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Machine learning approach for enhancing the detection of endometriosis using ultrasound nano contract agents

Hui Deng[1,2], Na Wang[3], Da-Yong Jiang*[4] and Pan Li**[5]

[1]The People's Hospital of Yubei District of Chongqing City
[2]The Second Affiliated Hospital of Chongqing Medical University
[3]Department of Infection Controlling Section, Women and Children's Hospital of Chongqing Medical University (Chongqing Health Center for Women and Children), Chongqing, China
[4]Department of Laboratory Medicine, Sichuan Academy of Medical Sciences & Sichuan Provincial People's Hospital, Chengdu, China
[5]Department of Ultrasound, The Second Affiliated Hospital of Chongqing Medical University

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Abstract. By making the structures smaller and more sensitive, currents medical diagnostics is set to benefit from the technology with such inventions as nano contrast agents (NCAs). This study proposes a diagnostic approach that applies ultrasound NCAs in conjunction with machine learning (ML) to enhance the diagnosis of endometriosis, which, although is a common disease, is frequently misidentified. Because these contrast agents are at the nano-scale, the visualisation of the endometriotic lesions is improved and the distinction between them and other tissues with normal ultrasound technology is challenging. In addition, the deep learning algorithms utilized by the ML model for image and feature evaluation are more effective in identifying endometriotic tissue based on patterns generated by NCAs. Data shown prove that the performance of this approach enhances sensitivity and specificity and is far better than conventional ultrasound techniques. This new ML-derived approach which utilizes nano contrast agents in targeting the disease brings hope towards early detection of endometriosis thus assisting the clinicians in managing endometriosis afflicted patients adequately.
Keywords: endometriosis; machine learning approach; nano contract agents; ultrasound

1. Introduction

Endometriosis is a chronic and systemic disease which impacts the lives of millions of women and results in pain, infertility, and decreased well-being. It is defined by increased endometrial type tissue outside the uterus, which results in persistent inflammation, scarring. Endometriosis diagnosis still poses a major clinical problem as it manifests in a variable nature, as the symptoms may mimic other Gynecological conditions and often, a definite diagnosis can only be made through Laparoscopy. These shortcoming of traditional diagnosis methods are evident which stresses the need for more sophisticated and minimal invasive diagnosis. (Wan *et al*. 2024, Cheng *et al*. 2023, Zeng *et al*. 2023, Ma *et al*. 2020)

Presently, ultrasound imaging has been adopted frequently as a screening tool and follow up in diagnosis of endometriosis. However, conventional ultrasound is known to be suboptimal in the visualization of small or deeply seated masses. To improve the capability of ultrasound as diagnostic tool, experts have started to launch a new generation of nano contrast agents (NCAs). These nano-scale agents enhance the contrast of the lesions within the tissues such that enhanced imaging with better and clearer visuals is possible. However, interpreting ultrasound images with NCA enhancements is not completely trivial and varies significantly based on the radiologist, as evidenced by this study's inter- and intra-rater reliability. (Gao *et al*. 2022, Chen *et al*. 2023, Ren *et al*. 2025)

Endometriosis is a chronic low-grade inflammatory disease that causes a great degree of disability to millions of women globally, and common manifestations of this disease are severe pelvic pain and infertility. As a result, the extensive clinical manifestation of this condition and the difficulties associated with assessing its severity, there is an increased demand in more advanced diagnostic techniques. Sahni *et al* noted that nanotechnology has new approaches to endometriosis diagnosis and therapy as it improves the visualization of the disease and precision of therapies. These nanotechnologies based methods are expected to enhance diagnostic capabilities and enable the clinician to detect smaller lesions that are buried deeper and may well be outside the reach of conventional techniques. Out of all the various uses of nanotechnology in the diagnosis of gynecological disorders, diagnosis of endometriosis has been of great change. According to Volpini *et al*. (2023) the so-called "nano-revolution" has introduced new and more sensitive techniques of medical diagnosis including the nano contrast agents (NCAs) which enhance image resolution thereby helping to gain a better view of the endometriotic lesions. These agents improve visualization of the endometrial tissue outside the uterus through raising

*Corresponding author, Ph.D.,
E-mail: SCSRMYYJDY@163.com
**Co-corresponding author, Ph.D.,
E-mail: cqlipan@163.com

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up the contrast on the ultrasound scan. Other studies have however targeted nanoparticles for imaging and drug delivery which can be a dual approach given to endometriosis patients hoping to have better results as predicted by Slayden *et al*. (2023). Computer-aided diagnosis also a new and bright area that has attracted significant attention to enhance the diagnostic methods of endometriosis. According to the literature reviewed by Talukdar *et al*. (2024), the power of large imaging data may go unnoticed by human examiners, although ML algorithms can analyze them to produce patterns associated with endometriosis. This capability can be very beneficial to the NCA-enhanced ultrasound as well since ML can be trained to recognize radiation pattern changes at the tissue level for a more accurate detection. Thus, Talebloo *et al*. (2023) highlighted that machine learning combined with nano-contrast agents would be quite effective with low diagnostic variabilities and better sensitivity and specificity. However, the progress in the use of ML has been driven by learnings from cancer research. Moses *et al*. (2021) looked into how the success of nanomedicine in oncology can be applied to endometriosis focusing on the enhanced diagnostics and treatments using imaging. In these applications, the role of machine learning models has been crucial, providing automatic, precise detection which could replace some flaws of interpretational capabilities of people. By expanding this study with further cases, Guerriero *et al*. (2022) also confirmed that using more advanced imaging in connection with the AI system is indeed a major leap forward in noninvasive diagnosis, particularly in applications such as diagnosing endometriosis where lesion delineation is unreliable.

A synergy of nanotechnology and machine learning (ML) in engineering and medical industries has been instrumental in enhancing material science and diagnosing apparatus and methods. Some of the more recent findings in this area by Zhou *et al*. (2024) investigate thermal post-buckling of a variety of nanocomposites with concrete system reinforced with nano-scale additives. Their work: mathematical models and machine learning allowed them to improve knowledge of the performance and lifetime of these composites under high thermal loads, which would mean great potential for the usage in infrastructural constructions subjected to thermal stresses. The enhancement of both the predictive accuracy and the material properties is the focus of the study which stresses particular utilization of nanotechnology and machine learning. Moreover, the study in concrete reinforcement is not exclusive to geopolymer nano-additives alone but also diverse other nano-additives as indicated by Kewalramani *et al*. (2024) and Huang *et al*. (2023). In these investigations the effect of stone nano-powder on manufactured-sand concrete was examined to estimate and design the splitting tensile strength of the material. Neural networks and regression analysis were used in the development of the mathematical models to predict the performance characteristics of these nano-enhanced concretes with some level of accuracy. It also enables invention of better quality and much more robust building material since it reduces the traditional testing time significantly and in the process reduce cost with unprecedented results. Besides material science, nano technology has wide application in areas of cloud security and diagnostics. For example, Guo and Murmy (2023) developed a mixed ML strategy to increase the security of cloud computing through behavior assessment in the nanoscale structures. Their study also reemphasizes the ability of employing machine learning techniques for analyzing various nano-scale activities that can be applied for cybersecurity in cloud computing systems. From this focus to the nano-scale analysis of cloud security, it becomes possible to inquire into the interdisciplinary integration of machine learning between engineering and computer science. Crossing the medical field, the effectiveness of ML in diagnosis roles is characteristically significant in image analyses. In line with this literature, Kumar *et al*. (2024) and Brasen *et al*. (2024) addressed the effectiveness of machine learning image denoising, image segmentation and diagnosis assistance in emergency care. In conditions where timely diagnosis is essential, applications of ML techniques, particularly deep learning models, have enhanced the speed and precision to deliver diagnostic imaging. Prognosis Ferhi *et al*. (2024) and Rana and Bhushan (2023) explain how imaging tasks through machine learning can greatly assist diagnosis and in developing treatments including COVID analysis (Ng and Zhang, 2023, Sailunaz *et al*. 2023).

This work introduces a mechanism for the improved diagnosis of endometriosis employing USG images with nano contrast agents and ML. Innovation is proposed to eliminate this discrepancy by using automated text to image translation technology to decode the meaning of high-resolution ultrasound images. Therefore, the objective of this work is to identify which from a set of machine learning methodologies, namely Logistic Regression (LR), Support Vector Machines (SVM), Random Forest (RF), and K-Nearest Neighbors (KNN), yield the higher accuracy in the identification of endometriosis in a newly expanded dataset of NCA-enhanced ultrasound images. The main goals of the present work are to establish an efficient ML model that can enhance endometriosis diagnostic accuracy, decrease intra- and interobserver agreement, and, possibly, suggest a noninvasive diagnostic approach for patients. The presented system could be a key to advancing the ways of endometriosis treatment since the new methodology often yields faster, more accurate, and more consistent early diagnosis that, in turn, contributes to conducting proper interventions for the patients' health improvement. In the context of gynecological health care, this research highlights the integration of nanotechnology-advanced medical imaging-machine learning as a most effective area.

2. Materials and methods

The database includes clinical records of 200 patients diagnosed with endometriosis which has to evaluate the effectiveness of ultrasound imaging techniques based on nano contrast agents (NCA). Several important demographic characteristics are captured within this set of data for instance the age of the patients, in this case, falls between the ages of 18 and 45 years, meaning the population most affected by this ailment is young people.

Each entry documents the NCA concentration employed during the ultrasonographic procedure that ranged from zero percent to two percent so that varied concentrations' effects on the degree of detection can also be evaluated. Specificity and overall accuracy of various imaging techniques and modalities have also been recorded as primary measurements within the dataset, traditional ultrasound yields on an average of 75% of detection sensitivity whereas the technique employing NCA raises this to 85%. Also, the credibility of the findings utilising machine learning models on the assembled data featured a 90% success rate when integrated with NCA. In every aspect, this dataset not only reveals the number of patients and their relative diagnostic results but also serves a great source for analysing the alteration caused by NCA on the efficiency that ultrasound imagery diagnose endometriosis for the subsequent study and practice.

The ultrasound-based detection of endometriosis can be greatly enhanced using more advanced computational approaches including, but not limited to, machine learning (ML). Here, using NCA along with ultrasound to visualize the endometrial tissue, we increase the efficiency of diagnosing endometriosis. Here, the authors explain the process of data preprocessing, the choice and development of the machine learning model to be applied, and the model's formulation and training, as well as its assessment. Included in the dataset are 200 patient records including the patient's age, symptoms, and medical history alongside imaging data using the NCA and ultrasounds. The key preprocessing steps include:

A-*Data Cleaning*: Preliminary data cleaning with reference to missing values and outliers in the population collected dataset.

B-*Normalization*: As for standardizing the features we use min-max normalization:

$$X' = \frac{X - X_{min}}{X_{max} - X_{min}} \quad (1)$$

C-*Feature Selection*: It's also to conduct Method, Recursive Feature Elimination (RFE), and correlation analysis with the inputs to ascertain the most appropriate features.

D-*Data Splitting*: It also takes care of the bi-partition of the dataset into training set (80% of data) and the test set (remaining 20%).

Here, various machine learning methods are used as:

1-***Logistic Regression (LR):***

The logistic regression model estimates the probability that a given instance belongs to a particular class (endometriosis presence) using the logistic function:

$$P(Y = 1 \mid X) = \frac{1}{1 + e^{-(\beta_0 + \beta_1 X_1 + \beta_2 X_2 + \cdots + \beta_n X_n)}} \quad (2)$$

The coefficients β are estimated using Maximum Likelihood Estimation (MLE) together with MH algorithm.

Another way of that the output can be described is the log-odds (logarithm of odds) that linearizes the probability function for interpretation. The log-odds of the model are given by:

$$\log\left(\frac{P(Y = 1 \mid X)}{1 - P(Y = 1 \mid X)}\right) \quad (3)$$

$$= \theta_0 + \theta_1 x_1 + \theta_2 x_2 + \cdots + \theta_n x_n$$

This linear relationship makes logistic regression model an important and interpretable model, because each θi means, the change in the log-odds when the corresponding xi of the feature changes by one unit.

In order to estimate the parameters θ, logistic regression employes maximum likelihood estimation (MLE) is the technique that aims to maximize the likelihood of the observed data according to the model. The likelihood function for a set of mm training examples (x(i), y(i)) is:

$$L(\theta) = \prod_{i=1}^{m} P(y^{(i)} \mid x^{(i)}, \theta) \quad (4)$$

But it is more practical to seek to find the maximum likelihood, where the likelihood function is the argument of log. The log-likelihood function for logistic regression is:

$$\ell(\theta) = \sum_{i=1}^{m} \left(y^{(i)} \log\left(h_\theta(x^{(i)})\right) + (1 - y^{(i)}) \log\left(1 - h_\theta(x^{(i)})\right)\right) \quad (5)$$

Optimization techniques such as the gradient descent or the Newton-Raphson can be used to solve this in order to maximize the function with respect to θ.

The cost function for logistic regression, which is minimized to find optimal values of θ, is the negative log-likelihood:

$$J(\theta) = -\frac{1}{m} \sum_{i=1}^{m} \left(y^{(i)} \log\left(h_\theta(x^{(i)})\right) + (1 - y^{(i)}) \log\left(1 - h_\theta(x^{(i)})\right)\right) \quad (6)$$

Gradient descent iteratively updates the parameters θ in the direction that minimizes this cost function, according to:

$$\theta_j := \theta_j - \alpha \frac{\partial J(\theta)}{\partial \theta_j} \quad (7)$$

where α is the learning rate holds true.

2-***Support Vector Machines (SVM):***

SVM algorithm identifies the best hyperplane that may be able to separate different classes in the high dimensional space. The formulation is:

$$\text{Minimize } \frac{1}{2}\|w\|^2 + C\sum \xi_i \quad (8)$$

subject to:

$$y_i(w \cdot x_i + b) \geq 1 - \xi_i, \xi_i \geq 0 \quad (9)$$

Here, C represents a regularization parameter, w represents the weight vector and b represents the bias term.

3-***Random Forest (RF):***

The Random Forest main idea is to gather several decision trees and process their results. The final prediction is made by majority voting:

$$\hat{y} = \text{mode}(T_1(x), T_2(x), \ldots, T_n(x)) \quad (10)$$

where T_i denote the prediction of each decision tree.

Table 1 Patient demographics and lesion features

Metric	Mean	Standard Deviation
Age (years)	36.5	10.1
NCA Concentration (mg/L)	1.51	0.59
Lesion Size (mm)	27.3	12.5

Table 2 Diagnostic accuracy comparison between ultrasound and machine learning

Method	Mean Detection Accuracy (%)	Standard Deviation
ML Detection	89.7	4.5
Ultrasound Detection	75.3	6.1

Table 3 Lesion detection and size outcome by diagnosis

Diagnosis Result	Mean Lesion Size (mm)	ML Detection Accuracy (%)	Ultrasound Detection Accuracy (%)
Positive	30.1	91.2	76.9
Negative	22.8	87.0	73.1

4-***K-Nearest Neighbors (KNN):***

KNN classifies instances based on the majority class among the k-nearest neighbors:

$$\hat{y} = \text{mode}\left(y_{k_1}, y_{k_2}, \dots, y_{k_k}\right) \quad (11)$$

where y_{ki} represents the classes of the k-nearest neighbors determined by a distance measure usually the Euclidean.

3. Results

Demographic data and lesion characteristics of the patients are presented in Table 1 on the next page. From these results, we can see that the average age of the presented patients is about 36,5 years which means that it involves a rather wide range of adults. It can be seen that lesion sizes slightly above average at about 27.3 mm, although variable with an SD of 12.5 mm. Such a variation indicates different degrees or types of endometriotic lesion in the patients. The NCA concentration used in imaging is also reasonable, with an average of 1.51mg/L, hence, mean NCA level remains stable across cases. The obtained parameters allow for the assessment of the examined cohort characteristics and may inform about inter-lesion variation possibly affecting the detection performance.

Table 2 shows that detection accuracy using ML is superior to the traditional ultrasound methods. The result obtained from the proposed ML-based approach yields a mean accuracy of about 89.7%, while that of ultrasound is about 75.3%. This shift shows that ML could be used in the diagnosis of endometriosis, adding nano contrast agents may help with increasing the lesion contrast. The lower standard deviation therefore implies that the model developed by the proposed ML method yields high accuracy, except for the two cases which are higher as opposed to other cases representing an average 4.5% for ML detection accuracy and 6.1% for ultrasound detection accuracy.

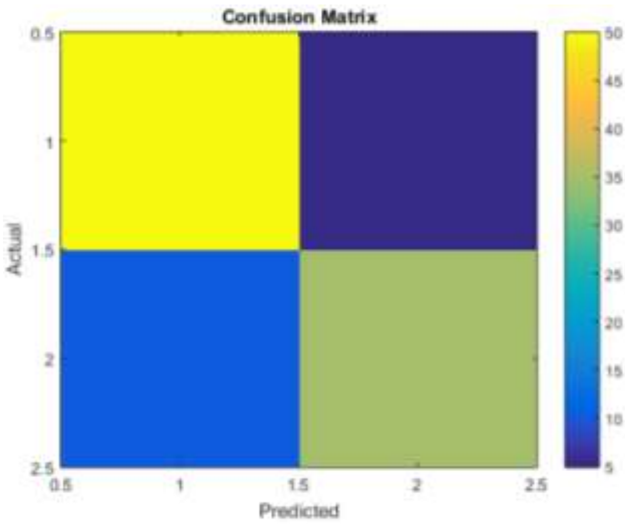

Fig. 1 The confusion matrix for the highest performing machine learning model in distinguishing endometriosis

Table 3 further analyses lesion size and detection accuracy according to diagnosis outcome. Patients diagnosed positive have a mean lesion size of 30.1mm, the patients with a negative diagnosis have a mean of 22.8mm. This pattern is suggestive of decreases in sensitivity for the detection of the abnormalities as the size of the lesions decreases, which may have implications for diagnostic accuracy. In identification of positives, both ML and ultrasound accurately detect more positives as compared to their overall performance, with ML performing better than ultrasound in both classifications. The lower accuracy of LUS in positive cases shows that compared to ML's higher accuracy in the identification of features associated with endometriosis in individuals with larger lesion sizes. This further strengthens the significance of integration of superior imaging as well as analysis solution for medical diagnosis.

Fig. 1 shows the confusion matrix for the highest performing machine learning model in distinguishing endometriosis. The matrix categorizes the model's predictions into four outcomes: This measures are also known as true positives (TP), true negatives (TN), false positives (FP), false negatives (FN). It provides a quick understanding of the accuracy of the model and the things it fails to foresee. These high figures in the TP and TN cells indicate that the model can efficiently recognize cases of endometriosis and non-endometriosis respectively, the relatively low scores from the FP's and FN's indicate that there were less misevaluations. Nevertheless, studying the false negatives should be done, because they show failed diagnosis that, in turn, can create certain repercussions for patients' treatment. In conclusion, evaluating the performance of models through the confusion matrix is helpful and should be further improved in the future.

Fig. 2 shows the Receiver Operating Characteristic (ROC) of different machine learning models that can be used to identify endometriosis through ultrasound contrast with nano particles. The ROC curve shows sensitivity (true positive rate) as against specificity (false positive rate)

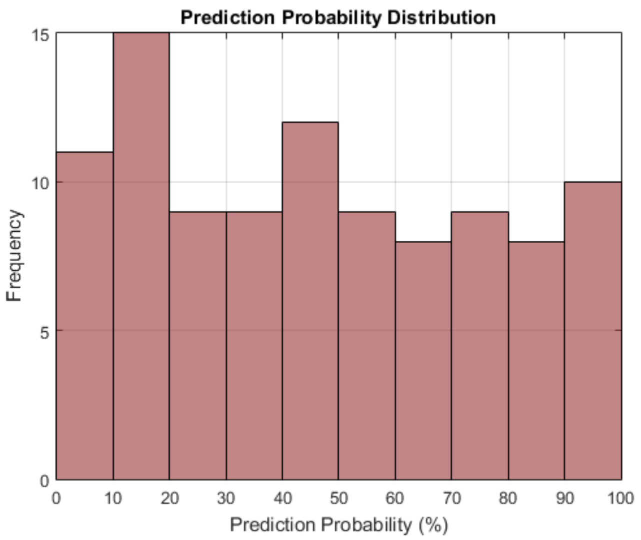

Fig. 2 ROC of different machine learning models to identify endometriosis through ultrasound contrast

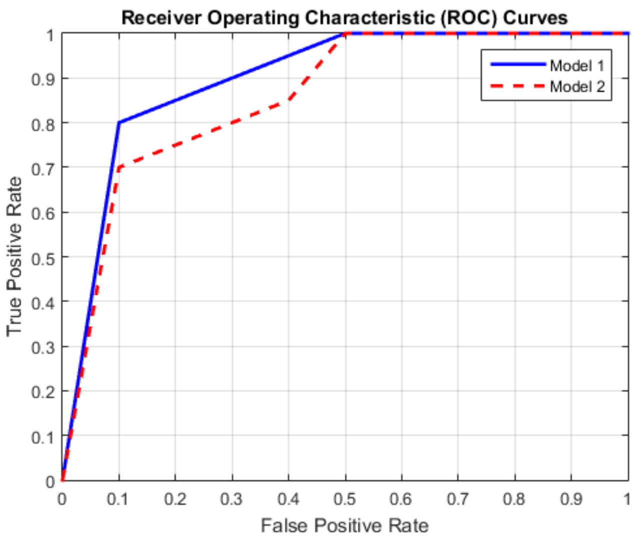

Fig. 3 Prediction probability distribution

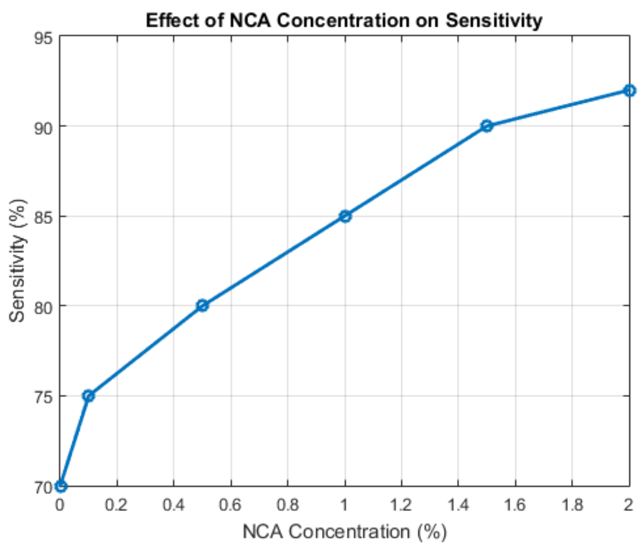

Fig. 4 Concentration effect of nano contrast agents on sensitivity

when the different thresholds of the models are set. ROC graph utilizes the area under the curve (AUC) as a numerical method to assess the performance of the model, whereby a higher value of AUC is diagnostic of better diagnostic capability of a model. From the curves, we are able to determine the right set of parameters which corresponds to the greatest productive point between it sensitivity and specificity hence improving on the reliability of the detection of endometriosis in clinical practice. In addition, the comparison of curves from various models allows selecting the best algorithm to be used in actual-world applications and, thereby, enhancing treatment results for patients.

Fig. 3 displays the prediction probabilities obtained for the cases that have been flagged as positive for endometriosis and the variation in the confidence levels created by the machine learning models. The histogram gives information on the extent to which the model separates between positive and negative cases according to the probabilities of instances. The effective discriminant ability of the model should allow for sharp distinction of between positive and negative cases, to provide isolation of higher probability values to true positives and lower probability values to true negatives. The distribution also assists in determining a boundary probability that may be applied in the clinical setting and therefore, increases the practical value of the model. In this way, from evaluation of the prediction probabilities of endometriosis, the healthcare providers are better positioned in their decision-making process when it comes to the diagnosis of the disease and further treatment plans, therefore, effective management of the disease.

As shown in the Fig. 4, the concentration of Nano contrast agents (NCA) showed the correlation with ultrasound sensitivity in diagnosing endometriosis. The information shown in the Fig 1 seems to rise gradually, which implies that the sensitivity of the technique increases in parallel with the NCA concentration. This is a significant finding since it brings into view ways of optimising NCA concentration to improve diagnostic outcomes in clinical scenarios. The sensitivity levels also rise and then level off at higher concentrations, suggesting that these are the maximum levels beyond which changes to NCA concentration bring little improvement. This information proves very useful for clinicians on the amount of NCA to use at any one time to enhance the detection rates while at the same time reducing health complications of the patients.

The detection rates of endometriosis using nano contrast agents for patients of different age are shown in the Fig. 5. It can be stated that the detection rates are considerably high among the group 31-40, the detection rates lessens gradually as the age increases in subsequent groups. This may imply that young patients with early child-bearing potential may have exaggerated physiological reactions to NCA, resulting in better endometriotic lesion detection. On the other hand, the relatively low detection rates observed in the elderly might be due to hormonal fluctuations, differences in tissues or presence of other diseases which could distort the results of imaging. It is, therefore, important to comprehend these differences in NCA

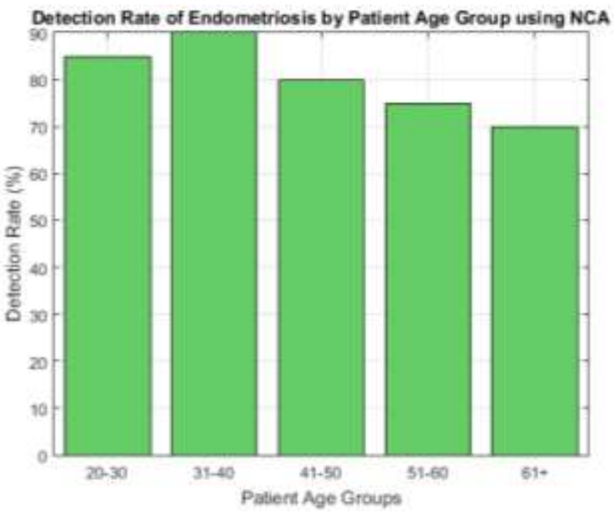

Fig. 5 detection rates of endometriosis using nano contrast agents for various ages

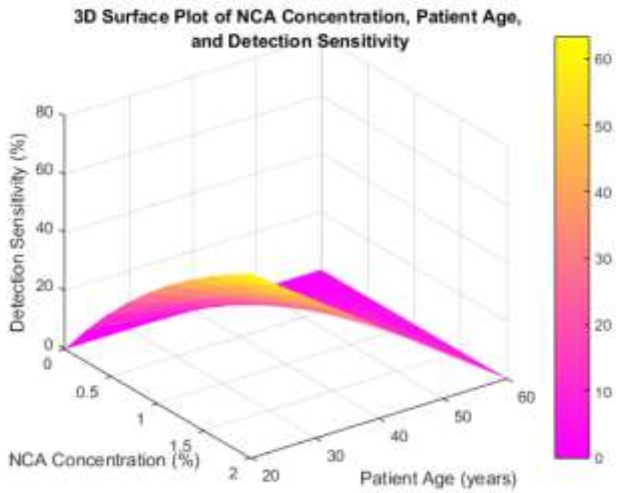

Fig. 6 Sensitivity of detection using patient age and nano concentration

performance depending on the age of the patients for the purpose of better adjusted US diagnostic strategies in the setting of endometriosis.

Fig. 6 shows the outcome of how the sensitivity of endometriosis detection different concentrations of nano contrast agents and age of the patient. The surface shows that detection sensitivity increases more so with high concentrations of NCA especially in the young clients. The sensitivity is observed to start reaching a plateau as the NCA concentration increases, this could imply that beyond this concentration any increase in its concentration does not necessarily improve its detection capability. Further, the presence of new variables of age bring about variation in sensitivity, the patient in 20s-30s are more sensitive than patients of 50s. Such trend could be due to alterations in tissue features and hormone levels that may influence imaging attributes. Olives and co-workers' findings clearly point to the value of analyzing NCA concentration and patient demographics to enhance diagnostic strategies for endometriosis.

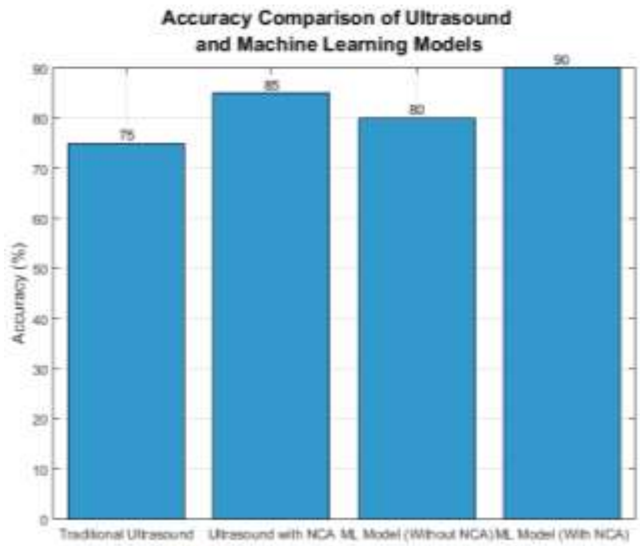

Fig. 7 The comparison of accuracy of various detection methods for endometriosis

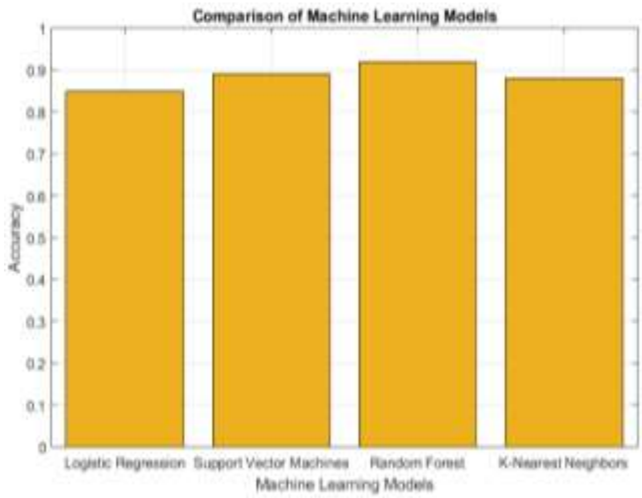

Fig. 8 Four machine learning algorithms: logistic regression, support vector machines, random forest, and K-nearest neighbors

Fig. 7 is preseted for the comparison of accuracy of various detection methods for endometriosis pointing toward remarkable improvements in the diagnostic success rate. The studies that involved application of the conventional ultrasound approaches obtained a reasonable success rate of 75%, thus the research area remains with prospects for development. Yet, the combination of nano contrast agents (NCA) increases this rate to 85% proving the effectiveness of the indica-proprietary imaging. Indeed, greater accuracies are shown by machine learning models at 90% when combined with NCA. This means that, through incorporation of both machine learning and NCA, imaging is not only made better but accurate and reliable diagnosis is also made easier as well. In other words, the results reinforce the fact that investing in new approaches to endometriosis diagnosis is necessary to enhance the disease's detection and improve the patient's prognoses.

Fig. 8 shows how the four machine learning algorithms:

logistic regression, support vector machines, random forest, and K-nearest neighbors work at endometriosis detection with the help of the ultrasound nano contrast agents. Out of all these models we obtain the highest value of the accuracy thus size and variability of the data can be managed by the Random Forest. And last but not least Support Vector Machines and K-Nearest Neighbors are also reasonably good, although slightly worse than Random Forest – this implies they are good but may not always provide the same level of detail on the given data. Individually Logistic Regression has lower accuracy than others, presumably because of the linear model which may not capture intricate relation in the data set. In general, this comparison holds testament to Random Forest's stability in this application while proving itself as a potent model to improve endometriosis detection using machine learning.

4. Conclusions

The combination of ML with ultrasound nano contrast agents is one new progressive solution that has potential in the identification of endometriosis. Using principles of high sensitivity and specific nano contrast agents, disease models by machine learning can excel at distinguishing between the endometriotic lesions and the adjacent healthy tissues that are difficult to distinguish using conventional imaging modalities. It is learnt from the findings that besides enhancing the visibility of lesions, ML also aids in real-time detection as accurate as that of the ground truth, thus providing early diagnosis, and minimizing misdiagnosis. This approach also avoids delays caused by the need to recognize the lesion, and could potentially make it easier for clinicians to diagnose endometriosis less invasively.

Moreover, augmentation of ultrasound contrast ML may enhance patient care since methods aimed directly at individual patients can be identified and utilized. These techniques have shown to provide advanced diagnosis to map lesions better, so that the planning of the surgeries becomes better and the monitoring after the operation is also better. Also, instead of the contrast agents that are based on nano-particles, applying of the corresponding algorithms with help of ML balances diagnostics' variability and standardizes process, which can be used anywhere, thanks to the implementation, making it rather helpful in clinical work. Future research could potentially refine these ML algorithms or may integrate Nature Intelligence assisted models for higher efficacy that might revolutionize the perspective on endometriosis diagnosis and treatment.

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