies is the connection that radiomic must establish among current features and progression of tissue lesions to customize treatments[44]. Depending upon AI methodology two procedures are used to undertake radiomic experiments. In traditional or ML-based radiomic characteristics are preset for retrieval, while, in DL-based radiomic characteristics are not specified and retrieved from data autonomously.

Region of interest (ROI) is selected from USG, CT, MR, and/or PET images and subsequently lesion is segmented manually, i.e., delineated with computer-assisted remodeling performed by a skilled practitioner[45]. Picture data is subjected to preprocessing, such as gray-level partitioning, to improve reproducibility of results. Characteristics of spatial interaction between various saturation levels, diverse structures, shape, and links of tissue lesion with surrounding structures are all employed to extract statistical imaging features. Most significant predictive characteristic is subsequently identified using a feature evaluation approach. A characteristic profile, also known as quantitative imaging biomarker, has several benefits with predictive or qualitative research. Selected traits are examined to create categorized models for predicting consequences alone or in conjunction with other data, such as demographics, comorbidities, or genetic data[46].

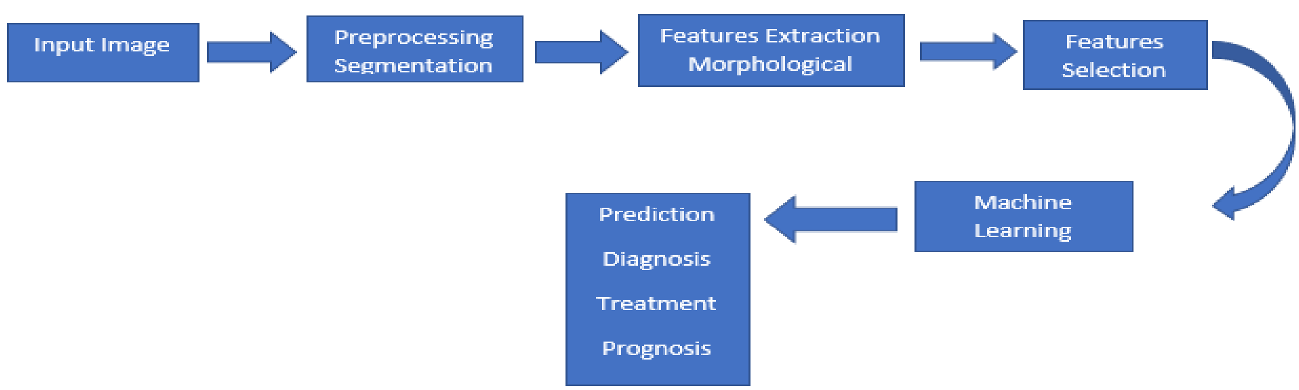

Figure 2. Schematic flowchart of radiomic approach.

Segmentation is an essential requirement in radiomics since many retrieved characteristics are dependent on region of interest[43]. Specialists physically draw ROI in various radiomic investigations. A few methods have been devised for semi-automatic categorization. Use of geographical area algorithm and grey-scale cutoff point method is common for ROI identification. Manual demarcation by a professional is considered gold standard despite time-consumption and sensitivity to interobserver heterogeneity. Team of physicians or multiple methods can be utilized to eliminate potential bias.

Radiomic properties are classified as morphological. It is predicated on the ROI's geometric parameters, such as volume, largest surface area, and circumference[47]. First-order estimates, also known as histogram statistics, characterize dispersion of grayscale intensity using histograms without regarding spatial relationships within ROI. Grey level refers to maximum, minimum, and percentiles. GLCM displays number of times same intensity combinations appear in two pixels divided by certain length in a particular direction[48]. Wavelet or Fourier transformations are examples of transformation and filtration that show recurring motifs, histogram-oriented trends, or local derivative patterns. Image biomarker standardization initiatives (IBSI) provide explicit definition of radiomic characteristics[48].

To avoid overfitting learning precision is enhanced and calculation time is decreased. Radiomic features are exposed to a feature representation. Glitchy, non-informative, or duplicate characteristics should be eliminated throughout recruitment process. Method of selection is divided into three categories. Methods which evaluate utility of a given feature using range of data tests to determine relationship with end characteristic are discussed in this article.

Wrapper procedure scores distinct subsets of features. These features are predicated on their classification results using an exterior classification technique. It is an engrained method where feature extraction is innate to model training, i.e., features are selected to optimize performance of proposed learning algorithm[49]. Filter approaches are simple, clear, and efficient but they treat characteristics as separate entities without interactions. Wrapper approaches have lesser risk of generalization but require more computing power[50]. Embedding is more efficient and robust since selection technique is part of training process. Least absolute contraction and choice activator is a common integrated algorithm used in radiomic investigations.

Selected attributes used to create a statistical model can predict the known medical outcomes. Selection of a good modelling methodology has a certain criterion, including sample and study outcome. It is beneficial to add variables in the model other than radiomic, such as clinical data and/or other "-omics" including genetic information[51]. Mathematical formula makes it easier to construct a personalized care by incorporating data from numerous sources, such as medical imaging, disease conditions, therapy, and follow-up details. As previously stated, radiomic investigations are used to determine either a current characteristic (tumor phenotype) or forecast a prospective (therapeutic efficacy)[52]. Characteristically,

radiomic research employs feature-based ML algorithms. In functionality ML algorithms link input data and intended outcome through training process. SVM algorithm is amongst the most commonly used. Use of DL-based radiomic enables extraction of feature representation to give desired outcome. All processing stages outlined in ML-based model are performed by various components of DL framework including extraction features, choice and model execution[53]. Most popular design used in radiomic investigations is CNNs. Evaluation is an essential part of both traditional and DL-based radiomic. Before use training set should be evaluated by cross-validation.

Description	Cohort	Method	Performance	Reference
Classification Benign/ Malignant Thyroid Nodules 730 features extracted and 66 selected US	1609 Patients	ML-Based Radiomic	Accuracy 77.8% Sensitivity 70.6% Specificity79.8%	54
Classification Benign/ Malignant Thyroid Nodules US	8339 Patients	DL- Based Radiomic	Accuracy 89.1% Sensitivity 94.9% Specificity 81.2%	55
Evaluation of extrathyroidal extension (ETE) in patients with papillary thyroid carcinoma; 479 features extracted; 10 features selected US	132 Patients	ML-Based Radiomic	Accuracy 83% Sensitivity 65% Specificity 74%	56
Evaluation of extrathyroidal extension (ETE) in patients with papillary thyroid carcinoma MRI	102 Patients	ML-Based Radiomic	Accuracy 79% Sensitivity 75% Specificity 80%	57
Classification Benign/ Malignant Thyroid Nodules US	106 Patients	ML-Based Radiomic	Accuracy 75.5% Sensitivity 69.7% Specificity 78.1%	(Zhao et a., 2021)

Table 3. Radiomic studies.

AI AND RADIOMIC IN THYROID DISEASES

Ultrasound imaging is the preferred approach for identification and treatment of thyroid abnormalities due to cost effectiveness, efficacy and lack of radiation exposure. It is widely recognized as the first imaging tool for detection of thyroid diseases. Artificial intelligence (AI) technologies are gaining popularity in medicine and playing a role in decreasing invasive diagnostic practice[58]. AI algorithms are mostly used to classify thyroid nodules as benign or malignant. Conclusion of these investigations contrast to radiologists' diagnoses. A study shows DL ability in capturing complicated patterns owing to significantly improved selectivity and precision when compared to feature-based ML traditional applications[59]. DL algorithms have shown results comparable to radiologists' conclusions in various investigations. Moreover, Jin et al. stated that application of computer algorithms enhances detection accuracy of novice radiologists and makes it comparable with transitional radiologists[60].

Radiomic is a viable tool for incorporating personalized medicine based on patient's personal qualities. CAD system focuses on distinguishing benign and malignant thyroid lesions, while, radiomic expands assessment to prediction and treatment success[57]. In addition, radiomic algorithms are used to examine prognosis and detect thyroid cancer with excellent precision (about 85 percent). Use of radiomic to ascertain tumor phenotypes or genetic mutations can be beneficial.

Radiomic characteristics have been studied to assess prevalence of metastasis or disease-free longevity[61]. Radiomic investigations aiming at classifying types of thyroid nodules are less reliable than traditional ML approach. It is worth mentioning that studies on thyroid lesions are still restricted. Table 3 enlists relevant studies of radiomic application for thyroid lesions.

DISCUSSION

Imaging techniques provide thorough details about tumors and play a crucial role in early-stage diagnosis, differentiate benign and malignant lesions, quantify risk and improve treatment outcome. Imaging is a non-invasive technique while biopsies being invasive techniques have risk of exposure to pathogens. Since past few decades medical images are transformed into statistical data and evaluated with AI techniques. Tumor samples gathered by biopsy may not accurately reflect changes in tumor since neoplasms exhibit intra-tumoral diversity62. AI approaches analyze entire image of a disease and have the capability to capture heterogeneity of tumors. AI can serve as a bridge between imaging and biopsy. However, AI systems require data of case-to-case variation for training. Inter-variability in patients makes it challenging to develop an AI system with accurate diagnosis of pathological conditions. Furthermore, prediction model is constructed using a constrained classification model[63]. Since, living cells have distinguished heterogeneity in inter-subjects and intra-subjects, limited training dataset cannot adequately represent range of cases that can arise in healthcare. Research is required to enhance generalization and precision of AI-based models. Dependence on AI technology for diagnosis is discouraged in healthcare system.

Various researches recommend that assessment of lesions should be done by both clinicians and use of ML or DL methods[64]. AI researches on thyroid diseases have used prospectively obtained data. In contrast, a few researches in this field have systematically tested AI prediction models for thyroid disease assessment. In retrospective research, cohorts are chosen amongst patients diagnosed with histological evaluation[21].

Additional research on AI models is required to reduce risk of generalization and enhance consistency of treatment outcomes. AI approaches rely on study of visual information to construct prediction models. ML is mostly used to distinguish between benign and malignant thyroid nodules. A study shows that TI-RADS method is effective in distinguishing benign and malignant thyroid nodules. Certain traits, such as calcifications and internal material, constitute a component that enhances reliability[56].

Retrieved characteristics in this research are morphological, first-order analytics, sensory, and elevated statics[65]. Wang and coworkers found that ETE diagnosis improves when factors associated to PTC diversity are considered. Guo et al., 2020 studied thyroid cartilage infiltration from laryngeal and hypopharyngeal squamous cell carcinoma and examined tumor interstitials while considering tumor heterogeneity. BRAF mutation can be studied using histogram-based and texture characteristics that indicate location of echogenicity and heterogeneity[66].

Various researches compare effectiveness of AI-based algorithms and capability of experienced doctors. Research shows that performance of DL algorithms is generally comparable to medical practitioners[67]. AI applications may improve precision of thyroid diseases diagnosis, particularly for junior radiologists. Evaluation of medical imaging by radiologists is strongly dependent on level of expertise. Responsiveness of junior radiologists is around 40% and 100%. While, precision ranges from 50 percent to 100 percent. Use of AI algorithms for characterization of thyroid lesions increases precision of junior radiologist from 82% to 87%. Peng and associates reported that using AI as feedback decreases fine needle aspiration by 27% and number of undetected cancers by 2%. Moreover, level of expertise of doctors has significant impact on performance of AI-based approaches[68].

ROI serves as input information for AI algorithms. Due to inter-operator heterogeneity in capturing images and classifying them it is widely regarded as essential sub-process[47]. Current findings suggest that semi- or completely automated approaches can increase performance of algorithms, however, detection and segmentation by specialists is still the most common practice. Most of ML-based thyroid investigations are associated with manual ROI segmentation. ML-based studies have established a semi-automated strategy in which initial automatic classification of a box-interconnected world relies on manual contouring by trained clinicians. In contrast, studies based on DL algorithms for imaging of thyroid gland used a manually selected box in area of interest[69]. Radiomic findings focused on hand contouring along boundary of thyroid tumors in order to eliminate artefacts [70].

Gilies and collaborators[44], provide an empirical rule to limit size of data in radiomic studies to avoid overfitting. It stated that roughly 10–15 patients are required for each radiomic feature under investigation[71]. AI approaches can help clinicians improve their diagnostic choices in future. When these approaches are combined with other "-omic" information they can help improve health risk assessment for personalized illness survival prediction[72]. Several initiatives have been taken to increase availability of an open-access library of annotated medical pictures to aid in the development of Intelligence forecasting analytics[73]. Improvement in Intelligence performance is a field of interest in United States[72]. Ultrasonography (USG) is widely recognized as the most important imaging method for evaluating thyroid nodules. US's has high sensitivity and specificity in differentiating benign and malignant thyroid lesions.

Significant number of thyroid goiters are found incidentally during non-thyroid imaging assessments (e.g., CT, MR, and PET/CT)[74]. These imaging processes have a poor or subpar ability in identifying benign and malignant tumors in adrenocortical thyroid epistasis, hence, substantial effort is being made to enhance their potential in recognizing patient's need for an urgent or non-urgent endocrine evaluation coupled with in-office US examination.

CONCLUSION

Medical imaging has a significant role to play in healthcare. Medical imaging assists doctors in deductive reasoning, understanding of pathological processes and assimilation of findings from previous investigations. Detection of thyroid nodules using diagnostic imaging relies heavily on physicians' expertise. Development of artificial intelligence (AI) approaches has led to significant advancement in visual identification. AI techniques can be used in healthcare to improve assessment of medical imaging. AI approaches can be used to detect biological anomalies, diagnose neoplasms, and predict response to therapy. However, diagnostic accuracy of these approaches is still a point of contention.

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