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Artificial Intelligence in Ultrasound Imaging: Current Research and Applications

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Abstract: Artificial intelligence (AI) is an area of computer science that emphasizes the creation of intelligent software or system based on big data information, machine learning and deep learning technologies. The rapid development of science and technology as well as internet communication has enabled AI and big data to gradually apply to many fields of health care. The modern imaging medicine is one of the first areas where AI can play an important role and applications. As cross-sectional imaging, ultrasound (US) is well suitable for AI technology to standardize imaging protocols and improve diagnostic accuracy. This article reviews current AI technology and related clinical applications in the fields of thyroid, breast and liver US.

Key words: Artificial intelligence; Machine learning; Deep learning; Ultrasound imaging, Thyroid; Breast; Liver

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Artificial Intelligence (AI) has attracted more and more attention not only from professional fields but also from the general public in recent years. Kaplan and Haenlein define AI as “a system’s ability to correctly interpret external data, to learn from such data, and to use those learnings to achieve specific goals and tasks through flexible adaptation” [1]. Thus, AI represents an approach to assist or even replace humans in a variety of tasks. In radiology, the induction of AI is less than a decade, but the expenses on AI have increased exponentially as well as its profound impacts on diagnostic accuracy, improved safety standards and increased time efficiency. Machine learning is an essential element that drives AI’s explosion and it has been widely applied in radiology. Whereas advanced technology is developed, machine learning is intended to be replaced by deep learning so that more complex radiological tasks can be accomplished. US imaging, a noninvasive, cost-effective and nonionizing technique, however, has limited AI applications compare to other imaging technologies in radiology. Thus, the development, technique, applications, and current performance of AI in US imaging are introduced and

summarized in this review paper.

Traditional CAD Systems and Deep Learning in US Imaging

With development of computer technology, the traditional Computer-Aided Diagnostic (CAD) System was developed in 1960s and helped radiologists to diagnose breast tumor from both their perspective and the computer’s perspective [2]. The traditional CAD system showed its usefulness by increasing diagnostic accuracy, keeping consistency of radiologic diagnosis, decreasing the load of radiologists and reducing image-read time consumption [3]. The traditional CAD system followed two main steps: detection and diagnosis [4]. Detection segmented lesions from healthy tissues and diagnosis examined lesions to provide diagnosis. There are four phases in traditional CAD system: image preprocessing, image segmentation, feature extraction, and lesion classification [5]. The most important and difficult phase is feature extraction since it is hard for a traditional CAD system to acquire data, and if the dimension of the feature is larger than the dataset,

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“curse of dimensionality” will occur and the system will become unreliable [6].

Thus, feature selection is crucial for the traditional CAD system and appropriate features can increase the

system’s accuracy and lower the system’s computational complexity. The categories that are utilized for feature selection in the traditional CAD system are shown in Table 1. Importantly, all these features are artificial.

Table 1 Categories for feature selections in traditional CAD system.

Categories	Description	Algorithms/ Methods
Texture	Reflects the surface characteristics of a lesion and it is frequently used in traditional CAD system.	<ul style="list-style-type: none"> • Laws Texture Energy (LTE) ^[7] • Contrast of Gray Level Values ^[5] • Gray Level Cooccurrence Matrix (GLCM) ^[5] • Local Binary Pattern (LBP) ^[8] • Wavelet Features ^[5]
Morphology	More focus on lesion itself. Such as smoothness of lesion margin, length and width ratio of lesion and so on.	<ul style="list-style-type: none"> • Speculation • Depth-to-Width Ration • Elliptic-Normalized Circumference (ENC) ^[9] • Elliptic-Normalized Skeleton (ENS) ^[9] • Long Axis-to-Short Axis Ratio (L: S) ^[9]
sModel-based	Statistical model of the backscattered echo that can indicates the character of backscattered echo from tissues.	<ul style="list-style-type: none"> • Nakagami model-based features • K-Distribution model-based features
Descriptor features	Different applications (diseases) create different descriptor features and features are generated by radiologist base on their experience.	<ul style="list-style-type: none"> • Shape • Calcifications • Posterior shadow or posterior echo • Echo characteristic

The lesion classification is the last phase in the CAD system, and provides a diagnosis following the lesion extraction phase. Numerous classifiers have been produced to classify lesions and each of them has their own advantages and limitations. Most classifiers

are designed to classify the lesion such as the breast tumor, liver fibrosis, and thyroid nodules [5]. Table 2 as shown below provides descriptions of characteristic on frequently used classifiers in the field.

Table 2 Frequently utilized classifiers to classify lesions.

Classifiers	Descriptions of characteristic
Linear Classifier	Linear discrimination analysis and logistic regression are two linear classifiers and reliable only with linear data.
Bayesian Classifier	It is involved in machine learning and it predicts posterior information base on analyzing previous data points.
Support Vector Machine	Kernel functions are utilized to find decision hyperplanes by computing the original data into the higher dimensional space. The complexity increases as dataset increases.
Decision Tree	Its structure is a flowchart and it computes classification rules from disordered data. The size of data and feature values affect the complexity of the decision structure.
Artificial Neural Network	It is a machine learning model base on human nervine system. The complexity of the network affects the training time.
AdaBoost	Integrating several weak classifiers and building a strong classifier based on prediction voting from weak classifiers.

The artificial neural network is a machine-learning model but it is directly related to the deep learning model since it is built according to the human nervous system and its appearance revealed the application of deep learning in US imaging fields and a more advanced approach for the CAD system [5].

The idea of deep learning was generated two decades ago, but it was firstly explained and modeled by Hinton et al. [10]. The deep learning system represented a multi-layer machine learning system. The machine learning system contained an algorithm to parse and learn data,

then it can make decisions based on what is learned. Deep learning systems will generate algorithms in layers to construct an artificial neural network then learn and make intelligent decisions by itself [11]. With advanced development in deep learning, image recognition, semantic analysis, and disease detection can be achieved precisely and efficiently. All these applications are closely related to the function of an US CAD system so that deep learning system will be a powerful tool to assist diagnostic US imaging [5]. Figure 1 represented a lesion recognition by both deep learning system and human

detection [12].

The most applicable deep learning algorithms to radiological imaging are called convolutional neural networks (CNNs) as these are very efficiently applied to image segmentation and classification [13]. A convolutional neural network (CNN, or ConvNet) is a class of deep, feed-forward artificial neural networks that explicitly assumed that the inputs are images, which encode certain properties into the architecture. The components of a CNN included an input layer, an output layer and one or more hidden layers. What makes CNN different from a regular neural network is that the neurons in the layers are in three dimensions, including height, width and depth. This permitted the CNN to process and transform an input volume in three dimensions to an output volume. The hidden layers are crucial for the ability and efficacy of feature extraction and classification for CNN [14]. The hidden layers are combined with convolutional layers, pooling layers, normalization layers and fully connect layers (Fig. 2). Convolutional layers are used to create feature maps from input images, then pooling layers subsampled from the feature maps. This reduces the memory consumption

of the neural network so that more convolutional layers can be used. Meanwhile, the pooling layers can limit translation and rotation invariance to enhance the ability to detect unusually placed objects. The normalization layers normalize all layer inputs to a mean of zero and variance of one. The fully connected layers connect all features that are generated from previous layers then allowed the classification [14].

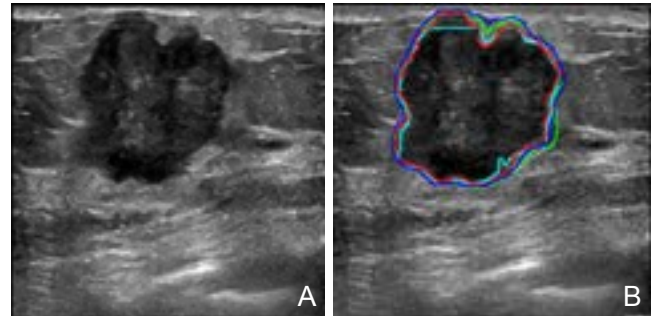


Figure 1 (A) The original US image contains an irregular shaped lesion; (B) red outline represents a manually segmented lesion, while blue, green and cyan outlines represent deep learning system with lesion segmentations (Reprinted with permission from [12]).

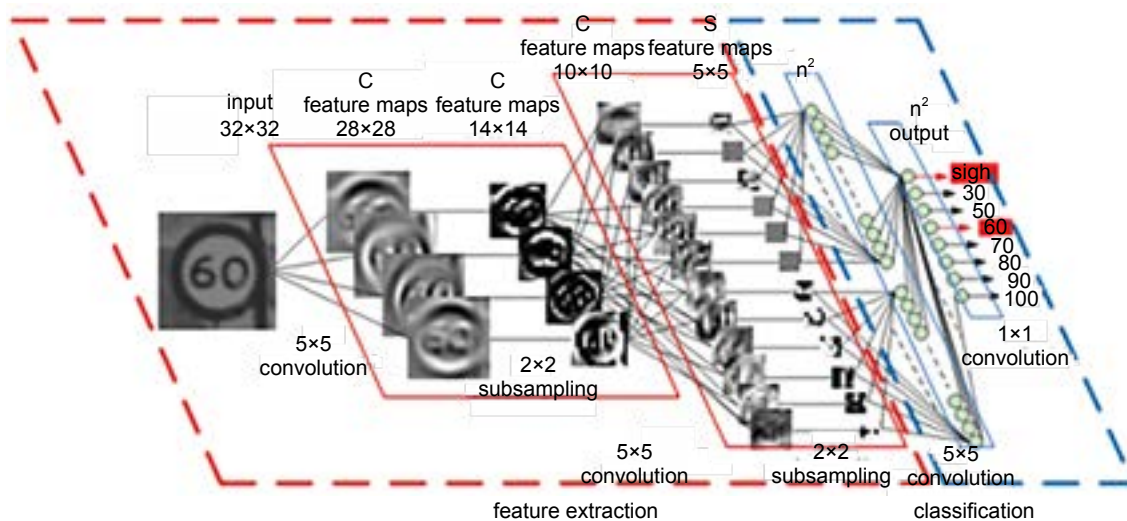


Figure 2 An example of showing that an input image is filtered by convolutional layer then creates 4 feature maps. Max pooling is utilized to subsampling these feature maps. Then the process ran again from convolutional layer and finally all generated features are combined in fully connected layer for classification. (Reprinted with permission from [14])

The main difference between the deep learning US CAD system and traditional US CAD system is that the features that are employed by the deep learning US CAD system are not artificial features. As mentioned before, the traditional US CAD utilized man-crafted features, such as gray features and texture features. As an alternative, deep learning techniques developed and applied to CAD system use features that are extracted by the deep neural network. This approach has been shown

to be more effective than the feature designed by the human [5].

Breast Cancer

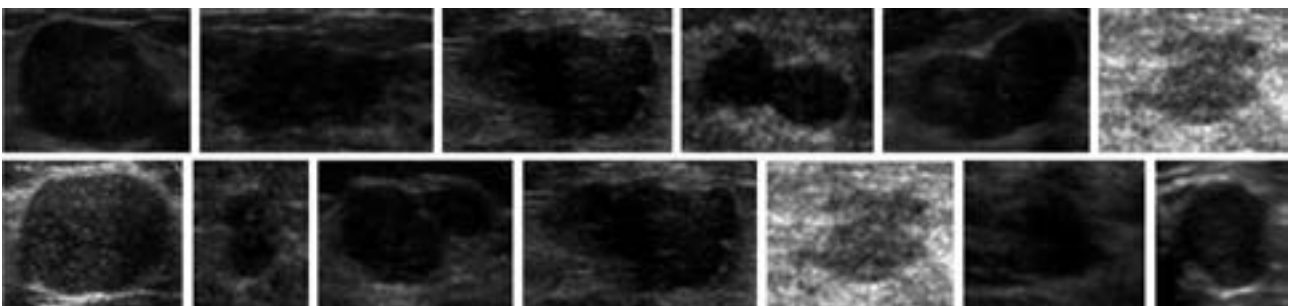
Breast cancer is one of the most common cancers in women. About 1 in 8 U.S. women (about 12.4%) will develop invasive breast cancer over the course of her lifetime. In 2018, an estimated 266,120 new cases of invasive breast cancer are expected to be diagnosed in

women in the U.S., along with 63,960 new cases of non-invasive breast cancer [15]. Utilizing US imaging is a safe, inexpensive and time-effective method to detect and characterize breast cancer [16] and early detection can significantly decrease the mortality rate of the breast cancer [17].

Deep learning techniques have been utilized by radiologist research teams to help them detect and evaluate breast tumors. Byra et al. classified breast tumor mass by employing several transfer learning techniques along with a matching layer and color conversion. The area under curve (AUC) is 0.936 with matching layer involvement and radiologists reading on same set of data is ranged from 0.806 to 0.882 [18]. Drukker et al. utilized gray-values to generate features for CAD systems and obtained an AUC of 0.90 and 100% sensitivity at 30% specificity [19]. Zhang et al. utilized the point-wise gated Boltzmann machine (PGBM) to extract the feature from shear-wave elastography (SWE) to classify the breast tumor. The deep learning feature reached 93.4% accuracy [20]. Cheng et al. utilized stacked denoising autoencoder (SDAE) technology to encode the US image and employed the softmax layer to classify the breast lesion [21] (Fig. 3 and 4). Shi et al. employed the deep polynomial network to extract the textural feature from the US image and reach the accuracy of 90.40% [22]. Gruszauskas et al. tested the performance of CAD system using a Bayesian neural network-based classifier. The result showed that

the differences in the area under the ROC curves are never more than 0.02 for the primary protocols and non-inferiority is demonstrated [23]. Ruey-Feng et al. built a learning vector quantization model with 24 autocorrelation texture features to classify tumors and reached 90% accuracy; sensitivity, 96.67%; specificity, 86.67%; positive predictive value, 78.38%; and negative predictive value, 98.11%. The performance of the CAD system is better than the radiologist with an accuracy of 86.67%, sensitivity of 86.67%, specificity of 86.67%, positive predictive value of 76.47% and negative predictive value of 92.86% [24]. Han et al. utilized the GoogLeNet to classify the breast image and reached 90% accuracy [25]. Hu et al. computed a novel automatic tumor segmentation model by combining dilated fully convolutional network (DFCN) with a phase-based active contour (PBAC) model. Then the model is compared with three existing state-of-art networks. The testing results gave a Dice Similarity coefficient of $88.97 \pm 10.01\%$, a Hausdorff distance (HD) of 35.54 ± 29.70 pixels, a mean absolute deviation (MAD) of 7.67 ± 6.67 pixels, and an AUC of 0.795 [26]. These data indicate the best segmentation performance that is close to manually segmentation [26]. These examples of deep learning in breast US show the potential of AI for improving breast cancer detection and characterization. In addition, the improving performance of deep learning CAD systems demonstrate a reliable future of automated diagnosis in US imaging.

Benign US Breast Lesion



Malignant US Breast Lesion

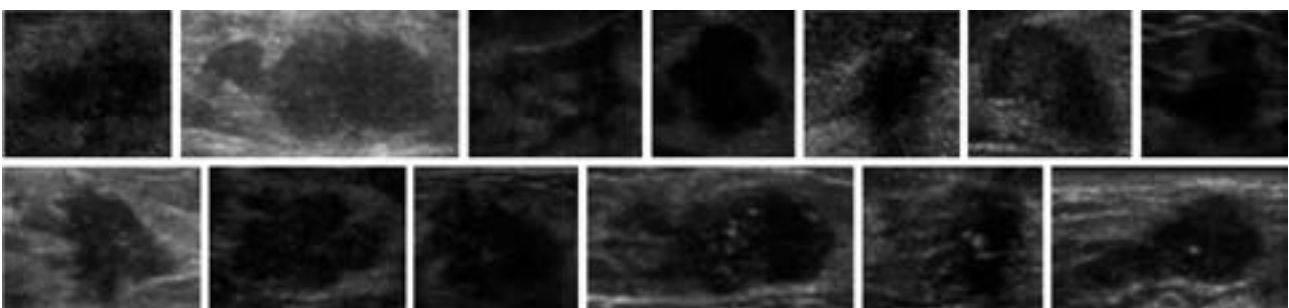


Figure 3 Stacked denoising autoencoder (SDAE) technology is used to encode US image of breast lesions in US images. (Reprinted with permission from [21])

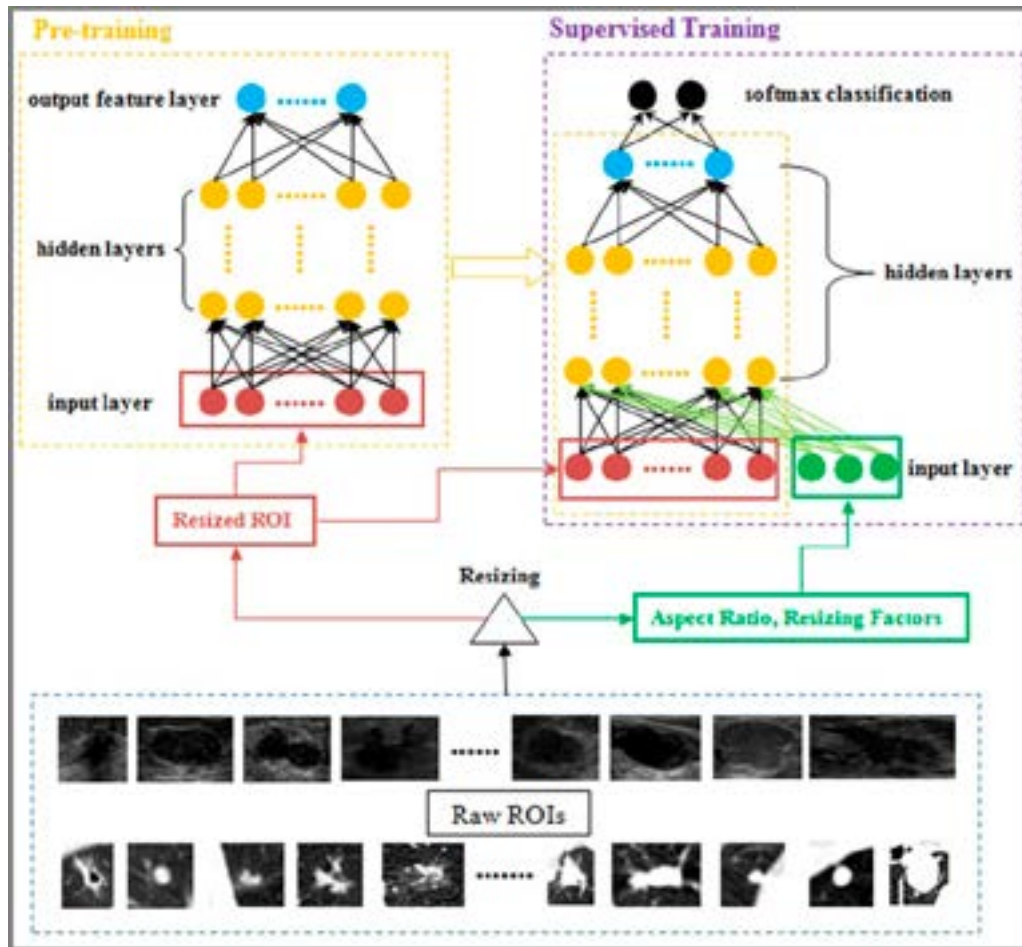


Figure 4 Flow-chart of the deep-learning-based CADx training framework. The pixels of resized (the region of interest) ROIs are fed into the network architecture at the pre-training step. The pre-trained network is then refined with the supervised training by adding three neurons carrying aspect ratio of the original ROI and also the resizing factors at the input layer. The final identification result can be made with the softmax classification. (Reprinted with permission from [21])

Thyroid Cancer

Thyroid cancer is a common disease worldwide. In 2018, it is expected that there are 53,990 new cases of thyroid cancer (40,900 in women, and 13,090 in men) and around 2,060 deaths (1,100 women and 960 men) [27]. Thyroid ultrasound is the main examination used for both detection and characterization of thyroid nodules [28]. In order to support radiologists to diagnose thyroid nodules with high accuracy and efficiency, deep learning CAD systems have been proposed. Ko et al. designed a deep convolutional neural network to examine malignancy of thyroid nodules and compared the testing results with experienced radiologists. The AUC for radiologists is 0.805-0.86 and the network achieved an AUC ranged 0.835-0.85. Thus, there is no significant differences between radiologists and the network (Fig. 5) [29]. Wang et al. utilized YOLOv2 neural network to achieve automatic thyroid nodule recognition and diagnosis. The performance of

YOLOv2 is compared with experienced radiologists. (TOLO?)YOLOv2 achieved a higher AUC (0.902) than radiologists (0.802), and the sensitivity (90.5%), positive predictive value (95.22%), negative predictive value (80.99%), and accuracy (90.31%) of YOLOv2 had no significant difference with radiologists but it had a higher specificity (89.91% vs 77.98%) [30]. Zuo et al. combined two improved methods, corresponding anti-pooling (unpooling) and deconvolution layers (deconv2D), with Alexnet convolutional neural network to extract calcification from US images of thyroid nodule. The approach achieved an extraction accuracy of 86% and much higher than traditional method [31]. Young et al. integrated AI (S-Detect for Thyroid; Samsung Medison Co.) into CAD US and examined 102 thyroid nodules from 89 patients. The CAD system showed a similar sensitivity as the experienced radiologist (90.7% vs. 88.4%, $P > 0.99$), but a lower specificity and a lower AUC (specificity: 74.6% vs. 94.9%, $P = 0.002$;

AUC: 0.83 vs. 0.92, $P = 0.021$) (Fig. 6) [32]. Ma et al. employed a system that included two CNNs into a single CAD system. The first CNN segmented thyroid nodules from processed US images and then the second CNN

classified the thyroid nodules. This method presented better performance than traditional deep learning systems but since the system required two CNNs, the training time lasted more than 106 hours [33].

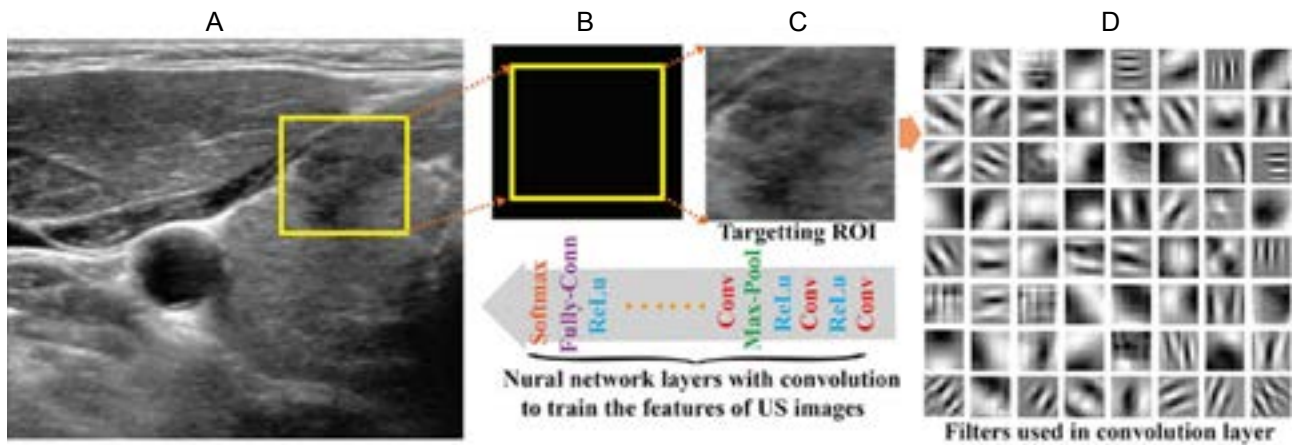


Figure 5 Implementation framework of convolutional neural network (CNN). (A) The region of interest (ROI) is drawn by a radiologist and (B) The position information of ROI is collected; (C) By using the position information, ROI is extracted; (D and E) The extracted ROIs are used either in training or testing deep CNNs. (Reprinted with permission from [29])

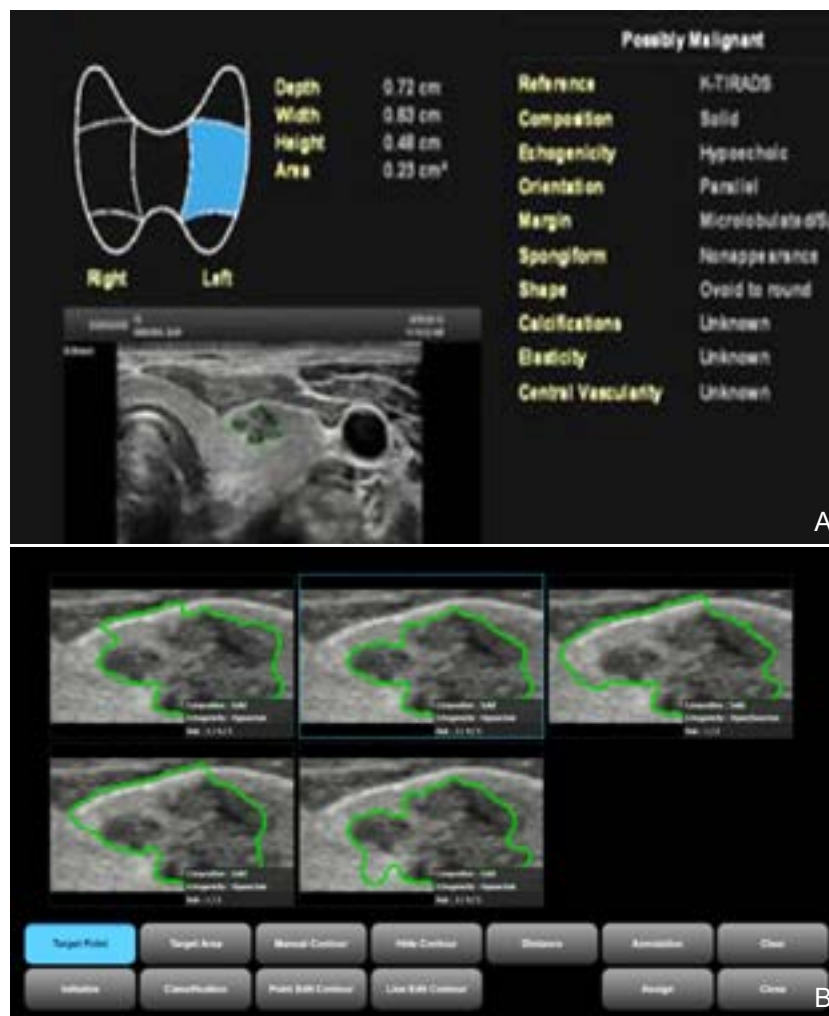


Figure 6 (A and B) US system RS80A (Samsung Medical) equipped with S-Detect function has used the ACR BI-RADS and TI-RADS classifications for the standardized analysis of suspected breast and thyroid lesions. (Provided by Samsung with permission)

Liver diseases

Liver disease has become a major concern worldwide. Approximately 31,000 people in the United States die each year from cirrhosis and other chronic liver diseases [34]. US imaging is an effective approach to detect liver cancer. With an increased demand, more time-effective and accurate methods with deep learning application into CAD systems has been proposed by researchers. Hassan et al. utilized the sparse autoencoder to acquire the representation of the liver US image and utilized the softmax layer to distinguish different focal liver diseases and their method reached a higher accuracy than support vector machines method [35]. Liver fibrosis classification is also a high priority. Meng et al. utilized the VGGNet and fully connected network (FCN) to differentiate the level of liver fibrosis [36]. To address the shortage of samples, Meng et al. employed the transfer learning (TL) technology. The group then divided the liver fibrosis level into three phases: normal, early stage fibrosis (S1–

S3), and late-stage fibrosis (S4). The accuracy of their method reached 93.90%. Similar to Meng et al., Liu et al. utilized deep learning technology to diagnose cirrhosis [37]. In this study CNN is employed as a tool to generate features from US images. The researchers adopted the SVM as the classifier to distinguish the normal liver and the diseased liver, and the accuracy of the proposed method reached 96.8% which is much higher than the accuracy of low-level features. Byra et al. utilized Inception-ResNet-v2 deep convolutional neural network to generate liver steatosis assessment, while comparing with hepatorenal index technique and the gray-level co-occurrence matrix algorithm. The network obtained an AUC of 0.977 and it is higher than hepatorenal (0.959) and much higher than gray (0.893). The Spearman correlation coefficient for network, hepatorenal and gray were 0.78, 0.80 and 0.39. The Inception-ResNet-v2 network showed the best performance among the three approaches (Fig. 7) [39].

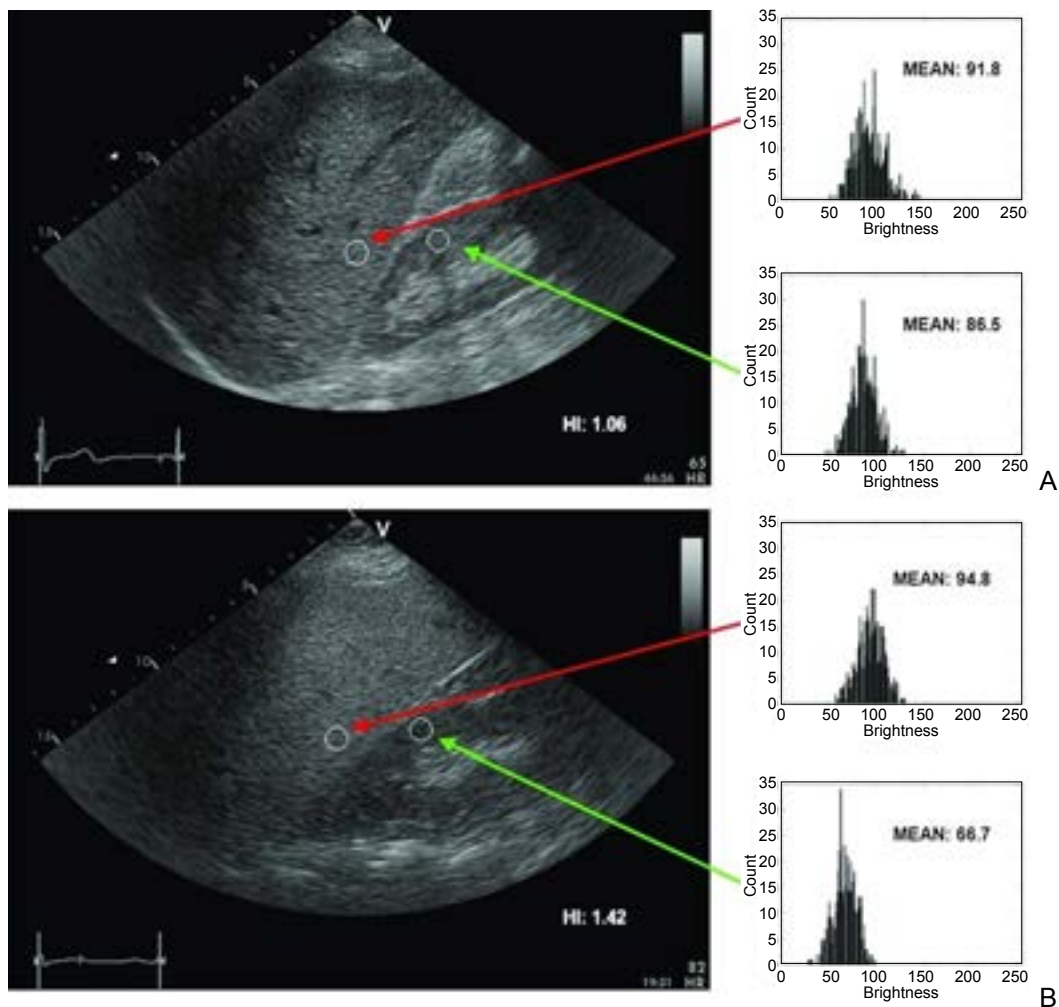


Figure 7 Liver B-mode images and the region of interest (ROIs) selected for hepatorenal sonographic index (HI) calculation, (A) steatosis level of 3% and (B) 25%, respectively. (Reprinted with permission from [38]).

Limitations

Even though the deep learning CAD system in US had shown promising performance, further improvement is expected. The current deep learning system can not only accomplish tasks that are impossible for radiologists but may also can make mistakes that a radiologist will not [39]. For instance, if radiologists make imperceptible alterations to the input data, these changes may not be detectable to human eyes, but still affect the result of classification from a deep learning system [13]. In other words, a small difference can cause a different determination or conclusion from a deep learning system.

In order to train deep learning CAD systems, a certain amount of consistent and standardized data with authenticated reference standard is needed for developers. Performing this via retrospective studies may create problems with annotated images. Meanwhile, the datasets are often not easy to obtain since the companies owned them will keep datasets as their proprietary and protect their intellectual properties [13]. The validation of a deep learning CAD system in the clinic can also be a challenge since it often required multi-institutional collaboration and effective communication between deep learning developers and radiologists [13]. In addition, validating a deep learning CAD system is both costly and time consuming. Finally, ethical and legal issues may be raised when large patient datasets are involved.

Conclusion

Prior efforts on the development of deep learning implantation into CAD systems for US have shown great potential to eventually become an intelligent tool that can surpass human performance. Although there are limitations with current deep learning systems, the benefits to date are encouraging. In the future, more US studies are needed to prove the functionality of applying AI. This includes development of improved AI models, creation of large, validated imaging data sets with reliable reference standards, and the validation of systems in prospective fashion. However, it is clear that US imaging and radiology as a whole is greatly altered following the refinement of these approaches.

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