Research Proposal of Machine Learning in Detection OF Osteoarthritis.

Introduction

Osteoarthritis (OA) is a joint disease which can occur in any joint of the human body (mostly found in hip joints and knee joints) (mayo clinic, 2021). OA affects cartilage and surrounding structure of the entire joint including trabecular bone, femoral head, bone tissues ligament, synovial fluids, hyaluronic acid (which helps synovial fluid lubricate the joint), subchondral bone (located underneath the cartilage).

Osteoarthritis (OA) has stage I-IV stages. **Stage 0** (Pre-OA) has no clinical sign of the joint pathology but is characterized by an appearance of cellular changes. No other surface lesion is observed but MRI might detect pre-OA. Treatment involves change in lifestyle. Early stage of OA, also referred to as **Stage 1**, exhibits negligible cartilage injury and development of bone spurs but patients rarely complain of pain. It is usually diagnosed by physical examination or imaging studies, and its treatment does not involve surgery; instead, it may involve modified diet and regular exercises or change in weight. Mild OA at **Stage 2** involves more the formation of bone spur as well as slight narrowing space in joint as well as frequent pain frequently. Diagnosis is done through X-ray and the treatment as suggested includes NSAIDs, braces and exercises. Moderate osteoarthritis (OA) is categorized in **Stage 3** characterized with major cartilage loss and worsening pain during and after the exercise. It may be diagnosed using MRI or arthroscopy or through a surgical procedure; the treatments are through drugs, physical therapy and administration of injections for patients in severe pain. **Stage 4** severely limits their movement and has constant pain and stiffness coupled with very minimal or no cartilage at all. This is diagnosed using images and osteotomy or joint replacement may be needed since cure usually necessitates intervention ((Bandoim, 2023; Surmachevska and Rubio, 2023; Horváth et al., 2023)).

Osteoarthritis (OA) is a complex and disabling condition that led to $140 billion in healthcare expenses and $164 billion in lost wages in the United States in 2013 alone (Murphy et el., 2018). Additionally, with an aging global population, the prevalence of osteoarthritis (OA) is continuing to increase [5]. Artificial Intelligence (AI) and Machine Learning (ML) can help clinicians to detect OA and its pathology where ML can also help with personalized treatments. This method allows us to use multidimensional and multi-source data to understand the nature of OA (Arbeeva et al., 2023).

The complexity and diversity in both the structural and clinical aspects of **osteoarthritis (OA)** have made it challenging to develop effective treatments to slow or stop the disease's progression. Due to this challenge, the focus on AI driven technology to detect OA at its earliest stage has been a considerable topic to discuss and to explore.

Literature Review

PubMed research was conducted from October 1 2024 to November 3 2024 this research was based on the key words Osteoarthritis and machine learning with the restriction of recent one year, we got 178 articles from those articles 43 articles where selected in terms of the title and abstract. After a detailed full text review done on those 43 articles 30 articles where selected as our area of interest. These articles where divided in 3 genre, (a)Lifestyle related ML Study, (b) Images related ML study and (c) Gene related ML study.

Research Proposal of Machine Learning in Detection OF Osteoarthritis.

(a) Lifestyle related ML Study

The study done by Widera and his colleagues, tried to determine patients with osteoarthritis (OA) who are likely to develop their disease more quickly. This is important because it will increase understanding of the factors that may affect the treatment efficacy through enrolment of these "rapid progressors" in RCTs (Randomized Controlled Trials). Cohort Hip and Cohort Knee which contained 1002 patients and Osteoarthritis Initiative (OAI) which contained 3465 patients were used on which Six types of ML algorithms are examined. These datasets were comprised of clinical data, and X-ray data results including Total Joint Replacement (TJR). The study established that the trained models outperformed conventional approaches to predicting OA progression in terms of pain, or structural alterations, or both. The lesson showed that the current methods of analysis had an accuracy of 20 percent, while the ML models had approximately 45 percent accuracy. This indicates that the designed ML models should be more effective in identifying patients who are likely to develop the worsening OA symptoms. However, the approach has not been validated for independent use and needs further testing in future RCTs to establish its practicality in the external environment (widera et al., 2020).

Few studies still hold hopeful about the integration of machine learning in successful OA risk prediction. Nielsen et al., (2024) in their study aimed to predict OA risk over 5 years using an XG Boost ML model that used diverse patient data using socio-demographic, and lifestyle information collected during recruitment apart from 5 years of longitudinal electronic health record (EHR) data. The performance metrics for the clinical model showed successful cross-validated results. An ROC-AUC of 0.72 (95% CI:0.71-0.73), predicting OA in 70% of future cases, further identifying a 66% of the cases as true positives.

On the other hand, for non-OA cases, 60% of them were correctly predicted, with a 67% true-negative rate. However, slightly lower accuracy was predicted in certain joint predictions, with ROC-AUCs ranging 0.67-0.73. Weight-bearing joints like knees (0.73) and hips (0.72) displayed the highest weight.

Shapley values identified age, NSAID use, and Body Mass Index (BMI) as top predictors of risk factors with other factors like self-reported health, walking speed, and Vitamin D levels. The patients were categorised into 14 subgroups through cluster analysis in the study, with unique risk profiles based on SHAP value clusters, showing varied risk patterns across OA subtypes.

(b) Image related ML Study

Dorraki and his team (2023) came up with a unique idea to detect OA by using Novel Network Approach inspired by Graph Theory. They focused on trabecular bone structures and their changes. They compared bones from people who have HOA (Hip Osteoarthritis) to healthy bones with no history of bone disease in the same age group of the people. Then they created a Machine Learning model to classify between OA affected to healthy bone. They used CNN architecture for image processing and to identify the pathology of OA. This approach helped to explain how certain patterns are linked to the occurrence of OA.

The need to predict cartilage loss in the knee as a manifestation of OA progression was the aim of the study by (Bonakdari et al., 2022). They focused on assessing bone curvature using MRI scans. The researchers paid particular attention to eight areas of the knee and employed gender-related simulation data. According to their outcomes, researchers discovered that cartilage degeneration most likely affect the medial condyle region, the interior portion of the knee. The results were highly accurate, with an R value of 0.78 in the test as well

as in the validation sets. The best ML algorithm deployed was an "adaptive neuro-fuzzy inference system"; however, it required many input variables (10 in this case) to increase the computational cost.

To see if the severity of knee osteoarthritis (KOA) can be classified and identified correctly using deep learning (DL) models, a study (Zhao et al., 2024) used a widely accepted standardized grading system known as Kellgren-Lawrence (K-L) grading scale, for accessing KOA severity. Ever K-L grade from 0-4 represents an increased severity, while a K-L grade of 0 represents no evidence of KOA, K-L4 being the most severe.

A total of 29 DL models with 19,745 X-ray images for K-L 0 (no KOA), 30 DL models with 8221 images for K-L1 (very mild KOA), 30 DL models with 11057 images for K-L 2 (mild KOA), 29 DL models with 6349 images for K-L 3 (moderate KOA), 29 DL models with 2630 images for K-L 4 (severe KOA) were tested to understand the accuracy of these DL models in classifying images and areas they made mistakes.

The study showed that the Data Learning models are effective in classifying the severity of KOA using X-ray imaging, especially displaying a better performance in identifying more severe grades i:e, (K-L3 and K-L4) than milder grades i:e, (K-L1 and K-L2). The misclassification rates resulted higher in distinguishing between adjacent grades, especially for mild cases, where the models often confused the very mild (K-L1) and mild (K-L2) KOA severity.

On the other hand, Leung et al., (2020), in their study predicting the likelihood of Total Knee Replacement (TKR) in patients over the next 9 years, identified that compared to different models multi-task DL models trained to analyse X-ray images using "transfer learning", a model that leverages knowledge from one task to perform better on a similar task, are highly effective in predicting the TKR outcomes, achieving the best balance of accuracy and reliability with an AUC of 0.87. This metrics outperformed their test results of other models such as KL grade analysis (AUC 0.74), Osteoarthritis Research Society International OARSI model (0.75). The KL model, however demonstrated high sensitivity (91%) but fell short on specificity with a low specificity (58%). The multi-model balanced this metrics better thereby reducing false positives and providing reliable predictions. It also showed an optimal performance in a "zombie plot" with a focus on key knee joint areas like joint space. Risk factors for TKR such as BMI, knee injury history, and pain scores, were included, with multitask DL model being the strongest predictor. Although, factors from contralateral knee initially corelated with TKR, they became less significant when combined with other variables.

(c) Gene related ML Study

In the further study conducted by Bonakdari et al., now the aim was to know whether structural knee OA could be accurately forecasted with other factors such as, SNPs and mtDNA haplogroups in combination with age and BMI (OA damage) which are the two main predictors of knee OA. In this study, the bonakdari focused on 901 participants from the OAI database to perform machine learning studies, where hybrid models helped boost prediction capability. These models were internally and externally validated on the data from the Tasmanian Older Adult Cohort Study. The outcome demonstrated excellent validity of the models as they scored above 95% in the initial experimental trials and 85% in the external test. This underscores the genetic factors in hitch with clinical findings as promising biomarkers for prediction of OA progressiveness. And the current research points to the development of a more focused, individualized approaches to OA treatments in the future, opening the door for similar studies in other populations and multiple

other genetic risk factors. In his research, Bonakdari draws attention on biomolecular data applicability to inform the development of machine learning algorithms in complexity of OA progression and treatment (Bonakdari H et al., 2022).

In the DNA Methylation and Biomarkers Study, the researchers aimed to identify biomarkers for osteoarthritis (OA) progression by analysing DNA methylation patterns, which are chemical changes in DNA that can impact gene expression. The study focused on predicting different types of OA progression, such as pain-only, radiographic-only (joint damage seen in X-rays), or both. The team used data from three independent groups: a subset of 554 patients from the Osteoarthritis Initiative (OAI), 128 individuals from the Johnston County OA Project, and an additional 56 participants from the OAI. The researchers applied elastic net regularized logistic regression to correlate methylation patterns with progression outcomes. They found that models based only on clinical features (like symptoms or X-rays) did not perform well, with an AUC of 0.54–0.68. However, when methylation data was included, either alone or combined with clinical data, the models performed much better, particularly in identifying patients with pain-only or pain plus radiographic progression. They identified 13 CpG sites (regions of DNA where methylation occurs) as reliable predictors of OA progression in both the original test and independent groups. The study is significant because it was validated with both internal and external data, making the results more reliable. These methylation biomarkers could serve as stable, time-independent indicators of OA progression, offering potential for more targeted and personalized treatment approaches in the future (Arbeeva L et al., 2023).

Another study's (Liu et al., 2024) approach to identifying biomarkers for OA starts with Weighted Gene Co-expression Network Analysis (WGCNA) to find gene modules linked to OA traits. The study uses an optimised threshold to build a network from gene expression data. ML techniques, LASSO and Random Forest were used to pinpoint cellular energy response genes which are critical for OA diagnosis. The findings of the study defined a panel of four gene biomarkers (HSPA5, UBL4A, ATF4, PPP1R15A) for diagnosing OA and employed the nomogram to quantify the diagnostic performance. The performance of the model was confirmed with an ROC curve was constructed and the AUC score was found to be high, suggesting good diagnostic capability. OA patient's immune cell proportions were evaluated using CIBERSORT, and these authors confirmed associations of immune cells with these biomarkers. The biomarker levels in OA tissues were further confirmed by qRT-PCR conducted on laboratory confirmation.

Discussion

In case of OA, the application of AI and ML is useful predicting the patterns and progression of the disease but there are challenges faced by researchers. That is; the AI models could be biased in many ways. This is possible where the data we use to train the AI belongs to a set of people or have some missing information. For example, electronic health records (EHRs) often have gaps or are designed for billing, not for detailed medical analysis, which can lead to inaccurate predictions . That is why when AI systems are developed in a particular population, applying it to a different or real patient population may not be effective.

Another challenge is that most AI models are not validated with other datasets. Notably, without this external validation, the results cannot always be trusted which limits the use of AIML in practical life (Ghassemi, Oakden-Rayner, and Beam, 2021; Wynants et al., 2020).

Research Proposal of Machine Learning in Detection OF Osteoarthritis.

Conclusion

Current ML algorithms and their structure are having a positive impact on OA diagnosis. However, for more practical and realistic approach we can introduce recent advance methodologies built around Reinforcement Learning, Active Learning, and Cloud Computing which can help to overcome certain deficiencies of current AI/ML models for OA. **Reinforcement learning** allows the system to improve through the results given to it, thus minimizing the biases and increasing the correct answers' rates as time goes by (**G**eeksforGeeks, 2021). **Active learning** makes certain that the model pays attention to the most difficult instances, and when in doubt, it seeks advice from doctors, which enhances the learning process through the integration of knowledge from the experts (Francois-Lavet et al., 2018). This feedback loop also helps maintain a human-in-the-loop again that keeps the model up to date and clinically sound. Additionally, **cloud computing** enables a combination of big databases and increases the system's adaptability and applicability; at the same time, it supplies the necessary computational resources for the processing of extensive medical data （Armbrust, 2010）. These techniques will help reduce biases from the ML Architecture and will make AI more trustable and a reliable source in Medical Applications.

Research Proposal of Machine Learning in Detection OF Osteoarthritis.

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Research Proposal of Machine Learning in Detection OF Osteoarthritis.