

Deep Learning Aided Diagnosis of Rheumatoid Arthritis

Deep Learning Project Report



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# Abstract

The past decade has seen some effort being directed towards the use of deep learning techniques to develop a way to automatically diagnose the severity of rheumatoid arthritis (RA) in a patient. However, there is still some work to be done for the development of an end-to-end system that can achieve this in a commercial setting and aid medical specialists. To further this cause, there is a need to analyze and compare present approaches to the problem and find improvements that can help in progress towards a system that can achieve good performance in RA diagnosis with less time, effort, and cost. This system will analyze the noteworthy approaches to RA diagnosis through deep learning and try to propose improvements to the current techniques.

# Introduction

Rheumatoid Arthritis (RA) is an auto-immune disease that is characterized by joint pain, stiffness, swelling, weakness, and fatigue. The disease usually occurs in the elderly above the age of 65 and affects small joints, such as those of hands and feet, causing severe deformities if left untreated. The manual method of RA diagnosis utilized by RA specialists includes assigning a narrowing and erosion score to each of the patient’s hand or foot joints. These scores are then utilized by the Sharp/van der Heijde (SvH) for determining the severity of the disease. For this method, the RA specialist regularly needs to monitor 44 joints (combined for both hands and feet) to assign 86 joint scores in order to observe the rate of progression of RA in a patient. However, this process is tedious, time-consuming, and requires a significant amount of effort. Furthermore, the entire process can only be completed by an RA specialist with a significant knowledge base.

Therefore, there is a need for an automated system that can speed up the process by automatically determining the narrowing and erosion scores along with other RA frisk factors to determine the severity of the disease in the patient. For such a system, there are mainly two tasks that are involved: (1) identifying joints in a patient’s X-rays, and (2) determining narrowing and erosion scores along with other risk factors to evaluate RA progression in a patient. For the purpose of developing such as system, significant work has been done in the past decade that can be utilized to build a system to be used in real-life. The aim of this paper is to present all the notable approaches to the development of an RA diagnostic system using machine learning and deep learning techniques. Furthermore, the paper will also use the understanding achieved by the analysis of current methods to propose improvements to the field of study.

# Literature Review

## Computer-Aided Diagnosis System for RA Using ML (2017)

The quality of life of a patient with RA can only be improved through timely treatment. However, that can only be achieved through proper measurement of the disease progression. Usually, a manual process is adopted to evaluate the modified Total Sharp Score (MTSS) and joint space narrowing (JSN) from patient X-rays. However, these X-rays must be taken and analyzed regularly to see RA progression in a patient. As this process can be tedious and time-consuming, there is a need for an automatic method. [1] proposes the use of Support Vector Machines (SVM) with histogram of oriented gradients (HOG) to detect the joints in fingers. The MTSS is then calculated using Support Vector Regression (SVR).

The method proposed in [1] uses a two-class SVM. The system extracts 140 patches from X-rays of each positive and negative class. The SVM is then trained on these positive and negative HOGs. For Joint Detection, the paper proposes using 100x100 pixel image patches from X-ray images. When fed into the SVM, this produces results in the range -1 to 1, where 1 means joint. The results from SVM for all patches are arranged in descending order, thus putting the joints at the top.

For MTSS calculation, the paper assumes that bone deformities in RA patients change the intensity gradients of finger joints in their X-rays. These changes in intensity gradients are used by the SVM to calculate MTSS, which is then compared to the manually evaluated JSN and MTSS to find the variance of the calculated value from the ground truth value.

When put to test on X-rays of 45 RA patients, the system proposed by [1] achieved finger detection with an average accuracy of 81.4%, showing better results in mild RA patients than severe ones. However, when it came to MTSS calculation, the system was only able to calculate erosion and narrowing scores with average accuracies of 50.9% and 64.3% respectively.

Therefore, even though using SVM yields decent results where joint detection is concerned, it provides uninspiring results when considering MTSS calculation. And since MTSS calculation is the backbone of determining disease progression, the method proposed by [1] is proved to be insufficient for commercial use.

## Finger Joint Detection Method in Hand X-ray Radiograph Images Using Statistical Shape Model and Support Vector Machine (2020)

The system proposed by [1] though is not in vain as it led to future work that utilized the base architecture to improve upon finger joint detection [2]. As a successor of [1], this paper introduced an improvement in joint detection and improved accuracy from 90.6% to 94.5% using a statistical shape model (SSM)[[1]](#footnote-2).

Where [1] failed to identify joints at image boundaries and fingertips, this paper proposed a new method to change the way the foreground was discriminated from the background. Furthermore, it combined SSM with SVM to offer better joint detection results even at the fingertips. Overall, the paper introduces a three-step method for better results: (1) Background bias reduction method in X-ray radiograph images, (2) Construct SSM of finger joint position coordinates, and (3) Automatically detect finger joints through SVM+SSM.

In the first step, the upper and lower borders are removed which significantly reduces background bias while evaluating results. Afterward, an SSM of the finger joints is used to normalize each subject’s joint shape vector by randomly choosing the shape vector of a subject to which the other subjects’ shape vectors are normalized. For the joint detection, the SVM is trained using a leave-one-out-cross-validation (LOOCV), where one subject is used for testing while the rest are used for training the SVM.

The differences in results achieved by [1] and [2] can be observed in Table 1.

|  |  |  |
| --- | --- | --- |
| Mean Accuracy | Only SVM [1] | SVM+SSM [2] |
| Finger Joint | 90.6% | 94.5% |
| Fingertip | X | 83.3% |
| Both (finger joint + fingertip) | X | 91.6% |

Table 1

Therefore, it is evident that the model proposed in [2] significantly improves the results for finger detection as compared to [1].

## Using Deep Learning to Assign Rheumatoid Arthritis Scores (2021)

The machine learning methods employed for the purpose of RA predictions have been achieved but not without their challenges as exhibited by [1] and [2]. The models proposed require much more information than just X-ray images to compute reasonable results. Furthermore, due to their dependencies on other information sources, these models also do not compute scores for all the joints of hands and feet, unlike the manual method that involves analysis and scoring of these joints.

[3] utilizes the data provided for the RA2-DREAM Challenge organized by the University of Alabama at Birmingham and Icahn School of Medicine at Mount Sinai to fill the gaps left by previous methods. As the dataset has images in different sizes, the images are preprocessed to 100x100x3. And since there are fewer patients with scores that indicate RA progression, the data is also augmented to get 2078 samples from the original 368. This dataset is then split into the train (1662 samples) and test (416 samples) sets.

Even though there are a lot of radiographic scoring methods for RA [4], this paper utilizes the Sharp-van der Heijde score [5] to find narrowing and erosion at each joint of the left and right hands and feet. For each hand/wrist image, 15 joints are assessed along with 6 joints from each foot to find the narrowing score. Similarly, for the degree of erosion, the model assesses 16 joints from each hand/wrist image and 6 joints from each foot. The erosion and narrowing scores are then used to find an overall damage score within the range 0-448 where a higher score means more damage. When done manually, this process of computing the scores can be time and effort-consuming, as well as expensive and subjective. Therefore, [3] proposed an automated model to calculate these scores.

As far as the model is concerned, the proposed architecture consists of the Input layer, CONV-8[3x3x3], MAXPOOL[2X2], MAXPOOL[2X2], CONV-32[3X3X16], FC-4, and Output Layer. The activation functions mainly utilized are ReLU at each convolutional layer and a Softmax at the end to get the classification output. The model proposed and tested in [3] was also compared against two other deep models: a 1000-node 1 hidden layer network, and a [1000,100,10]-nodes 3 hidden layer network that achieved more than 95% accuracy for the MNIST dataset [6]. On average, the model proposed by [3] achieved 90.8% accuracy with a 0.0469 root-mean-squared-standard-deviation (RMSD). As compared to this model, the single hidden layer model achieved 81.38% accuracy with 0.2106 RMSD, while the three-hidden layers network achieved 79.4% accuracy with a 0.2308 RMSD. This exhibits the superior performance of the architecture described above.

Even though this model achieved higher than benchmark results, it still has its shortcomings, the major one being that at the time of its proposition, the model was implemented in MATLAB. This means that the model cannot be utilized in commercial practice. Therefore, there is a need to implement the proposed architecture in Python and obtain similar results. This model can then be utilized in real-life predictions for patients and pave the way more achieving more accurate results with an increased dataset.

## Evaluation Method of Rheumatoid Arthritis by the X-ray Photograph using Deep Learning (2021)

While [3] established the baselines for how accurate a model for evaluation of erosion and narrowing scores can be, [7] took the work a step further by developing an end-to-end that doesn’t just do the classification of the condition but also automatically recognizes the joints. Not only this but the system can also be improved and modified by the doctor in diagnosis at the hospital in which the system is used, thus paving the way for further learning. Some key tasks for the development of this system include: (1) Generation of Training Data, (2) New Images Input, (3) Check Task of Medical Doctor, and (4) Improvement of Model Using Transfer Learning.

Unlike [3], this paper evaluated only the erosion score titled *destruction score* (DS) through the Sharp/can der Heijde scoring method. This score varies in a 0-5 range with 0 being a normal score, 1 indicating discrete erosion, 2-4 showing significant erosion, and 5 meaning complete disappearance of joint space and collapse of the bone.

For this identification and classification task, [7] makes use of a pre-trained object tracking model called YOLO (You Only Look Once). For the purpose of this system, YOLO V3 was used. The class for this YOLO model is set as 6 for emulating the range 0-5 and 30 training data images are used to train the model.

Now, for the training of this model on RA X-ray images, 5-dimensional data was collected per image in the form (position (x, y), size (width, height), score). This resulted in 20 data points per X-ray image. each image is an X-ray of size 1170x827.

The system works by taking an X-ray image as an input and then passing it through the trained model that draws the position of each joint along with their DS scores. The resultant image is then used for approval by the medical professional in charge. When checking the image, the medical professional can: (1) Delete a data point if the position is wrong, (2) Add a Data Point if the marker doesn’t exist, (3) Modify the Image if the position/scale are wrong, and (4) Modify if the score is wrong as shown in Figure 1.

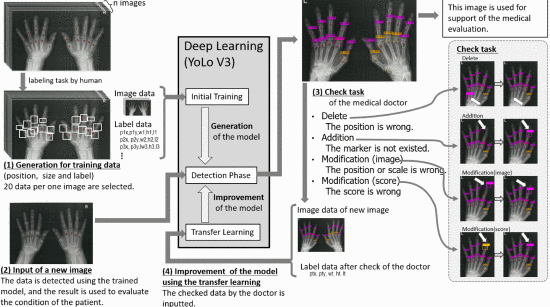


Figure 1

In the end, the prediction, as well as corrections, are fed back into the model for transfer learning so that the model can improve over time. As an end-to-end system with commercial applications, this feature makes the system an ideal candidate to be replicated with modifications for improved accuracy.

In terms of evaluation metrics, the model performs at a decent level since its lowest accuracy is 60% for score=3 and its average validity rate is 80%. However, as observed in [3], these metrics can be significantly improved through a fine-tuned model. Another gap in the system is also the lack of data available for training. With an increase in the number of data images, these results can see a significant improvement.

## Rheumatoid Arthritis Detection method based on Mask R-CNN (2021)

Instead of developing a deep network from scratch, [8] decided to utilize already existing object detection algorithms to locate and classify the joints affected by RA (usually hands and feet). For the purpose of this paper, the authors decided to utilize Mask RCNN. Mask RCNN is an extension of Faster RCNN that uses Region Proposal Network (RPN) unlike its predecessors that used selective search algorithm. Mask RCNN extends Faster RCNN in a model that is much simpler and computationally faster. It works for prediction and segmentation masks on each region of interest (ROI) in parallel with classification and bounding box regression already occurring.

Another benefit of using Mask RCNN over Faster RCNN is also that Mask RCNN used ROIAlign instead of ROIPool which can prevent any information loss that could tamper with joint detection.

For the dataset, the detection system proposed in [8] uses Digital Radiography (DR) images from 90 patients, including both male and female patients. DR images are just a digital form of X-rays and provide the same information as normal X-ray films. The manual annotation of diseased joints by medical professionals is saved in an XML file format that includes the left and right coordinates of the bounding box of affected joints.

For the Mask RCNN model, the segmentation layer is removed and only the detection layer is used as we only need to detect the joints. For evaluation of the model, COCO metrics[[2]](#footnote-3) were used. The paper compared Mask RCNN results with the Faster RCNN results and concluded that Mask RCNN achieves much better results as compared to Faster RCNN as evident in Table 2.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Model | Backbone | AP | AP50 | APm | APl |
| Faster RCNN | R-50-FPN | 19.62 | 66.51 | 19.07 | 23.02 |
| Mask RCNN | R-50-FPN | 19.82 | 69.12 | 20.72 | 21.24 |

Table 2

Additionally, different depth and backbone architectures of Mask RCNN were also compared and concluded that an R-50-FPN achieves the best results as shown in Table 3.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| MODEL | Backbone | AP | AP50 | APm | APl |
| Mask RCNN | R-50-C4 | 19.55 | 62.14 | 19.34 | 21.29 |
| Mask RCNN | R-50-FPN | 19.82 | 69.12 | 20.72 | 21.24 |
| Mask RCNN | R-101-C4 | 16.96 | 58.89 | 16.47 | 20.29 |
| Mask RCNN | R-101-FPN | 18.89 | 59.64 | 19.27 | 21.24 |

Table 3

When applied to test scenarios, this model was able to achieve confidence rates of up to 100% in identifying the diseased joints and drawing a bounding box around them. And as the model used Mask RCNN, the detection is quite fast and can be used in commercial settings for preliminary screening of RA patients.

## A Study on Automated Grading System for Early Prediction of Rheumatoid Arthritis (2021)

Like the analysis at hand, [9] compares different machine learning and statistical approaches for identifying RA in patients and evaluating the progression of the disease. The analysis showed significant favor towards deep learning methods such as the ones that use CNN as these methods provide approximately 85% percentage even in complex scenarios. As compared to these networks, statistical approaches, as well as machine learning approaches like use of SVM, yielded much lower accuracies. Therefore [9] suggests the continuation of using CNN and other deep learning models for evaluating disease progression in future research work. This recommendation, though, comes with a grain of salt as these deep learning approaches require a large amount of data to yield reasonable results. Therefore, not only is there a need for bigger and better datasets, but there is also a requirement for these methods to be optimized enough for commercial applications in medical setups.

## Detection of Rheumatoid Arthritis Using Machine Learning (2019)

Even though most of the work in the domain of RA detection has focused on supervised ML techniques and statistical models, there are still some outlier approaches to solve this problem. One such approach is presented by [10] which proposes the use of clustering techniques for the early detection of RA in patients. For the purpose of this study, the authors considered three types of clustering, namely, K-means, Hierarchical, and DBSCAN clustering.

According to this paper, there are many factors that can be used to detect and evaluate the stage of RA in a patient. From among these factors, the four most prominent were taken into consideration. These include, (1) values of Anti CCP[[3]](#footnote-4), (2) Rheumatoid Factor (RF), (3) ESR[[4]](#footnote-5), and Swollen Joint Count (SJC).

Clustering algorithms help to create clusters of patients that can provide insight into the trends of the above-mentioned four factors in patients with RA. These factors help analyze the danger in certain age groups, and gender for the development of RA. As mentioned by [10], analysis of these factors can help in the early detection of RA in risk groups. And early detection can prove itself valuable as it will most likely be followed by early treatment. Early treatment can not only slow down the progress of RA significantly but also improve the quality of life (QOL) in patients which is a vital part of medicine.

As a result of this comparative study, it was concluded that K-means and hierarchical clustering methods can only work well when data is cleanly separable. Furthermore, both of these methods tend to be very sensitive to outliers that can significantly reduce performance. Both these methods also require the user to specify the number of clusters beforehand which is tedious. In comparison, the DBSCAN algorithm performs well with outliers and doesn’t need the number of clusters beforehand for grouping the data.

When the time and space complexity of these clustering methods were compared, DBSCAN still performed better than K-means and hierarchical clustering with time complexity of O(n2) and space complexity of O(n). The complete comparison can be observed in Table 4.

|  |  |  |  |
| --- | --- | --- | --- |
| Algorithm | K-means | Hierarchical | DBSCAN |
| Time | O(n2) | O(n3) | O(n2) |
| Space | O((m+k)n) | O(n2) | O(n) |

Table 3

These clustering techniques to identify patient trends can be combined with other machine learning or deep learning techniques proposed by work that came afterward to create an end-to-end diagnostic system that can raise red flags in case of risk patients so that doctors can monitor them closely and provide treatment where necessary. This will help not only in the treatment of patients but also in early detection which can have huge effects on continued QOL in RA patients.

## Broad Learning with Attribute Selection for Rheumatoid Arthritis (2020)

Another unique approach to identifying risk factors for RA with notable accuracy was presented by [11] to determine the risk factors associated with RA that could help with the evaluation of its prognosis. For this purpose, the authors proposed a novel approach called a broad learning attribute selection system (BLAS) to diagnose the risk factors. The intuition behind using this architecture instead of a deep one was the simultaneous investigation of desired connection weights that could be achieved in a much more efficient way through a broad architecture.

A broad learning system (BLS) is essentially flattened architecture instead of a deep one. As deep architectures usually suffer from complexity and huge time constraints because of a large number of connected parameters involved, BLS serves to prevent that complexity altogether through incremental learning algorithms [12].

The basic system developed for rheumatology works by extracting the clinical data of rheumatology patients from the electronic medical database. This data including missing or noise values is then preprocessed. Afterward, the dataset is divided into three categories depending on the severity of symptoms, and the risk factors are determined through the ranking of attributes. This process is based on multi-attribute reduction with entropy and a rough set.

The study took data from 5000 patients and this data included every relevant detail that could help with diagnosis including age, gender, height, weight, blood pressure, morning stiffness, joint pain number, pretreatment information, and diagnosis date among others. For determining the progression of the disease through risk factors, a total of 8 risk factors were considered. These included CCP, CRP, HAQ, DS28, SSA-antibody, RF, Anti-CCP, and Larson Score. Depending on the values of these factors, three progression levels were determined where a *low* value indicates slight RA disease, *medium* levels indicate RA but not in a serious condition, and a *high* value is indicative of serious disease status.

As far as the broad learning model is concerned, it was trained using 10-fold cross-validation. The number of mapping nodes and enhancement nodes used was 10 and 100 respectively, while the output dimension of the model was set to 10. The model was evaluated using the F1 score. Overall, the broad model showed significant improvement over other models such as SVM, Naïve Bayes, ForestPA, and Dendritic Neuron Model (DNM) by showing the best mean accuracy at 99.67% with 0.32% absolute error.

Though the model presented in [11] shows hopeful results for future work in both broad learning and its application in the medical classification field, there is still room for improvement. Some gaps include an imbalance in the dataset and the size of the dataset. Future works can build upon these shortcomings to introduce a more robust method for determining risk factors and using them for finding disease progression.

# Pros & Cons

Analysis being the basis of this paper, some of the promising novel techniques as well as their gaps need to be discussed for a better overview. [1] displays good results for joint detection through SVM with an accuracy of 90%. However, it falls short when compared with other novel methods that involve deep learning [3] or broad learning models [11] as discussed in this paper. The system also performs poorly in MTSS calculation.

[2] improves upon the model presented in [1] by using statistical shape models (SSM) to improve the accuracy of joint detection for further evaluation of RA progression in a patient’s scans. This improved model yield good results by achieving an accuracy of 94.5% on average. This improvement can be utilized in the development of an end-to-end system for RA diagnosis.

Since the application of machine learning techniques in the field of rheumatology is quite recent, it was a natural thing to shift from ML models to more robust deep learning models. A tentative effort to utilize deep learning models for RA detection can be observed in [3] where the proposed model achieved 90.8% accuracy in determining the progression of RA. This proposed system however was implemented in MATLAB and thus cannot be utilized in more robust end-to-end systems for future commercial use. Therefore, there is a need to replicate the system in Python and achieve similar results.

[7] took a step further in the development of a complete end-to-end system with the base thought of developing a system that could not only assist in a commercial setting but also improve with time. And this is where their proposed deep learning model with an improvement component through transfer learning comes in. The idea, though not unique, is a step in the right direction for the development of RA detection and diagnosis systems that can prove useful in real medical scenarios. Though the approach presented by [7] was good in its consideration of real-life scenarios and improvement, the performance achieved by the presented model is decent at best. However, the system can be significantly improved upon by fine-tuning the model. Another constraint for the poor results was also the lack of training data. Therefore, one dimension of improvement can be to develop a dataset for RA that can help in future model development.

Another interesting approach to determine RA progression in patients was through Mask RCNN as presented in [8]. This method proves to be faster as compared to other deep learning models as it utilizes a pre-trained object detection model tuned for the identification of joints. The best thing about the proposed model is that it also achieves great results even in the case of severe RA patients. However, there is still a need to test the system on a larger dataset to see if the results are replicated or not.

As the purpose of this paper was to give an overview of the developments in the application of deep learning to the field of rheumatology, some unique approaches to the problem were also considered in [10] and [11] in the form of clustering and broad learning. However, it should be noted that both approaches are for determining risk factors for RA that can help in the diagnosis of RA in patients. There is still a need to combine these models with diagnostic models for a complete system.

[10] presented how different clustering techniques could be utilized to group patients into different categories ranging from mild to severe conditions based on the values of various risk factors. [11] also presents a solution for the same task but with a different approach by utilizing a broad learning architecture to determine the most impactful risk factors in RA diagnoses of different groups. While both approaches show a new way of tackling the diagnosis problem from the ground up, there is a need to apply them to a bigger dataset to observe whether similar accuracies and performance are displayed or not.

# Conclusion & Future Work

With the development in the different architectures of deep learning to solve trivial day-to-day problems as well as complex issues, it is only natural to utilize these advancements for the automation of medical procedures and diagnoses. The work presented in this paper gives a thorough overview of the different deep learning as well as machine learning systems being applied to the field of rheumatology. Though the work is yet in its initial stages, the results are promising and encourage more experiments for the development of systems that can assist doctors in determining RA in patients earlier as compared to orthodox methods. Not only this, but the development of such systems shows promise to one day be able to monitor the progression of diseases in patients with enough accuracy which can then be utilized for early treatment of patients and to improve their quality of life.

As far as any input to improve upon the already presented techniques is concerned, the author of the paper proposes that the system presented in [3] should be replicated in python to observe its performance. Furthermore, the approach presented in [8] shows the most promise for efficient joint detection. So, it can be combined with the diagnostic component of [3] to shape an end to and system, the performance of which can then be evaluated in combination. Furthermore, the author also feels the need to add a component of continued learning in the end model, which can be hard to achieve with a deep model. Therefore, if the performance time of [3] is too long then the broad learning approach presented in [11] can be utilized as broad architectures provide much faster learning with the addition of new inputs. Understanding all the constraints of present systems and the space for improvement, the author is interested in approaching the problem with a systematic view, utilizing the best current models for the development of a system with decent performance.

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1. Statistical Shape Models (SSMs) are geometric models that describe a collection of semantically similar objects in a very compact way. SSMs represent an average shape of many three-dimensional objects as well as their variation in shape [↑](#footnote-ref-2)
2. Average Precision (AP) – precision for determining true positives correctly [↑](#footnote-ref-3)
3. Positive CCP and Positive RF means patient has developed RA

   Positive CCP and Negative RF means patient is in early stages of developing RA [↑](#footnote-ref-4)
4. Greater than normal rate of ESR indicates there is inflammation in the body [↑](#footnote-ref-5)