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# An Extensive Review on the Utilization of Lidocaine in Cataract Surgery

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## ABSTRACT

Cataracts are a disease that causes a gradual decrease in visual prowess and requires surgery when the symptoms progress to an abortive state. This disease can be treated through surgical procedures that use anesthetics, such as lidocaine. Through inhibiting sensory nerve propagation to the brain, lidocaine plays an invaluable part in reducing pain for patients that undergo cataract surgery. Current clinical practice commonly utilizes 2% lidocaine with fentanyl as a combination agent. However, recent studies have reported that concentrations higher than 1% can cause substantial alteration to corneal epithelium cells. Additionally, fentanyl is cited as an extremely addictive opioid inappropriate for continual use in cataract surgeries. In this review, the authors examine the application and concentration of lidocaine, along with the various combination agents that were reported in several studies that describe the usage of the anesthetic during cataract surgery. Within the review, it was found that most surgeons generally only use lidocaine gel on the corneal epithelium tissue of patients during cataract surgery. Perhaps this standard could change over time as it is generally known that using intracameral injections in conjunction with topical anesthesia produces better patient outcomes. The authors find that although anesthetics and surgical treatment for cataracts are generally beneficial for patients, there are still many adjustments that could be implemented to enhance patient outcomes.

## INTRODUCTION

A cataract is an ocular disease that occurs when the lens of a patient's eye becomes cloudy. Cataracts generally occur as a result of the aging process. In fact, it is estimated that one out of every five individuals from the ages of 65 - 74 has a cataract [1]. It is theorized that due to ultraviolet (UV) light exposure over time, the collagen within the eye's lens deteriorates which causes the normally clear lens to become cloudy in appearance. In fact, one study has shown that high exposure to UV light can cause a 60% increase in the risk of developing cataracts [2]. This deterioration caused by UV light can lead to hazy vision and lower perception during the night. Cataracts generally cause a gradual decrease in vision over time but don't cause physical pain. Although cataracts are a treatable disease, they are also the leading cause of blindness within the developing world due to a lack of access to surgery. Cataracts can be surgically removed from a patient and replaced with an intraocular lens (IOL). It is estimated that over 10 million cataract surgeries are performed each year around the world [3]. In order to diminish the pain that patients may experience during an operation, it is quite common that surgeons use anesthetics when performing this procedure. One of the more popular anesthetics for this procedure is lidocaine. Due to the fact that this anesthetic is quite commonly used for this procedure, it is important to outline and understand the proper standards and protocols that are necessary when utilizing this medication in order to protect and maintain patient health. The purpose of this review is to analyze the current usage and application of lidocaine on patients during cataract surgery.

## METHODS

This review utilized a systematic approach to examine the application and concentration of lidocaine, as well as the various combination agents reported in several studies that describe its usage during cataract surgery. A comprehensive literature search was conducted in electronic databases, including PubMed, MEDLINE, and Google Scholar, using appropriate keywords. The search was limited to English-language studies focusing on lidocaine application during cataract surgery. The selected studies were carefully reviewed, and relevant data on lidocaine application techniques, concentration, combination agents used, and reported outcomes were extracted and analyzed. The findings were synthesized to provide a comprehensive overview of current practices and potential adjustments for enhancing patient outcomes.

## RESULTS

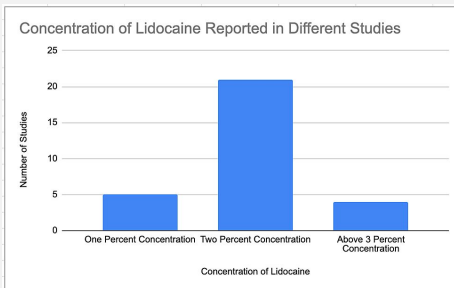


Figure 1: Lidocaine Concentration Distribution of the Studies Within the Literature Review

## Key Findings

- University of Berlin study found use of lidocaine for cataract surgery to be effective and non-harmful, given that doses were administered at 1%. However, there was substantial corneal endothelial alteration in pig corneas at lidocaine 5% and complete endothelial necrosis with lidocaine at 10%.
- University of Florida study found that, compared to the use of epinephrine with lidocaine 1% as the control, use of phenylephrine and ketorolac 1.0%/0.3% with lidocaine 1%, decreased the likelihood that patients experienced moderate-to-severe pain or requested for fentanyl for additional pain relief.
- Phenylephrine, tropicamide, tetracaine, povidone-iodine, and fentanyl were the most commonly used combination agents with lidocaine in cataract surgeries
- The most common area of application for lidocaine is the corneal epithelium.
- Few reported studies injected lidocaine into the intracameral region of patients' eyes. This could potentially be for faster visual rehabilitation and decrease in room turnover time for patients.
- The most common concentration of lidocaine that was used was at 2%, indicating this concentration is the bare minimum that needs to be utilized in order to achieve an analgesic effect
- Few studies utilized lidocaine at concentrations of 1% and 1.5%, potentially indicating that different patients have different thresholds to achieve the analgesic effect or that different procedures with variable combination agents require a lower concentration of lidocaine to ensure the safety of the patient.
- Few articles utilized lidocaine at concentrations of 2.5%, 3.5%, and 4%, potentially indicating that a higher concentration of the anesthetic is needed for cataract surgeries that are more invasive.

## CONCLUSIONS

- Understanding the usage of anesthetics, such as lidocaine, during cataract surgery can help improve the current standard of patient care.
- Lidocaine is a commonly used anesthetic in cataract surgeries because it is efficient and requires little to no preoperative preparation.
- Most physicians in the explored studies used lidocaine concentrations of 2% on the corneal epithelium.
- Most commonly used combination agents with lidocaine in cataract surgeries were phenylephrine, tropicamide, tetracaine, povidone-iodine, and fentanyl.
- Current studies have suggested that lidocaine is most beneficial when used both topically on the corneal epithelium and through an intracameral injection.

## CLINICAL IMPLICATIONS

- Cataract surgery is crucial to protect the eyesight of many individuals.
- Despite all the current research conducted on application and usage of lidocaine on cataract surgery patients, additional studies are needed in order to determine more ideal standards that can be used for these procedures in order to minimize side effects that patients may experience.
- Current standard concentration of lidocaine during cataract surgery is 2%; however there is no mechanism or system to follow if this concentration needs to be adjusted to accommodate specific patient needs.
- Supplementary research involving combination agents, such as ethylenediaminetetraacetic acid (EDTA), may be needed.
- Appropriate usage of anesthetics is important to reduce pain patients experience during surgery, but to protect the safety of cataract surgery patients, further research on effects of lidocaine must be continued.

## ACKNOWLEDGEMENTS

The authors express their gratitude to the individuals cited in this review for their valuable contributions to the advancement of science. No other acknowledgments are necessary at this time.



# Efficacy of GLP-1 Receptor Agonists in Reducing Urine Albumin-to-Creatinine Ratio in Type 2 Diabetes Patients

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## ABSTRACT

As diabetes mellitus becomes increasingly prevalent globally so does diabetic nephropathy, a complication leading to one of the world's leading causes of end-stage renal disease (ESRD). Current research has linked an increase in the urine albumin-to-creatinine ratio (UACR), a marker for kidney damage, to a greater risk of adverse renal outcomes and ESRD in patients with diabetes. Of the diabetes medications studied and implemented in clinical settings, glucagon-like peptide-1 receptor agonist (GLP1-RA) drugs have been shown to not only help control HbA1c in diabetic patients but have also demonstrated numerous cardiovascular, hepatic, and renal benefits. The objective of our study was to assess the efficacy of GLP1-RA drugs in reducing UACR in patients with type 2 diabetes mellitus (T2 DM) to determine if GLP1-RAs could be used to provide renoprotection in diabetic nephropathy in addition to their glucose-lowering effects. Upon a comprehensive review of the literature, we conducted a statistical analysis to determine the efficacy of GLP1-RA monotherapy and combination therapy in reducing UACR in comparison to placebo and not in comparison to insulin glargine. GLP1-RA therapy could serve as an alternative treatment in diabetic nephropathy to insulin glargine, which carries a higher risk of hypoglycemia and weight gain.

## INTRODUCTION

Diabetes mellitus (DM) is a chronic metabolic disorder characterized by elevated blood glucose (hyperglycemia). With DM afflicting approximately 11% of the global population and the percentage expected to grow rapidly over the coming years, there has never been a stronger need to focus on diabetes and its multitude of adverse health effects. Type 1 diabetes (T1 DM) is caused by an absolute deficiency of insulin secretion owing to an autoimmune pathologic process occurring in the pancreatic islets. Type 2 diabetes mellitus (T2 DM) is due to both an increased resistance to insulin as well as insufficient compensatory insulin secretion. Other causes of diabetes may include gestational diabetes mellitus, genetic disorders, and those caused by drugs, chemicals, or infection. Diabetic nephropathy develops in approximately 40% of those with diabetes, making it a leading cause of end-stage renal disease (ESRD) globally. There are two key markers for chronic kidney disease (CKD): the urine albumin-to-creatinine ratio (UACR) and the estimated glomerular filtration rate (eGFR). UACR estimates 24-hour urine albumin excretion. UACR values above 30 mg/g are positive for albuminuria and are sensitive markers for CKD. Drugs that decrease UACR are associated with improved cardiovascular outcomes in addition to improved renal outcomes. Treatment options for diabetic patients with ESRD are limited; for patients with deteriorated renal function, common oral hypoglycemic agents like metformin are not recommended. GLP1-RAs are a class of incretin-based therapies that have been widely studied for their effects on HbA1c, cardiovascular disease (CVD), and nonalcoholic fatty liver disease (NAFLD). One of the mechanisms by which GLP1-RAs have been shown to have renal-protective effects is natriuresis. Natriuresis is the increased urinary excretion of sodium, which can lead to a reduction in blood pressure and a decrease in heart workload.

## METHODS

A comprehensive search was conducted on PubMed to obtain an all-encompassing query on using various GLP1-RAs in patients with T2 DM and their respective effects on changes in UACR. In the identification stage, using a combined total of nine different searches, an aggregate total of 1646 papers published after 2010 were identified. Citations were imported to Mendeley Reference Manager, through which duplicate studies were manually found and removed, resulting in a reduction of 246 papers and an aggregate total of 1400 unique papers. Of the non-duplicate papers, each title and abstract were individually scanned for relevance, and it was found that only 143 papers studied relevant topics. One hundred and twenty-five papers were further eliminated due to specific calculations in the UACR not being provided, so 18 papers were left to be used for analysis.

## RESULTS

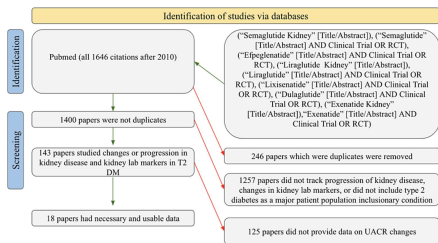


Figure 1: PRISMA diagram to provide a visual representation of the study screening process  
PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses; RCT: randomized clinical trial. Figure independently designed by authors.

## Key Findings

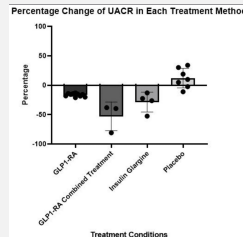
While current research does not have a definitive stance on the effect of GLP1-RAs on GF, there has been strong evidence to show that they provide a marked reduction in UACR, notably seen by 14 of the 16 unique trials and observational studies. Upon statistical analysis, it was determined that the use of a GLP1-RA drug was able to significantly decrease UACR values compared to a placebo in T2 DM patient populations. While the maximally administered dosage appears most beneficial, even doses as low as half the maximally administered dosage prompted considerable decreases in UACR vs. placebo. Interestingly, when insulin glargine was used as a comparator drug to GLP1-RAs, there was no statistical difference in the reduction UACR between the two medications. The GLP1-RA combined treatment group consisted of three studies from that studied exenatide taken in combination with either insulin glargine, metformin (biguanide), or dapagliflozin (SGLT2 inhibitor). Our review provides context to clinicians regarding the use of GLP1-RA drugs in patients with or at risk of DKD to reduce UACR and help prevent adverse renal outcomes or the precipitation of ESRD in patients with T2 DM. Although the small sample size of studies was a notable limitation, a greater problem was the lack of substantive studies focused specifically on patients with DKD. While GLP1-RAs have been extensively studied as a means to reduce HbA1c, their cardiometabolic and hepatic benefits have only been discovered recently, and studies are currently being conducted specifically on the use of GLP1-RAs on DKD.

## CONCLUSIONS

While the data showed no significance between the efficacy of GLP1-RA compared to insulin glargine or GLP1-RA combination therapy compared to insulin glargine, the use of GLP1-RAs was statistically more effective than a placebo in reducing UACR. Although there was no a statistical difference in the efficacy of GLP1-RA monotherapy or combination therapy in reducing UACR versus insulin glargine, GLP1-RA treatment is a promising alternative to insulin therapy in DKD due to the lower risk of hypoglycemia, the induced weight loss instead of weight gain with insulin therapy, and a possible reduction in cost. If further data reveal that GLP1-RA combination therapy is more effective in reducing UACR than GLP1-RA monotherapy or insulin therapy, GLP1-RA combination therapy could be the first line of glycemic control and renoprotection in diabetic patients at risk of progression to CKD.

## CLINICAL IMPLICATIONS

Current research supports the use of GLP1-RA in combination with a lower dose of insulin to more effectively reduce HbA1c while mitigating weight gain from insulin and lower the risk of hypoglycemia, all with no change in adverse gastrointestinal issues from the use of GLP1-RA independently. Further investigations should look closely at the ongoing clinical trial FLOW, expected to be completed in August 2024, investigating semaglutide versus placebo in patients with T2 DM and CKD. Literature on the combined usage of GLP1-RAs and insulin in DKD is limited, but their concurrent use in diabetes is promising and could significantly reduce UACR. Exenatide with metformin and exenatide with dapagliflozin demonstrate these combinations as effective options for reducing UACR.



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# A Systematic Review on the Effects of Diet on Alzheimer's Disease

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## ABSTRACT

Alzheimer's disease (AD) has been very difficult to prevent and cure using the medicine available today. However, there has been some hope with using a ketogenic diet (KD) to reduce the cognitive and quality of life decline experienced by patients with AD. In this review, the authors discuss the research done on the effect of a KD on AD to provide some potential avenues for future research and to determine a KD that can be best adopted by patients. The authors also go over the effects of KDs and low-carbohydrate diets (LCDs) on the cognitive function of healthy patients and on patients without AD to determine the similar and dissimilar effects of the diets. The authors found that the KD was able to improve the cognitive abilities and quality of life of patients ranging from mild to severe AD. Several types of memory were improved as a result of the diets. Further research needs to be conducted to determine the cause behind these improvements. However, the several studies that were done were mostly in agreement that once ketosis was reached, cognitive improvements were observed in patients ranging from mild to severe AD or mild to moderate cognitive impairment. Through the use of a KD, potential mechanisms can be found to reduce the cognitive decline of patients with AD, and potentially even prevent the damaging effects of cognitive decline from AD altogether.

## INTRODUCTION

Alzheimer's disease (AD) is currently the sixth-leading cause of death in the U.S. [1]. Around 6.2 million Americans are living with the disease in 2021, and about eleven percent of the population over 65 years of age have the disease [1]. Advancements have been made on reducing and eventually preventing the effects of AD, and the one effect focused on in this paper is cognitive decline. Ketogenic diets are currently being studied as a method to help reduce or prevent the onset of cognitive decline in Alzheimer's patients [2].

The ketogenic diet's goal is to reduce one's reliance on using glucose as fuel for the brain and instead use ketones [2]. Since AD could potentially reduce the number and overall function of glucose transporters in the brain [3], ketones could provide an alternate avenue to supply the brain with energy in patients with AD. The studies on the several diets that induce ketosis have some discrepancies. The purpose of this paper is to determine the best ketogenic diet that has been tested currently for preventing the harmful effects of AD. This paper looks at the cognitive improvements associated with the different diets. For example, whether medium-chain triglycerides are used and the effects of using a ketogenic diet and not another diet that does not achieve ketosis.

While prevention of Alzheimer's disease may be very far in the future, our effort to reduce its prevalence in the population will undoubtedly benefit the world and future families that could suffer from the disease. This review is set apart from others because it looks at the cognitive effects of a KD and LCD on people without AD as a method of comparison.

## METHODS

Randomized controlled trials were searched using PubMed with the search terms "((Alzheimer's) AND (ketogenic diet) AND (cognitive function)) OR ((ketogenic diet) AND (cognitive function)) OR ((low-carbohydrate diet) AND (cognitive function)))". Only articles in English were included in the analysis, and papers not focusing on the cognitive changes within human patients while on a low-carbohydrate diet were not included. The 1995 paper by Wing et al. was not included as only an abstract could be found. Only literature published online within PubMed was included in the review. Using the search terms and criteria mentioned, only 21 of the 25 papers found were used in the literature review.

## RESULTS

Table 1. Methodological analysis of ketogenic and low-carbohydrate diets within the literature review.

Author (year)	Experimental Diet Used (percentage of total calories)	Presence of MCTs in Diet	Dropout Rate of Low-carb Diet	Patient Population Tested	Presence of Ketone Body Increase	Cognitive Improvements Observed
Branch (2019) [5]	Modified Atkins with MCTs	Yes	20	Mild AD	Yes	Yes
Brinkworth (2009) [15]	LCD (61% Fat, 35% Protein, 4% Carb)	No	58	Overweight or Obese Adults	N/A	No
de la Rubia Otri (2018) [6]	Mediterranean Diet with Coconut Oil (30% Fat, 15% Protein, 55% Carbs)	Yes	N/A	Mild-Moderate AD and Severe AD	Yes	Yes
El-Rashidy (2017) [9]	Modified Atkins with MCTs (60% Fat, 30% Protein, 10% Carb)	No	33.3	Children With Autism Spectrum Disorder	Yes	Yes
Emilien (2017) [11]	High Protein LCD (30% Fat, 40% Protein, 30% Carb)	No	0	Healthy Adults	N/A	No
Fischer (2004) [12]	LCD (100% Fat) and LCD (100% Protein)	No	N/A	Healthy Adult Men	N/A	Yes
Fortier (2021) [20]	KD with MCTs	Yes	38	Adults and Mild Cognitive Impairment	Yes	No
Haybaron (2007) [17]	LCD (61% Fat, 35% Protein, 4% Carb)	No	7.69	Overweight or Obese Adults	Yes	Yes
Henderson (2020) [7]	50% Caprylic Triglyceride AC-1204 Formula	Yes	24.3	Mild-Moderate AD	No	No
Holloway (2011) [10]	LCD (73.6% Fat, 24.6% Protein, 1.6% Carb)	No	N/A	Healthy Adult Men	N/A	No
Iacobucci (2019) [9]	LCD (60% Fat, 25% Protein, 15% Carb)	No	8.3	Healthy Adults	Yes	No
Ulf (2016) [18]	LCD (61% Fat, 20% Protein, 20% Carb) and KD with MCTs (Fat is 30% MCTs)	Yes	0	Children and Adolescents with Refractory epilepsy	N/A	Yes
Kakoschke (2021) [16]	LCD (58% Fat, 28% Protein, 14% Carb)	No	3.45	Obese Adults with T2DM	N/A	No
Karl (2015) [13]	LCD (39% Fat, 42% Protein, 28% Carb)	No	0	Healthy Adults	N/A	No
Lee (2021) [22]	KD with MCTs (37.3% Fat, 15.7% Protein, 47.0% Carb)	Yes	0	Adults with Primary Progressive Multiple Sclerosis	Yes	No
Markus (1999) [23]	Protein Rich Carbohydrate Poor Diet (32% Fat, 27% Protein, 41% Carb)	No	0	High and Low Stress Post-Students	N/A	No
Morrison (2020) [21]	LCD (68.2% Fat, 24.4% Protein, 7.3% Carb)	No	0	Adults with HIV and Mild-to-Moderate Cognitive Impairment	Yes	Yes
Phillips (2021) [4]	LCD (58% Fat, 29% Protein, 7% Carb)	No	19	Mild AD	Yes	No
Torossyan (2021) [4]	40g Caprylidene	Yes	29	Mild-Moderate AD	Yes	N/A
Yomogida (2021) [14]	KD with MCTs (87.16% Fat (48.31% MCTs), 18.83% LCTs), 8.09% Protein, 4.79% Carb)	Yes	N/A	Healthy Elderly Individuals	Yes	Yes

## Key Findings

- In all studies but one, diets that resulted in increased ketone body levels improved cognition in patients with Alzheimer's Disease [5, 6.]
- In studies where cognition was improved in Alzheimer's Disease patients, medium-chain triglycerides were implemented in the diet as a ketogenic factor [5, 6]
- In the henderson et al. and Phillips et al. studies, 50% Caprylic Triglyceride and a low-carb diet did not induce ketogenesis, which both resulted in no cognitive improvement. Latter study went into the COVID-19 lockdown, which could have impacted results. [4, 7]
- Torossyan et al. found increased cerebral blood flow with ketogenesis induced by 40g of Caprylidene [4]
- Healthy adults given low-carb diets showed no cognitive improvements [9-13]
- One study with healthy adults showed that the presence of ketone bodies did not improve their cognition [9]
- Ketogenesis induced by a low-carb diet in obese adults with type two diabetes mellitus showed improvements in cognition [17]

- Healthy elderly patients who consumed a low-carb diet with medium-chain triglycerides showed improved cognition with ketosis
- Low-carb diets with medium-chain triglycerides also showed improved cognition with ketosis in children and adolescents with refractory epilepsy [18], children with autism [19], and patients with mild cognitive impairment associated with and not associated with HIV [20, 21].
- Dropout rates in some studies were high due to medium-chain triglycerides, which are known to cause gastrointestinal issues upon ingestion [5, 7, 20]

## CONCLUSIONS

- A ketogenic diet has the potential to improve the cognitive function of patients with Alzheimer's Disease and improve their quality of life if ketosis was achieved.
- Ketosis was the probable factor that improved cognitive function
- Medium-chain triglycerides may be a factor in improving cognition in Alzheimer's Disease patients
- Healthy adults may not be affected cognitively by ketosis or low-carb diets
- Healthy adults could potentially benefit cognitively from medium-chain triglycerides like the Alzheimer's Disease patients
- Many cognitive and metabolic conditions can benefit from ketogenic diet
- We propose a longitudinal study with two groups of participants: one consuming a ketogenic diet and another consuming normal control diet. The health and cognitive faculties of the individuals can be accessed. Groups can be further broken down into two categories: at risk for Alzheimer's Disease and not at risk for Alzheimer's Disease.

## CLINICAL IMPLICATIONS

- Alzheimer's Disease is a neurodegenerative disease that causes many cognitive problems in patients and is the 6th leading cause of death in the United States
- There is currently no cure for Alzheimer's Disease
- This study provides insight on many diets and their effects on patients with Alzheimer's Disease and other cognitive and metabolic conditions
- Ketogenic diets and medium-chain triglycerides may contribute to cognitive improvement in patients with Alzheimer's Disease
- The ketogenic diet can be used for many other cognitive conditions to determine the chemical pathways being affected

## ACKNOWLEDGEMENTS

The authors express their gratitude to the individuals cited in this review for their valuable contributions to the advancement of science. No other acknowledgments are necessary at this time.



# Advancing Myocardial Infarction Diagnosis through Machine Learning: Leveraging Electrocardiogram Images for Early Detection

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## ABSTRACT

Myocardial infarction (MI) detection is crucial for timely intervention and improved outcomes. This study aimed to develop a machine-learning model using electrocardiogram (EKG) images to detect MI. A dataset of 2172 EKG segment images was utilized, and the model achieved an average precision of 0.977 with a precision and recall value of 92.2% each. The high accuracy demonstrated the potential of machine learning algorithms in MI detection using EKG images. The model exhibited a sensitivity of 96.1% and a specificity of 88.5%, highlighting its efficacy in accurately identifying MI-positive cases and normal EKG images. Early MI detection is essential for prompt management, and integrating accurate MI detection models into clinical practice can improve patient care. However, limitations such as dataset size and algorithm selection should be considered. Further research and validation using diverse datasets are necessary to enhance the model's generalizability. In conclusion, our study demonstrates the potential of machine learning algorithms in improving MI detection using EKG images. The developed model exhibited high accuracy, precision, recall, sensitivity, specificity, and overall performance, warranting further research and integration into clinical practice to facilitate early detection and improved management of myocardial infarction.

## INTRODUCTION

Myocardial infarction, commonly known as a heart attack, remains a significant global health concern with profound implications for morbidity and mortality [1]. It occurs due to the obstruction of blood flow to the heart muscle, leading to ischemic injury and potentially irreversible damage [2]. Myocardial infarction predominantly affects individuals with risk factors such as hypertension, hyperlipidemia, smoking, and diabetes [3]. Prior to the COVID-19 pandemic, myocardial infarction accounted for a substantial proportion of cardiovascular-related deaths worldwide, surpassing other cardiac conditions in terms of its impact on mortality [4]. Electrocardiogram (EKG) imaging has emerged as a vital tool for diagnosing myocardial infarction, allowing for the assessment of cardiac electrical activity and the detection of characteristic EKG changes associated with myocardial ischemia and infarction [5, 6]. EKG images provide valuable insights into the extent and location of myocardial damage, facilitating timely intervention and appropriate treatment strategies [7, 8]. However, the interpretation of EKG images by human experts can be subjective and influenced by individual expertise and experience, potentially impacting diagnostic accuracy [9]. Advances in machine learning and deep learning algorithms offer promising opportunities to improve myocardial infarction diagnosis through the analysis of EKG images using artificial intelligence (AI) techniques. These algorithms can learn intricate patterns and features indicative of myocardial infarction, leading to more accurate and consistent detection. This study aims to develop a myocardial infarction detection model utilizing EKG images. By creating a reliable and accurate myocardial infarction detection model, we seek to revolutionize the diagnosis of this life-threatening condition by providing a standardized and objective tool for healthcare professionals [10]. Such models have the potential to support early detection, prompt intervention, and the implementation of effective treatment strategies. Furthermore, integrating AI-based myocardial infarction detection models into clinical workflows could particularly benefit regions with limited access to specialized cardiologists and healthcare resources [11]. This investigation explores the potential of machine learning algorithms to enhance myocardial infarction diagnosis using EKG images. By leveraging AI technology, we aim to develop a robust myocardial infarction detection model that enhances the accuracy and efficiency of diagnosis, ultimately contributing to global efforts in combating this cardiovascular disease.

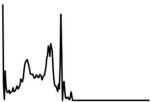


Figure 1: TB x ray

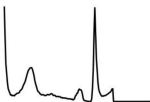


Figure 2: Normal chest X ray

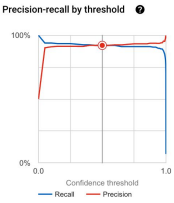


Figure 3: AUC Graph

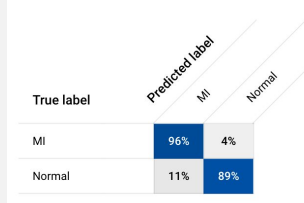


Figure 4: Confusion Matrix

## METHODS

This study aimed to develop a myocardial infarction detection model using a dataset of 2172 EKG segment images obtained from Kaggle.com. The dataset was carefully divided into three subsets: 80% for training, 10% for validation, and 10% for testing. These subsets ensured a representative distribution of both myocardial infarction-positive and normal cases across each phase of model development. Leveraging Google's Collaboration Platform, machine learning algorithms were applied to analyze the EKG images and identify specific patterns associated with myocardial infarction. The model was trained on the training set to learn and recognize these patterns, validated on the validation set to fine-tune its performance, and finally evaluated on the testing set to assess its accuracy and generalizability. Further validation studies and research efforts are needed to fully explore the potential of the model and its integration into clinical practice, with the aim of enhancing myocardial infarction diagnosis and improving patient outcomes.

## RESULTS

The developed myocardial infarction detection model achieved excellent performance in terms of accuracy and precision. The average precision of the model was measured at 0.977, indicating its ability to effectively classify myocardial infarction-positive and normal cases. The precision value of 92.2% indicates the high proportion of correctly predicted myocardial infarction cases among the identified positive cases. The recall value, also 92.2%, reflects the model's capability to accurately identify and retrieve true positive myocardial infarction cases. Sensitivity, calculated at 96.1%, represents the model's ability to correctly detect individuals with myocardial infarction. The model also demonstrated a specificity of 88.5%, highlighting its proficiency in correctly classifying individuals without myocardial infarction. The F1 score, combining precision and recall, was computed at 0.921, indicating the overall effectiveness of the model in detecting myocardial infarction cases. Finally, the model's accuracy was determined to be 92.17%, reflecting the proportion of correct predictions made by the model. These results affirm the model's robustness and potential for enhancing myocardial infarction diagnosis, contributing to improved patient outcomes.

## DISCUSSION

Myocardial infarction (MI), commonly known as a heart attack, is a leading cause of morbidity and mortality worldwide. Early and accurate detection of MI is crucial for timely intervention and improved patient outcomes. In this study, we aimed to develop a myocardial infarction detection model using electrocardiogram (EKG) segment images and evaluate its performance as a potential tool for enhancing MI diagnosis. The results obtained from this study demonstrate the potential of machine learning algorithms in improving MI detection using EKGs. EKGs are widely utilized in clinical practice for assessing cardiac function and detecting abnormal cardiac patterns. Our model, trained on a dataset of 2172 EKG segment images, achieved an average precision of 0.977, indicating its high accuracy in classifying MI-positive and normal cases. The high precision and recall values of 92.2% each suggest that the developed model effectively identified MI-positive cases while minimizing false positives and false negatives. This accuracy is crucial in avoiding unnecessary invasive procedures and ensuring prompt treatment for MI patients. The sensitivity of the model, calculated at 96.1%, highlights its ability to correctly detect MI-positive cases, minimizing the risk of missed diagnoses. Moreover, the model demonstrated a specificity of 88.5%, indicating its proficiency in accurately classifying normal EKGs and reducing the likelihood of false-positive MI diagnoses. The balanced performance of the model, as reflected by the F1 score of 0.921, further confirms its ability to capture both true positives and true negatives effectively. The high accuracy and performance metrics of the developed model suggest its potential as a valuable tool in MI detection using EKGs. By leveraging machine learning algorithms, we have harnessed the power of data-driven approaches to enhance MI diagnosis and improve patient care. The use of EKGs as a diagnostic modality for MI is advantageous due to its non-invasive nature and widespread availability in clinical settings. However, it is important to acknowledge the limitations of our study. Firstly, the performance of the model may be influenced by the size and diversity of the dataset used for training and evaluation. Additionally, the choice of deep learning algorithms and hyperparameters can impact the model's performance. Further research and validation studies using larger and more diverse datasets are warranted to assess the robustness and generalizability of the developed model across different populations and EKG systems. Furthermore, while the developed model achieved high accuracy, it is crucial to evaluate its performance in real-world clinical settings. The application of the model in a clinical environment would require addressing potential challenges, such as the integration of the model into existing healthcare systems and the consideration of factors that may affect performance, such as variations in EKG quality or patient demographics. In conclusion, this study demonstrates the potential of machine learning algorithms in improving MI detection using EKGs. The developed model exhibited high accuracy, precision, recall, sensitivity, specificity, and overall performance, suggesting its utility as an adjunct tool in MI diagnosis. Further research and validation efforts are necessary to enhance the model's generalizability and facilitate its integration into clinical practice, ultimately aiding in the early detection and improved management of myocardial infarction.

## CONCLUSIONS

In conclusion, our study highlights the potential of machine learning algorithms in improving myocardial infarction (MI) detection using electrocardiogram (EKG) segment images. The developed model demonstrated high accuracy, precision, recall, sensitivity, specificity, and overall performance, suggesting its utility as a valuable tool in MI diagnosis. Early and accurate detection of MI is crucial for timely intervention and improved patient outcomes. By harnessing the power of data-driven approaches, we have leveraged EKGs as a non-invasive and widely accessible diagnostic modality for MI detection. Our model, trained on a dataset of EKG segment images, achieved remarkable performance with an average precision of 0.977, indicating its high accuracy in classifying MI-positive and normal cases. The high precision and recall values of the model ensure its proficiency in identifying MI-positive cases while minimizing false positives and false negatives. The sensitivity of 96.1% indicates the model's ability to correctly detect MI-positive cases, reducing the risk of missed diagnoses. Additionally, the model demonstrated a specificity of 88.5%, reflecting its capability to accurately classify normal EKGs and reduce the chances of false-positive MI diagnoses. The results of our study contribute to the ongoing efforts to improve MI diagnosis using machine learning algorithms. The development of a reliable MI detection model using EKG images can assist healthcare professionals in making informed decisions, facilitating early intervention and appropriate management of MI cases. This can potentially lead to better patient outcomes and reduced morbidity and mortality associated with MI. However, it is essential to acknowledge the limitations of our study. The performance of the model may be influenced by factors such as the size and diversity of the dataset, as well as the choice of deep learning algorithms and hyperparameters. Further research and validation studies using larger and more diverse datasets are necessary to ensure the robustness and generalizability of the developed model across different populations and EKG systems. Furthermore, the application of the model in real-world clinical settings requires careful consideration of factors such as integration into existing healthcare systems, variations in EKG quality, and patient demographics. Additional validation studies and collaborative efforts between researchers, clinicians, and policymakers are necessary to evaluate the model's effectiveness in diverse clinical settings and facilitate its integration into routine practice. In conclusion, our study demonstrates the potential of machine learning algorithms in improving myocardial infarction detection using EKG images. The developed model exhibited high accuracy and performance metrics, suggesting its utility as an adjunct tool in MI diagnosis. Further research, validation, and clinical implementation efforts are warranted to enhance the model's effectiveness and realize its full potential in improving the detection and management of myocardial infarction.



# Advancements in Metastatic Melanoma Treatment: Optimizing Outcomes through Targeted Therapies and Combination Strategies

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## ABSTRACT

This literature review examines the impact of targeted therapies, immune checkpoint inhibitors, and combination approaches on metastatic melanoma. Advancements in treatment have improved patient outcomes, but challenges in achieving durable responses remain. Factors influencing melanoma metastasis and the importance of early detection are discussed. This investigation provides valuable insights into current treatment strategies and emphasizes the need for further research in metastatic melanoma management.

## INTRODUCTION

Metastatic melanoma, a highly aggressive form of skin cancer, has historically presented a bleak prognosis with limited treatment options. However, recent years have witnessed significant advancements in the management of this disease, primarily driven by the development and utilization of targeted therapies and immune checkpoint inhibitors. These pharmaceutical breakthroughs have revolutionized the treatment landscape, offering new hope and improved outcomes for patients with metastatic melanoma.

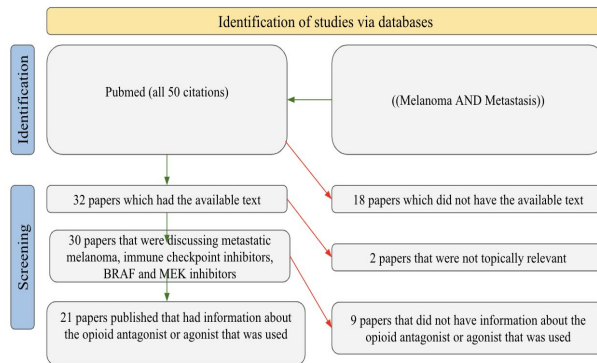
Furthermore, the introduction of targeted therapies, particularly BRAF and MEK inhibitors, has further revolutionized the treatment landscape for patients with BRAF-mutant metastatic melanoma. The COLUMBUS trial, for instance, demonstrated the superior efficacy of combination therapy with dabrafenib plus trametinib compared to monotherapy with dabrafenib alone, resulting in an overall survival rate of 44%. These targeted therapies specifically inhibit key molecular pathways involved in melanoma development, providing a targeted approach to tumor suppression.

This investigation aims to analyze various factors influencing the progression of metastatic melanoma by reviewing and synthesizing findings from previous studies. By exploring the impact of targeted therapies, immune checkpoint inhibitors, and their combinations, we seek to elucidate the current treatment landscape and identify areas for further research.

## KEY FINDINGS

- Combination therapies, incorporating both targeted therapies and immune checkpoint inhibitors, have shown enhanced efficacy compared to monotherapy in terms of overall survival and progression-free survival.
- Despite advancements in treatment, preventing melanoma recurrence remains a challenge, as none of the drugs studied showed complete effectiveness in preventing recurrence.
- The investigation emphasizes the importance of ongoing research and the development of novel combination strategies to improve long-term responses and prevent recurrence in metastatic melanoma.

## METHODS



**Figure 1.** PRISMA: Preferred Reporting Items for Systematic reviews and Meta-Analyses

DRUG	Recurrence Free Survival (RFS)
Pembrolizumab	37.5%
Nivolumab	40.9%
Ipilimumab	36.9%
Placebo	37.4%

**Figure 1.** Association between Drug used and Recurrence Free survival (RFS)

This figure illustrates that drugs used to treat melanoma are ineffective in preventing recurrence

## CONCLUSIONS

The analysis of multiple studies revealed the significant improvement in patient outcomes with the use of targeted therapies, including BRAF and MEK inhibitors, and immune checkpoint inhibitors. Combination therapies have also shown promise in extending overall survival rates compared to monotherapy. However, the durability of response remains a challenge, as patient response rates are often short-lived. Therefore, combining BRAF and MEK inhibitors with immune checkpoint inhibitors has been explored as a potential solution to achieve both higher response rates and more durable responses.

Factors influencing melanoma metastasis to different regions of the body were highlighted, emphasizing the need for early detection and intervention. Lymphatic spread to regional lymph nodes increases the risk of further metastasis and can lead to lymphoedema. Distant metastasis, which involves the bloodstream and affects organs such as the lungs, liver, brain, and bones, presents additional challenges in treatment.

The investigation of recurrence rates revealed that none of the drugs studied in the literature were entirely effective at preventing recurrence, including pembrolizumab, ipilimumab, and nivolumab. However, ipilimumab demonstrated the lowest likelihood of recurrence among the drugs analyzed. Surprisingly, the placebo groups within the studies also had a similar recurrence rate, suggesting the need for further research to improve overall prevention of melanoma recurrence.

## CLINICAL IMPLICATIONS

The findings of this investigation have significant clinical implications for the treatment of metastatic melanoma. The use of targeted therapies, immune checkpoint inhibitors, and combination strategies has improved patient outcomes and should be considered as standard treatment options. However, the limitations in response duration call for ongoing research and the development of novel therapeutic approaches. Early detection of melanoma and tailored treatment interventions based on the site of metastasis are vital for optimizing patient care and improving survival rates. Further studies should focus on refining existing therapies and exploring innovative combination strategies to enhance long-term responses and prevent recurrence in patients with metastatic melanoma.

## ACKNOWLEDGEMENTS

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# An Examination of Anesthetic Use and Postoperative Outcomes in Laser In Situ Keratomileusis (LASIK) Procedures

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## ABSTRACT

When laser in situ keratomileusis (LASIK) surgery is employed for myopia, hyperopia, and astigmatism, the process requires the usage of anesthetics to ensure that there is minimal patient harm and negative consequences once the procedure is complete. Statistical analysis was conducted as part of this review to evaluate the application of and distinctions between the different analgesics used for LASIK surgery by compiling and filtering information from multiple research studies. Typically administered oxybuprocaine and proparacaine were found to be the most commonly used anesthetics for LASIK, according to the data included in the review. It was also determined that there were no significant differences in terms of patient outcomes and drug concentrations when proparacaine was substituted for oxybuprocaine. This is particularly intriguing given their different chemical compositions. Temporary dry eyes were the most commonly reported adverse effect of LASIK when the anesthetic was employed. Perhaps cocaine derivatives produce similar anesthetic and post-surgical effects, but further investigations are needed to verify this hypothesis.

## INTRODUCTION

Laser in situ keratomileusis (LASIK) surgery is among the most frequently performed procedures worldwide. Nearly 60% of adults in the United States are affected by a refractory error, and approximately one million individuals undergo corneal refractive surgery annually [1]. Among US Food and Drug Administration (FDA)-approved LASIK device studies, 97% of patients achieved uncorrected visual acuity (UCVA) of 20/40, and 62% of patients achieved UCVA of 20/20. LASIK alters the cornea's refractive power in myopic, hyperopic, and astigmatic patients. This is achieved by utilizing a laser to create a hinged corneal flap from the epithelium, Bowman's membrane, and the superficial part of the corneal stroma [3]. Currently, the standard of care in terms of anesthesia for LASIK varies as there is no singular anesthetic that is universally used for every LASIK procedure. Conventional regional anesthetics include eye drops that inhibit pain signals to the ocular nerve. In some cases, concomitant administration of topical anesthesia has improved the quality of care for patients. Overall, the choice of anesthetic is largely based on preoperative factors (i.e., comorbidities, surgeon's preference, availability) that may influence patient safety, comfort, and outcomes [6]. To date, few studies have effectively compared the use of anesthetics historically used in LASIK surgery. In light of this, this review aimed to elucidate the benefits and outcomes of various anesthetics administered during ocular surgery.

## METHODS

We conducted a search on PubMed to find studies on the use of anesthesia in LASIK surgery. Exact searches were done with the keywords "laser and anesthesia," "analgesia and laser," and "laser surgery." We placed no restrictions in terms of time frames in the search. The search elicited a total of 237 studies, of which 79 were not duplicates, 56 had full text available, 46 were topically relevant studies, and only 36 had the relevant information needed and fulfilled the analysis criteria of our review. The data collected from these 36 studies included the type of anesthetic that was used, the dosage of the anesthetics that were used, the area of anesthetic application, and relevant information about post-treatment patient outcomes. Studies that did not provide sufficient information about at least two of these categories were excluded.

## RESULTS

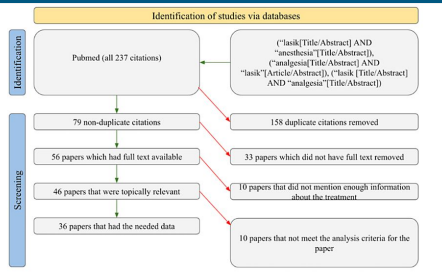


Figure 1: PRISMA Article Filtration Diagram

Group comparison	t value	P-value
Concentration of oxybuprocaine vs. proparacaine	0.4017	0.694
Side effects of dry eye in oxybuprocaine vs. proparacaine	0.8033	0.4343

Table 1: Oxybuprocaine vs. Proparacaine Concentration and Side Effects

## Key Findings

- LASIK surgery is typically performed under topical anesthesia using eye drops.
- Topical anesthesia is preferred due to its localized numbing effects and fewer side effects compared to other types of anesthesia.
- Recovery time is shorter with local anesthesia due to the shorter duration of nerve blocking.
- Topical anesthesia may not provide complete anesthesia, leading to discomfort, pain, and possible movement during the procedure.
- Proparacaine and oxybuprocaine are the most commonly used anesthetics in LASIK procedures.
- They are effective as local, topical anesthetics and are used at various concentrations (0.5%, 1%, 0.4%, and 2%).
- Despite functional differences, oxybuprocaine and proparacaine produce similar anesthetic effects at similar concentrations.
- The incidence of dry eye post-LASIK was not significantly different between oxybuprocaine and proparacaine.
- Both anesthetics have proven to be safe and efficient, with minimal complications reported.
- Eyelid closure can help spread the medication across the eye's surface, enhancing the anesthetic effect.
- Post-surgical complications in LASIK are generally rare, with severe complications such as blindness having a very low incidence rate.
- Dry eye syndrome (DES) is a common post-surgical complication, typically transient and lasting 6-12 months on average.

## CONCLUSIONS

- A review article was conducted on anesthetics used in LASIK surgery, compiling and analyzing multiple studies.
- Proper and effective anesthesia administration was associated with favorable patient outcomes in LASIK surgery.
- Dry eyes for a brief period of time was the most commonly reported negative consequence when anesthesia was used during LASIK surgery.
- Topically applied anesthetics oxybuprocaine and proparacaine were found to be the most commonly used anesthetics in LASIK procedures.
- Statistical analysis revealed no significant differences in patient outcomes and drug concentrations when proparacaine was used instead of oxybuprocaine, despite their different chemical compositions.
- Future studies could investigate the effect of using cocaine derivatives as anesthetic agents on patient outcomes after LASIK surgery.

## CLINICAL IMPLICATIONS

- This study provides information on different historically used anesthetics for LASIK, allowing physicians to have a wider range of options for anesthesia selection.
- Comparing outcomes and associated risks of different anesthetics helps in selecting the most suitable option for each patient.
- Varying dosages of anesthesia can be adjusted based on the collected data to balance efficacy and minimize side effects.
- This study emphasizes the importance of considering different areas of application for anesthesia administration to optimize efficacy.
- Consolidated information on post-surgery complications assists physicians in comparing and analyzing data from LASIK procedures.
- Recovery time is shorter with local anesthesia due to the shorter duration of nerve blocking.
- Despite functional differences, oxybuprocaine and proparacaine produce similar anesthetic effects at similar concentrations.
- Topically applied anesthetics were commonly associated with post-surgical complications of dry eye.
- The incidence of dry eye post-LASIK was not significantly different between oxybuprocaine and proparacaine.
- Both anesthetics have proven to be safe and efficient, with minimal complications reported.
- Prevalence of dry eye symptoms prior to LASIK is high, likely due to contact lens intolerance in some patients.
- Proper anesthetic administration is crucial for minimizing pain in LASIK patients, while early identification of myopia is important for optimizing surgical outcomes and reducing health implications.

## ACKNOWLEDGEMENTS

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# A Comparison of DASH Scores Resulting From Different Treatment Options For the Intra-articular Distal Radius Fracture in the Geriatric Population

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## ABSTRACT

There exist three main methods of treating distal radius fractures: closed reduction, open reduction internal fixation, and percutaneous fixation. 10 studies in the geriatric population comparing closed reduction and ORIF, and ORIF and methods of percutaneous treatment were found. DASH and PRWE scores from these studies at 1 year followup were compiled and means were compared via independent T tests. DASH scores in the ORIF and percutaneous treatment groups were better than the open reduction, although ORIF and percutaneous treatment groups were not significantly different. PRWE score analysis revealed a significant advantage of ORIF compared to percutaneous treatment, and percutaneous treatment over closed reduction and casting.

## INTRODUCTION

The distal radius fracture has one of the highest incidence rates across all age groups, contributing to 25% of all fractures in the pediatric population, and 18% of fractures in the geriatric population.

There are three main treatment options for the distal radius fracture: the closed reduction, the open reduction internal fixation (ORIF), and the percutaneous fixation. Depending on measures such as angulation of the distal fragment, comorbidity of an ulnar fracture, step off distance, and preexisting conditions, the scientific community has some understanding of which procedures should be done. However, consensus has not been completely reached about which procedures must be done when the cases do not fall within currently accepted guidelines. Minimal research exists comparing all three treatments in terms of indications, patient outcomes, and price.

When comparing three distinct procedures and the patient outcomes associated with each, it is essential to narrow down measures of comparison to clear variables that can be measured. The literature suggests measures of volar tilt, ulnar deviation, and grip strength are indicative of functional outcome. However, these metrics are difficult to compare due to differences in units and methods of measuring.

The primary metrics used to evaluate functional outcomes of the procedures were DASH score and PRWE score. The Disabilities of the Arm, Shoulder and Hand (DASH) outcome measure is a highly standardized self report questionnaire, evaluating difficulties the patient has in various categories such as feeling pain, having difficulties performing certain tasks, and being impacted socially. It is a scale from 0-100, with 0 indicating no disabilities. Because it relies on patient self reporting, it is susceptible to patient based variation. However, large sample sizes are correct for the variation. PRWE score is slightly more sensitive to patient differences than the DASH score for particularly distal radius fractures, which is an advantage of evaluating PRWE score [9]. While DASH and PRWE are both reliable and valid, DASH had better test-retest reliability (ICC .91), compared to PRWE (ICC .87).

As opposed to young adults, distal radius fractures in the geriatric population are much more serious because there are higher rates of osteoporosis. Because of the greater risks present in the geriatric population, this literature review will focus on data for the intra articular distal radius fracture in the geriatric population by analyzing DASH and PRWE scores.

## METHODS

Searches on pubmed were conducted using the keywords “open reduction internal fixation”, “external fixation”, “closed reduction”, “volar locking plate”, “K-wire”, “percutaneous” “casting”, “distal radius”, “elderly”. Literature reviews and studies about non-radial fractures were excluded. The data collected specifically concerned the geriatric population. It was made sure that the studies included information on postoperative DASH score or PRWE score. These scores were compiled into tables and it was noted whether the studies found a statistically significant difference with  $p < .05$  between the outcomes of the treatment groups. All data was retrieved from other studies which had proper patient consent. No personal information was included in this meta analysis, and only values of mean DASH and PRWE scores were retrieved from the studies included. Once all the DASH and PRWE values were compiled into the tables, averages for each group were found. 95% confidence intervals were also found for each group, and independent T tests comparing groups were performed to find p values to assess significance between the outcomes. P values resulting from the independent T tests comparing groups are listed on table 3.

## RESULTS

Table 1: DASH score at 1 year follow-up

study	# patients	p<.05	Closed Reduction	ORIF	Percutaneous Fixation
Arora 2009	130	no	11.6	11.1	N/A
Arora 2011	73	no	8.0 ± 9.3	5.7 ± 11.1	N/A
Saving 2019	140	yes	23.1 ± 19.8	15.6 ± 17.0	N/A
Huard 2010	38	no	N/A	21	17
Jubel 2005	55	no	N/A	17	17
Hollervolter 2011	40	no	N/A	14 ± 16	13 ± 20
Voigt 2006	89	yes	N/A	17	7
Ma 2016	123	no	N/A	16.81 ± 5.98	18.79 ± 5.54
Navarro 2016	140	no	N/A	11 ± 7	13 ± 8
Average:	828		15.6687 ± 0.828	13.8155 ± 0.366	14.1352 ± 0.517

Table 2: PRWE score at 1 year follow-up

study	# patients	p<.05	Closed Reduction	ORIF	Percutaneous Fixation
Arora 2009	130	n	16.9	9.3	N/A
Arora 2011	73	n	14.6 ± 22.8	12.8 ± 23.2	N/A
Saving 2019	140	y	22.4 ± 21.4	12.7 ± 15.0	N/A
Lawson 2021	166	n	21.5	19.8	N/A
Huard 2010	38	n	N/A	16	25
Navarro 2016	140	n	N/A	13 ± 9	14 ± 7
Average:	687		19.5929 ± 0.364	14.0247 ± 0.384	16.3483 ± 0.936

Table 3: statistical significance between group means

Group comparison	DASH p value	PRWE p value
1 vs 2	<.001	<.001
1 vs 3	<.001	<.001
2 vs 3	.312	<.001

Closed reduction (1), Percutaneous fixation (2), ORIF (3)

## RESULTS

10 studies were obtained for analysis, consisting of data from 828 geriatric patients for DASH score and 687 patients for PRWE score. The average DASH score for closed reduction, ORIF, and percutaneous fixation were 15.6687 ± 0.828, 13.8155 ± 0.366, and 14.1352 ± 0.517, respectively. The percutaneous fixation group had significantly better outcomes than the closed reduction group ( $p < .001$ ), and the ORIF group had significantly better outcomes than closed reduction group as well ( $p < .001$ ). However, there was no significant difference between the DASH scores of the ORIF and percutaneous fixation groups ( $p = .312$ ). The average PRWE scores for closed reduction, ORIF, and percutaneous fixation were 19.5929 ± 0.364, 14.0247 ± 0.384, and 16.3483 ± 0.936, respectively. All three groups were significantly different from each other, with ORIF offering the best results, followed by percutaneous fixation, and then by closed reduction. The p value was <.001 for all three comparisons.

## CONCLUSIONS

- Conservative treatment should be performed when the fracture is nondisplaced, incomplete, extra articular and can be reduced, or if surgery is too dangerous for the patient.
- K-wires when there are more than 2 fragments resulting from the fracture that are properly reduced. Another indication is old age, as there is a greater risk of infections resulting from more invasive procedures.
- Intra-articular step-off of greater than or equal to 2mm is an absolute indication for ORIF in patients under 65 years of age.
- Some studies show closed reduction vs ORIF not significant at 1 year, but some studies do. These studies differ in frequency of types of fractures (type A vs C).
- ORIF leads to significantly more infections in the geriatric population, necessitating replacement and further antimicrobial treatments, which hinder the healing process.
- ORIF vs percutaneous fixation: most studies found no significant difference in DASH and PRWE scores at 1 year post treatment
- In the geriatric population, the correlation between clinical outcome and anatomical differences is not as pronounced, which may explain the similarities between the functional outcomes found in the studies analyzed in this paper
- ORIF took 121 minutes on average. K-wire treatment took an average of 56 minutes. Closed reduction took the least time, at 24 minutes.

## CLINICAL IMPLICATIONS

- In the geriatric setting, treatment choice lies more in minimizing complications than restoring joint kinematics.
- Current guidelines are appropriate.
- In the ER setting, percutaneous fixation and closed reduction should be preferred.
- DASH and PRWE scores should both be measured in future studies.

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I would like to thank my dad, who funded my expensive education, and instant rice, which fed me while I wrote this paper.





# The Use of Antibody Treatment for Creutzfeldt-Jakob Disease

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## ABSTRACT

Creutzfeldt-Jakob Disease (CJD) is an incredibly rare but deadly neurodegenerative disease characterized by misfolded proteins that impair function and folding of wild-type proteins, causing a chain-reaction and subsequent accumulation in neural tissue. Most commonly, these misfolded proteins, or prions, are acquired sporadically, with no clear cause. However, they can also be transmitted hematogenously through infected blood, by oral consumption of infected meat, often bovine brain matter, or iatrogenically through contaminated surgical tools.

The prion at fault for CJD is PrPsc, an isoform of the wild-type PrPc. PrPc is a normal protein found on the cell membrane of all healthy cells in the body. The mechanism behind the transformation from PrPc to PrPsc is not completely understood. It is theorized that the symptoms of CJD is caused by the lack of wild-type PrPc as well as the accumulation of the atypical PrPsc in neural tissue causing neurodegeneration.

## INTRODUCTION

The presentation of CJD varies widely including cognitive symptoms, mood irregularities, psychological deficits and muscular abnormalities among others. However, what CJD patients have in common is rapid decline and eventual death, usually within 1 year of onset of symptoms.

In order to combat the rapid neurodegeneration seen in CJD, several treatments have been developed to slow the progression of prion proliferation. Some of these include RNA interfaces and antisense oligonucleotides aimed at preventing prion production. Some of these treatments have been shown to extend the lifespan of prion-infected mice, however none have been shown to reduce mortality.

One novel treatment for CJD that has shown promise is the use of antibodies to prevent the interaction between PrPsc and normal PrPc. This treatment uses antibodies to bind to specific regions of wild-type PrPc to prevent the misfolding chain reaction by PrPsc. This also reduces the overall levels of both PrPc and PrPsc, thus reducing slowing the progression of CJD.

The primary complication of antibody treatment for CJD is that many drugs have difficulty crossing the blood-brain barrier. The purpose of this literature review is to analyze the various antibody treatments for CJD for both their general efficacy and ability to cross the blood brain barrier.

## METHODS

The articles used in this literature review include all articles we could find pertaining to antibody treatment of CJD. A Pubmed search was performed using the following search terms: "Creutzfeldt-Jakob disease", "antibodies", "blood-brain barrier", "drug treatment", "PrP", "prion", "PrPc".

## RESULTS

**Table 1: Dissociation rate constant ( $k_{off}$ ) and equilibrium constant (KD) of the Fabs that bind to PrP (Senatore et al., 2020).**

Fab	$k_{off}$ (1/s)	KD (M)
Fab_POM1	2.96E-04	2.01E-09
Fab1	2.88E-03	1.21E-08
Fab2	1.58E-03	1.01E-08
Fab3	2.46E-03	7.72E-09
Fab4	1.93E-03	1.41E-08
Fab6	1.44E-03	9.89E-09
Fab7	2.41E-03	1.76E-08
Fab8	3.62E-03	1.79E-08
Fab10	2.61E-03	1.41E-08
Fab12	3.20E-03	1.71E-08
Fab13	4.98E-03	4.56E-08
Fab15	3.76E-03	1.27E-08
Fab25	2.42E-03	4.71E-08
Fab28	1.08E-03	1.28E-08
Fab29	3.15E-03	1.04E-08
Fab30	1.76E-03	4.76E-09

## KEY FINDINGS

Each antibody treatment was compared using the dissociation rate constant and equilibrium constant. Antibodies that have a smaller dissociation rate constant, such as Fab\_POM1 at 2.96E-04, have the highest affinity for PrP, leading to better efficacy. Likewise, antibodies that have a higher equilibrium constant tends to favor the bound form of PrP-antibody. Table 1 outlines the dissociation rate constants and equilibrium constants for the binding of PrP to various antibody treatments, outlining their efficacies.

Of note, all of the antibodies studied have a similar dissociation rate constant and equilibrium constant. Each value differs by not much more than a factor of 10, with the exception of Fab\_POM1 having a dissociation constant far lower than the others. This demonstrates that the overall efficacy of most of the antibody treatments do not change much from one to the next.

However, it is important to note that, while these antibody treatments are effective to varying degrees at preventing PrPsc propagation and extending the lifespan of patients suffering from CJD, none have been shown to improve mortality. In fact, to our knowledge, there has been yet to be discovered a treatment for CJD that cures and/or reverses the neurodegeneration caused by CJD.

In fact, some studies have shown that antibody treatments and other drug regimens for CJD can cause the development of drug-resistant prions, similar to how antibiotics can bring about antibiotic-resistant bacteria. These newly drug-resistant PrPsc can lead to paradoxically faster neurodegeneration and death.

## CONCLUSIONS

Antibody treatment for CJD represents a novel method at treating an otherwise tragically lethal disease. This treatment did in fact show promise in extending the lifespan of affected individuals by a statistically significant margin. However, despite many attempts to find a successful treatment, there still remains no cure.

Additionally, treatments targeted at prion disease has been shown to produce treatment-resistant prions that can cause faster rates of symptom progression and eventual death. This can lead to a disease course that starts with promising improvement of symptoms, but with an asymptotic decline as the prion proteins become resistant. As a clinician treating CJD, it is important to understand this disease course to better prepare the patient and their family.

## ACKNOWLEDGEMENTS

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# Exploring Naltrexone as Adjuvant Therapy in the Management of Opioid-Induced Hyperalgesia

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## ABSTRACT

Opioid-induced hyperalgesia (OIH) is a condition characterized by heightened pain sensitivity experienced by patients following opioid use. Opioids are widely prescribed for pain management, but they can paradoxically increase pain sensitivity. The concurrent use of low doses of the opioid antagonist naltrexone has shown promise in reducing OIH. This review analyzes the current role and effectiveness of naltrexone in managing OIH and explores the underlying mechanisms that allow naltrexone to reduce OIH while preserving the analgesic effects of opioids. The review highlights the prevalence of OIH and emphasizes the need for further study to optimize the use of naltrexone as a treatment alongside opioids for pain management.

## INTRODUCTION

Opioids are extensively prescribed in the United States for chronic and postoperative pain. However, a long-term consequence of opioid use is opioid-induced hyperalgesia (OIH), which can paradoxically increase pain sensitivity in patients on chronic pain medication. This heightened nociception can be caused by an exacerbated response to pre-existing pain via the endogenous transition from inhibitory to excitatory G-protein-coupled receptor responses in the context of long-term opioid use.

Although there is currently no definitive treatment for OIH, trials have explored the concurrent use of opioid antagonists to prevent or treat OIH. Naltrexone, a pure opioid receptor antagonist, is currently primarily used for substance abuse treatment. Recent research has shown naltrexone efficacy in treating OIH when administered in low doses. However, high doses of naltrexone can cause side effects and should be administered under healthcare professional guidance. The cold pressor test (CPT) is used to objectively measure pain and evaluate the effects of naltrexone as a treatment for OIH. This review highlights the effectiveness of naltrexone in alleviating OIH symptoms.

Research suggests that co-administration of opioids and low-dose naltrexone can enhance analgesic effects and decrease opioid dosage. Continuous supplementation of exogenous opioids have shown to shift  $\mu$ -opioid receptor (MOR) G-protein coupling from inhibitory (Gi/o) to hyperalgesic excitatory (Gs) states, contributing to OIH. Clinically recommended doses of opioids can induce this shift, resulting in increased pain propagation. Co-treatment with naltrexone allows for lower doses of opioids to achieve analgesic effects by helping prevent unwanted G-protein conformational changes. Studies have demonstrated enhanced analgesic potency when opioids are combined with ultra-low-dose naltrexone. Implantation of naltrexone pellets has shown prolonged effects in elevating naltrexone plasma levels and increasing the time between opioid doses, effectively enhancing both the analgesic duration and potency of co-administered opioids. Furthermore, several studies have elucidated that combining opioids with ultra-low-dose naltrexone helps reverse the MOR-G-protein conformational transition and reduce analgesic tolerance, withdrawal symptoms, and opioid dependence.

Future research should focus on developing more permanent treatments for OIH and exploring alternative medications and diagnostic methods. Naltrexone holds promise as a preventative medicine for opioid dependence and OIH, and its use should be considered alongside opioid prescriptions to prevent withdrawal symptoms and mitigate opioid-related risks.

## METHODS

PubMed searches were conducted using the keywords “opioid abuse,” “naltrexone,” “opioid-induced hyperalgesia,” and “tolerance.” Studies not involving naltrexone or naloxone-related treatment of opioid-induced hyperalgesia were excluded. Duplicate studies or literature reviews were removed, leaving a total of 23 studies in which data was extrapolated from.

## RESULTS

Author (year)	Opioid agonist	Effective dosage of the agonist	Opioid antagonist	Effective dosage of the antagonist
Apfel et al. (1995) [14]	N/A	N/A	Naloxone	15.0 mg/kg
Augusto et al. (2019) [15]	N/A	N/A	Naltrexone	10.0 mg/kg
Beaumont et al. (2005) [16]	Morphine	1.0 $\mu$ g/kg	Naloxone	2.0 mg/kg
Campillo et al. (2011) [17]	Remifentanyl	80 $\mu$ g/kg	Naloxone	1.0 mg/kg
Corder et al. (2017) [13]	Morphine	10 mg/kg	Naltrexone	0.9 mg/kg
Crain and Shen (2008) [7]	Morphine	1.0 $\mu$ g/kg	Naltrexone	0.1 ng/kg
Crain and Shen (2008) [12]	Morphine	1.0 $\mu$ g/kg	Naltrexone	0.1 ng/kg
Cruciani et al. (2003) [8]	Oxycodone	5.0 mg every 6 hours	Naltrexone	1.0 $\mu$ g x 2 per day
Harris et al. (2004) [4]	Morphine	10 mg/kg	Naloxone	2.5 mg/kg
Jackson et al. (2021) [2]	Morphine	N/A	Naltrexone	0.1 mg/kg
Juni et al. (2006) [19]	Morphine	0.1 $\mu$ g/kg	Naltrexone	100 $\mu$ g/kg
Largent-Miles et al. (2008) [6]	Oxycodone	10 mg/kg	Naltrexone	1.0 $\mu$ g/kg
Le Roy et al. (2011) [20]	Fentanyl	50 ng/kg	Naltrexone	1.0 mg/kg
Oaks et al. (2018) [3]	Morphine	4.5 mg per day	Naltrexone	0.1 mg x 2 per day
Pineda-Farías et al. (2017) [10]	Morphine	N/A	Naltrexone	0.5 ng/kg
Podolsky et al. (2013) [22]	Morphine	N/A	Naltrexone	1 mg/kg
Terashvili et al. (2007) [5]	Morphine	N/A	Naltrexone	2.3 $\mu$ g/kg
Van Dorp et al. (2009) [11]	Morphine	0.29 mg/kg	Naltrexone	10 mg/kg
Walwyn et al. (2016) [23]	Morphine	19 $\mu$ g/kg	Naltrexone	10 mg/kg
Wang et al. (2005) [9]	Morphine	2.5 $\mu$ g every 48 hours	Naloxone	1.0 mg/kg
Wang et al. (2008) [24]	Morphine	10 mg/kg	Naloxone	1.0 $\mu$ g/kg
Waxman (2009) [25]	Fentanyl	10 mg/kg	Naltrexone	0.05 mg/kg
Whitehouse (1985) [26]	Morphine	N/A	Naltrexone	10 mg/kg

**Table 1: Effective dosages of opioid agonists and antagonists reported in augmenting opioid-induced hyperalgesia (OIH) responses.**

## KEY FINDINGS

- Typically following opioid administration, subsequent G-protein signaling results in decreased levels of cAMP and hyperpolarization via increased efflux of potassium & decreased influx of calcium. OIH paradoxically recruits inhibitory (Gi/o) to stimulatory (Gs) pain pathways.
- The most commonly used combination of opioid agonist & antagonist was morphine with adjuvant naltrexone.
- The cold pressor test (CPT) is used as an objective measure of pain in evaluating the effects of naltrexone as a treatment.
- OIH is associated with a shift in opioid receptor-G-protein coupling, resulting in hyperalgesic effects. Co-treatment of opioids with low-dose naltrexone can reverse the transition from inhibitory to excitatory G-protein coupling, reducing OIH and tolerance.
- Ultra-low doses of naltrexone (as low as 0.3mg twice a day) can enhance the analgesic potency of opioids. Introducing naltrexone before or during opioid treatment can help eliminate withdrawal symptoms and maintain analgesic effects.
- Crain & Shen, Cruciani et al. show that morphine dosages 1,000x less than those required to attain analgesic properties are required to induce hyperalgesic effects. This is mitigated by naltrexone.
- While naltrexone is an opioid antagonist, less opioid agonist dosages are required to attain a similar level of analgesic effect due to naltrexone-assoc. reduction in G-protein conformational change.

## CONCLUSIONS

In conclusion, recent research has highlighted the potential of naltrexone and other opioid antagonists as effective treatments for opioid-induced hyperalgesia (OIH). Co-treatment with low doses of naltrexone alongside opioids can prevent and reverse the undesired shift in MOR-G-protein coupling, reducing the development of OIH and its associated symptoms. Furthermore, the addition of naltrexone has been shown to enhance the analgesic potency of opioids, allowing for lower opioid dosages while maintaining or even increasing pain relief.

While further research is needed to fully understand OIH and develop more permanent treatments, naltrexone and other opioid antagonists present a viable option for preventing and managing this condition. Future studies should focus on exploring the effects of naltrexone in combination with different opioids and gaining a deeper understanding of the underlying mechanisms of OIH. By prioritizing the investigation and utilization of naltrexone, healthcare practitioners can contribute to safer and more effective pain management strategies in the face of the opioid crisis.

## CLINICAL IMPLICATIONS

Overall, naltrexone and other opioid antagonists show promise in treating OIH when used in conjunction with opioids at low doses. This approach can help prevent OIH, reduce the overall dosage of opioids, and mitigate the risks associated with opioid over-prescription and abuse. It is crucial for healthcare providers to educate patients about the detrimental effects of opioids, including OIH and tolerance, and consider incorporating naltrexone co-treatment early on in opioid therapy to optimize pain management and minimize opioid-related risks.

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# Modifiable Preoperative Risk Factors Predict Postoperative Complications in Revision Joint Arthroplasty with Antibiotic- Loaded Spacers

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## ABSTRACT

**Purpose:** Evaluate the relationship between placement of antibiotic spacers in revision total joint arthroplasty (TJA) and renal complications.

**Methods:** NSQIP database was queried yielding 4,842 revision TJA patients.

**Findings:** Antibiotics impregnated in spacers utilized in TJA may be systemically absorbed and contribute to nephrotoxicity post operatively. Prevention may include excessive hydration.

## INTRODUCTION

As the prevalence of total joint arthroplasty increases with the aging population, the number of prosthetic joint infections are becoming more common, and antibiotic spacers have evolved to become the gold standard for infection eradication.

The use of high dose antibiotic spacers combined with systemic antibiotics may lead to systemic absorption and increase the risk of medical complications.

This study aims to identify risk factors to development of nephrotoxicity in the setting of TJA with spacer placement, as well as possible methods to ameliorate risks with preoperative nutrition and hydration optimization.

## METHODS

From 2006-2019, all knee and hip revision arthroplasties with insertion of spacer were queried from the National Surgical Quality Improvement Program Database. All patients with preoperative renal failure, dialysis, and serum creatinine >1.5 were excluded. 30-day postoperative adverse complications were identified, and preoperative baseline characteristics were assessed.

Analysis was performed using SPSS. ANOVA and linear regression models were used.

## RESULTS

Outcome	(n, %)	Variable	Adjusted OR	95% CI	P value
Total operation time in minutes (mean, sd)	134 (69)	BUN/Cr	0.93	0.83-1.04	0.25
Length of hospital stay in days (mean, sd)	6.1 (6.6)	BUN/Cr>20	2.04	0.41-10	0.37
Death	41 (0.8)	Hypoalbuminemia	1.7	0.57-5.01	0.33
SSI	457 (9.4)	Anemia	1.45	0.47-4.4	0.5
Superficial SSI	41 (0.8)	INR	0.6	0.08-4.23	0.61
Deep incisional SSI	94 (1.9)	INR>1.5	7.07	1.07-46.58	<b>0.042</b>
Organ space SSI	325 (6.7)	Diabetes	1.53	0.55-4.26	0.41
Pneumonia	35 (0.7)	PLT	0.99	0.99-1.003	0.708
Progressive renal insufficiency/Renal failure	43 (0.9)	BMI	0.99	0.93-1.05	0.79
UTI	50 (1)				
Stroke/CVA	4 (0.08)				
Bleeding transfusions	993 (20.5)				
DVT/PE	59 (1.2)				
Sepsis	259 (5.3)				
Reoperation	260 (5.3)				
Clostridium difficile (C.diff) colitis	23 (0.6)				
Periprosthetic fracture	23 (0.6)				

Table 1. 30-day outcomes.

Legend: SSI: Surgical Site Infection.  
UTI: Urinary Tract Infection. CVA: Cerebrovascular Accident. DVT: Deep Venous Thrombosis. PE: Pulmonary Embolism.

Table 2. Association between variables and the outcome of renal failure: multivariate logistic 144 regression analysis.  
Legend: Bolded values represent statistical significance (P < 0.05). BUN: Blood Urea Nitrogen. Cr: Creatinine. INR: International normalized ratio. BMI: Body Mass Index. PLT: Platelet Count

## DISCUSSION

There were 0.9% of patients in this cohort with renal failure, comprising 43 patients which is lower than previous studies.

Preoperative evidence of prerenal azotemia and anemia had a non-statistically significant positive predictive effect on development of renal failure within 30 days.

INR greater than 1.5 had a statistically significant predictive effect on development of renal failure. This may be related to anticoagulant nephrotoxicity which has been previously described in the literature.

## CONCLUSIONS

Acute kidney injury is a rare complication in revision total joint arthroplasty with antibiotic spacer placement. Although there is no definite mechanism, it is suspected that antibiotics impregnated within cement and spacers may seed into systemic circulation and exert their toxic effects.

Patients receiving antibiotic loaded spacers in the setting of TJA may have preoperative lab values associated with poorer outcomes. Early recognition and adequate optimization of the patient's preoperative care may result in a favorable change in risks for postoperative morbidity.

## CLINICAL IMPLICATIONS

Preoperative hydration may help reduce the risk of nephrotoxicity in the setting of TJA with antibiotic spacer placement.

Correction of deranged INR or cessation of anticoagulation prior to revision TJA may reduce the risk of nephrotoxicity.

## ACKNOWLEDGEMENTS

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# Miliary Pneumonia: How an Automated CBC Differential Can Give Us Clues

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## Introduction

- o Histoplasmosis is caused by the fungus *Histoplasma capsulatum*, which enters hosts through inhalation of spores from environmental sites inhabited by birds and bats
- o Clinical manifestations include fever, fatigue, malaise, weight loss, and respiratory symptoms
- o Physical exam often reveals lymphadenopathy, hepatomegaly, and/or splenomegaly as well as skin and oral lesions, which are less common
- o The most common causes of miliary pneumonia include TB, *cryptococcosis*, *histoplasmosis*, and primary varicella pneumonia
- o Exposure risk includes immigrants and travelers from endemic areas (regions of North America, Central America, and South America)

## Initial Presentation

- o A 23 year-old Hispanic male, who immigrated to the US from Guerrero, Mexico 1.5 years prior, with no significant medical history presented to the emergency room with:
  - o 1 month history of loss of appetite and weight loss
  - o 5-day history of fevers, chills, night sweats, submandibular swelling, and productive cough
- o He stated the cough was accompanied by rust-colored sputum and frequently interrupted his sleep
- o The patient was found to be febrile and in septic shock at the time of presentation

Review of Systems: unremarkable, negative for chest pain, myalgias, arthralgias, sinus congestion, diarrhea, and rash

Physical Exam: He appeared fatigued and younger than stated age. Exam notable for diffuse non-tender bilateral submandibular lymphadenopathy, dark brown macules bilaterally on fingertips, and tenderness in right upper quadrant

Vitals: T - 102.6°F, BP - 81/52 mmHg, Pulse - 132 bpm, RR - 28 breaths/min, SaO<sub>2</sub> - 92% on 2L nasal cannula

## Imaging & Figures



Fig. 1. CT pulmonary angiogram. This figure shows extensive miliary nodules in the bilateral lungs, with diffuse interstitial prominence.

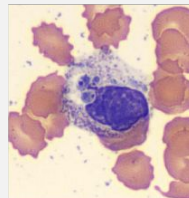


Fig. 2. CellaVision automated differential of a flagged macrophage which shows a macrophage with multiple intracellular yeast that are between 2-4  $\mu$ m, which is consistent with *H. capsulatum*.

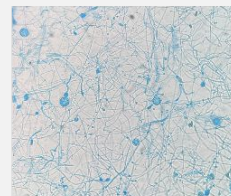


Fig. 3. Lactophenol cotton blue test (fungal blood culture) performed on a colony of *H. capsulatum*. This figure shows branching hyphae with microconidia and tuberculate macroconidia.

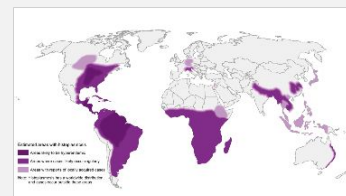


Fig. 4. This figure shows the CDC's current estimate of where the fungi that cause histoplasmosis live in the environment worldwide.

## Hospital Course

- o The patient continued to be in septic shock and was admitted to the intensive care unit, and due to respiratory failure, he was intubated
- o He was newly diagnosed with HIV/AIDS, with viral load of 62,901 copies/mL and a CD4 of 7 cells/ $\mu$ L (10.1%)
- o A bronchoscopy with bronchoalveolar lavage was performed which revealed:
  - o Positive *Aspergillus* galactomannan antigen index with optical density 7.1 (ref. range <0.5)
  - o Positive *Pneumocystis jirovecii* PCR, but negative *Pneumocystis jirovecii* direct fluorescence antibody
- o A bone marrow biopsy was performed w/ Grocott's methenamine silver stain and Periodic acid-Schiff stain, along with a peripheral blood smear with Wright-Giemsa stain which revealed:
  - o Neutrophils and macrophages with intracellular yeast; their size consistent with *Histoplasma capsulatum* rather than *Cryptococcus neoformans*
- o The patient was started on liposomal Amphotericin B, and Flucytosine was added on while trying to differentiate the morphological appearance of *Histoplasma* vs *Cryptococcus* in the bone marrow biopsy and bronchoalveolar lavage fluid
- o Unfortunately, the patient continued to develop worsening respiratory failure and septic shock
- o He passed away on hospital day 3 due to cardiac arrest

## Discussion

- o Our patient presented with miliary pneumonia and septic shock in a setting for which HIV was likely to have been present for years
- o Based on clinical presentation and epidemiologic history, differentials included: *Histoplasmosis*, *Coccidioidomycosis*, *Cryptococcosis*, and TB
- o Automated CBC Differential flagged intracellular macrophage showed intracellular yeast consistent with *Histoplasma* (2-4  $\mu$ m) vs *Cryptococcus* (4-10  $\mu$ m)
- o Due to the similarity between galactomannans in their cell walls, the *Aspergillus* galactomannan antigen assay may cross-react with *Histoplasma*, *Blastomyces*, *Fusarium*, *Talaromyces*, and *Penicillium*
- o Fungal blood and bronchoalveolar lavage cultures from our patient grew *Histoplasma capsulatum* post-mortem
- o Severe infection from histoplasmosis is treated initially with liposomal Amphotericin B

## Conclusion

- o We emphasize the importance of direct microscopy, which can be performed on specimens such as peripheral blood smears, bronchoalveolar lavage, and cerebrospinal fluid
- o It offers rapid turn-around times which is helpful in disseminating *Histoplasma* infection in patients with high susceptibility
- o HIV/AIDS patients are at risk for reactivation of latent *Histoplasma* infection, especially if the CD4 count is less than 150 cells/ $\mu$ L
- o Overall, immunosuppressed patients are at a 10-fold increased risk for developing disseminated histoplasmosis





# Exploring Sick Sinus Syndrome in Patients with Situs Inversus with Dextrocardia: A Case Report

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## INTRODUCTION

- Sick Sinus Syndrome (SSS) is a disorder characterized by an abnormality in the sinoatrial (SA) node, leading to impaired impulse generation and conduction within the heart.
  - Commonly due to age-related degeneration of the atrial myocardium, invasive procedures, congenital disorders, and preexisting arrhythmias [4].
  - To decrease the risk of atrioventricular block, patients with symptomatic SSS are indicated for implantation of a dual chamber pacemaker [1].
- Situs inversus with dextrocardia is a rare congenital condition in which the internal organs, including the heart, are mirrored in their anatomical position.
  - Exact cause is unknown but it has been linked to genetic disorders and environmental factors like maternal diabetes [2].
- Management strategies for SSS in patients with situs inversus with dextrocardia were found to be largely similar to those used in individuals without dextrocardia.
  - Special consideration was given to the unique anatomical and physiological characteristics of these patients.
  - Permanent pacemaker implantation emerged as a common therapeutic approach to restore adequate heart rate control.

## INITIAL PRESENTATION

- A 76-year-old female with situs inversus with dextrocardia presented to an outpatient cardiac electrophysiologist for consultation regarding worsening shortness of breath and fatigue upon exertion.
- Review of Systems:
  - Reports shortness of breath and fatigue. Negative for chest pain and syncope.
- Physical Exam:
  - Lungs were clear on auscultation
  - Auscultation of heart showed normal S1 and S2. % SM. No rubs or gallops.

**Figure 1:** Patient triggered event from 5-day Zio patch (remote cardiac monitor)



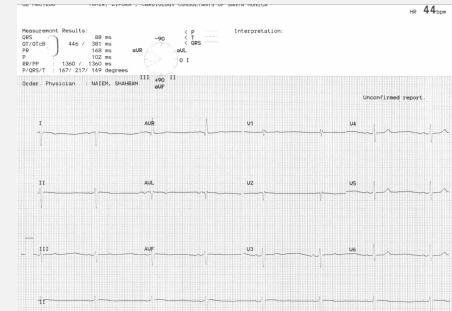
## KEY FINDINGS

- Exercise treadmill stress test
  - Maximum heart rate of 85 bpm reached after 5 minutes of exercise
- Outpatient EKG
  - Sinus bradycardia of 44 bpm at rest
- Ambulatory cardiac telemetry
  - Demonstrated bradycardia with heart rates ranging from 40-50 bpm at rest without any use of heart rate slowing medications
- CT angiography of chest and abdomen with contrast
  - Right sided aortic arch
  - Single left sided inferior vena cava
  - Superior vena cava entering the left side into the right atrium
- CT angiography of heart and coronary arteries with contrast
  - Right coronary artery is the dominant artery
  - Calcium score = 0
- The patient was diagnosed with sick sinus syndrome and had a Class I indication for a dual chamber permanent pacemaker implantation.

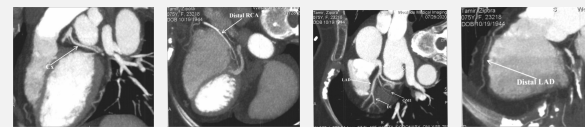
## PROCEDURE

- Due to the presence of a single IVC and SVC entering the left side of the right atrium, with no other abnormalities, access was gained via the right cephalic vein.
- The leads were successfully delivered and placed in the right atrium and the right ventricle, located on the patient's left side
- Device interrogation was performed and found satisfactory.
- Follow up Chest X-Ray PA/Lateral showed appropriate placement of dual lead cardiac pacemaker with lead tips projecting over the right atrium and right ventricle.

**Figure 2:** Outpatient EKG at rest: Sinus bradycardia at 44 bpm



**Figures 3a-d:** CT Angiography Heart and Coronary Arteries



## CONCLUSION

- Despite the challenges presented by dextrocardia, permanent pacemaker implantation remains a very effective treatment approach for patients with SSS leading to symptom improvement and favorable health outcomes.
- Further research is warranted to explore the underlying mechanisms and potential genetic factors contributing to the simultaneous occurrence of SSS and dextrocardia to improve diagnosis, treatment, and outcomes.

## ACKNOWLEDGEMENTS

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# The role of Sirtuin 1 (SIRT1) in Neurodegeneration

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## ABSTRACT

Sirtuins (SIRT) are a class of histone deacetylases that regulate important metabolic pathways and play a role in several disease processes. Of the seven mammalian homologs currently identified, sirtuin 1 (SIRT1) is the best understood and most studied. It has been associated with several neurodegenerative diseases and cancers. As such, it has been further investigated as a therapeutic target in the treatment of disorders such as Parkinson's disease (PD), Huntington's disease (HD), and Alzheimer's disease (AD). SIRT1 deacetylates histones such as H1 lysine 26, H3 lysine 9, H3 lysine 56, and H4 lysine 16 to regulate chromatin remodeling and gene transcription. The homolog has also been observed to express contradictory responses to tumor suppression and tumor promotion. Studies have shown that SIRT1 may have anti-inflammatory properties by inhibiting the effects of NF- $\kappa$ B, as well as stimulating upregulation of autophagy. The SIRT1 activators resveratrol and cilostazol have been shown to improve Alzheimer's Disease Assessment Scale-Cognitive Subscale (ADAS-Cog) scores in AD patients. In this review, we aim to explore the various roles of SIRT1 with regard to neuroprotection and neurodegeneration.

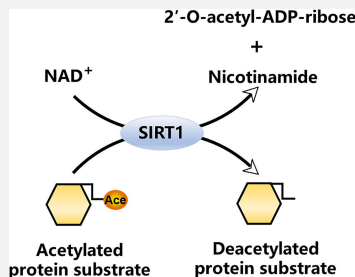
## INTRODUCTION

Sirtuins (SIRT) are a family of NAD<sup>+</sup>-dependent class III histone deacetylases [1]. There are currently seven mammalian sirtuin homologs identified, from sirtuin 1 (SIRT1) to SIRT7, which regulate important metabolic pathways and vary greatly in their functions and locations [2]. SIRT1s differ in length and sequence in their C- and N-terminal domains and thus localize differently. SIRT1 and SIRT2 localize in the nucleus and cytoplasm, while SIRT3-SIRT5 localize in the mitochondria [3,4]. They are best characterized by NAD<sup>+</sup>-dependent lysine deacetylation but have also been shown to remove other acyl groups such as succinyl, malonyl, and long-chain fatty acyl groups [5-8]. The enzymes are involved in several biological processes, including cell survival, proliferation, aging, longevity, senescence, apoptosis, DNA repair, and caloric restriction [9-11]. Recently, sirtuins have been considered potential targets for the treatment of a plethora of pathologies, including neurodegenerative, neoplastic, and cardiovascular diseases. Modulators of these enzymes have been of particular interest as they have been shown to have the potential for treating disorders such as type II diabetes, rheumatoid arthritis, cancer, and other aging-related diseases [12].

SIRT1 was the first sirtuin identified, which functions solely as a deacetylase and localizes in the nucleus and cytoplasm. This homolog is the best understood and most studied of the seven. It has been associated with neurodegenerative diseases and the following cancers: acute myeloid leukemia (AML), melanoma, glioma, lung adenocarcinoma, colon, prostate, ovarian, and breast [13]. With respect to Alzheimer's disease (AD), SIRT1 activation via resveratrol has been found to inhibit NF- $\kappa$ B and diminish amyloid- $\beta$ 's (A $\beta$ ) neurotoxic effect in microglia [14]. SIRT1 activity has also demonstrated a neuroprotective role in slowing neurodegenerative disease progression in pathologies such as Parkinson's disease (PD) and amyotrophic lateral sclerosis (ALS) by upregulating autophagy [15]. SIRT1 has also been shown to be a promising therapeutic target for inhibiting p53 involvement in neurodegenerative diseases [16].

## SIRT1 Mechanism of Action

SIRT1, like others in its family of class III HDACs, counteracts the actions of acetyl transferases by removing acetyl groups from histone and non-histone proteins. The catalytic reaction begins via the binding of the acetylated protein residue and NAD<sup>+</sup> between these two domains. In this deacetylation reaction, the acetyl group is transferred onto the ribose component of NAD<sup>+</sup>, forming nicotinamide (NAM) and 2'-O-acetyl-ADP-ribose or 1'-O-acetyl-ADP-ribose and 3'-O-acetyl-ADP-ribose [22]. SIRT1 activity is regulated directly by cellular NAD<sup>+</sup> levels, inhibition from its end product NAM, SIRT1-binding proteins, and post-translational modifications including ubiquitination, sumoylation, phosphorylation, glycosylation, nitrosylation, and glutathionylation. SIRT1 transcription is regulated by DNA methylation and a variety of transcription factors and cofactors, including p53, Hic1, E2F1, FoxO3a, and c-Myc [23,24]. SIRT1 expression also varies depending on different states of inflammation. It regulates inflammation through histone deacetylation of inflammatory cytokines and signaling pathways like NF- $\kappa$ B, HIF1a, AP-1, and P38MAPK [23].



## Neuroprotective role of SIRT1/AMPK in upregulating autophagy

Neurodegenerative diseases such as PD and ALS have common characteristic features of the accumulation of irregular proteins within neurons, leading to the formation of inclusion bodies and the accumulation of dysfunctional mitochondria. This leads to dysfunctional autophagy, which promotes the aggressive nature of neurodegenerative diseases. While the toxic role of the inclusion bodies is not completely understood, they are heavily correlated with symptoms of various neurodegenerative diseases [38,39]. Furthermore, dysfunctional autophagy in oligodendrocytes has been shown to cause abnormal levels of myelination, which are consistent with the findings in neurodegenerative diseases such as AD [40]. SIRT1/AMPK activity has been shown to play a key role in autophagy by inducing mitochondrial fragmentation, which serves a neuroprotective role in slowing neurodegenerative disease progression [15]. Experiments have shown that activation of AMPK increases the intracellular NAD<sup>+</sup>/NADH ratio, leading to enhanced activity of SIRT1 [41]. SIRT1 can deacetylate and activate LKB1 kinase, which enhances its phosphorylation of AMPK, leading to a downstream increase in AMPK activity [42]. This suggests a positive feedback loop between SIRT1 and AMPK, which can potentiate the downstream neuroprotective effects of AMPK.

## Drugs that target SIRT1 and their use in AD treatment

Several pharmacological agents have been studied with regard to their effects on SIRT1. However, resveratrol and cilostazol are two SIRT1 activators that have been explored in depth. Resveratrol is a phytoalexin occurring mainly in grapevine species and other fruits. Given its antioxidant, anti-inflammatory, and neuroprotective activities, it has garnered much attention with respect to AD, PD, and HD treatment [14]. AD treatment has been of particular interest as there is evidence that resveratrol can decrease the aggregation of A $\beta$  peptides in the hippocampus, prevent hippocampal damage, and promote neurogenesis [58]. Activation of SIRT1 by resveratrol has also been found to prevent A $\beta$ -induced microglial death, which contributes to improved cognitive function [35].

## SIRT1 inhibition of NF- $\kappa$ B in neurodegenerative diseases

It is known that the transcription factor NF- $\kappa$ B is involved in promoting an inflammatory response, with p65 being an important subunit of NF- $\kappa$ B that is activated in chronic diseases such as neurodegenerative pathologies. The p65 subunit has seven acetylation sites on different lysine residues that, when acetylated, activate NF- $\kappa$ B thus leading to an inflammatory state [34]. In AD, there is a buildup of A $\beta$  peptides that are presumed to cause microglial toxicity, leading to the neurodegenerative aspect of the disease. The buildup of A $\beta$  peptides has experimentally been shown to be associated with activation of the NF- $\kappa$ B inflammatory pathway in surrounding glia via acetylation of its p65 subunit; this plays a major role in A $\beta$ -dependent neurodegeneration in AD. The introduction of resveratrol, a SIRT1 activator, resulted in inhibition of NF- $\kappa$ B via deacetylation of p65 by SIRT1, thus diminishing A $\beta$ 's effect of neurotoxicity in microglia [35].

## CONCLUSIONS

Sirtuins have been linked to several neurodegenerative pathologies and malignancies. SIRT1 has shown the potential to provide protection against neurodegenerative pathologies that involve abnormal protein accumulation, such as AD, PD, and ALS. SIRT1's ability to inhibit NF- $\kappa$ B via deacetylation of p65 allows for mitigation of the inflammatory response, which can provide therapeutic benefit to patients suffering from these neurodegenerative disorders. In addition, SIRT1 promotes the phosphorylation of AMPK, which increases AMPK activity. This can provide a therapeutic effect through increased regulation of autophagy via mitochondrial fragmentation, which has been shown to slow neurodegenerative disease progression in PD and HD. In addition, SIRT1 has been shown to downregulate p53 activity, decreasing the amount of p53-induced cell death and helping to mitigate the effects of diseases like AD and ALS. The therapeutic effects of SIRT1 show promising potential for SIRT1 activators like resveratrol and cilostazol. These pharmacologic agents can be used to induce the effects of SIRT1's anti-inflammatory and regulatory effects to decrease the rate of neurodegeneration. However, given the role of SIRT1 in tumor formation, caution must be taken when investigating therapeutic agents that activate the enzyme. While SIRT1 has been explored in depth, future research is prompted regarding its roles in other disease processes, such as cancer.

# Allograft Versus Autograft for Hip Labral Reconstruction and Augmentation: A Systematic Review and Meta-Analysis

Muzammil Akhtar<sup>1</sup>

California Northstate University College of Medicine<sup>1</sup>

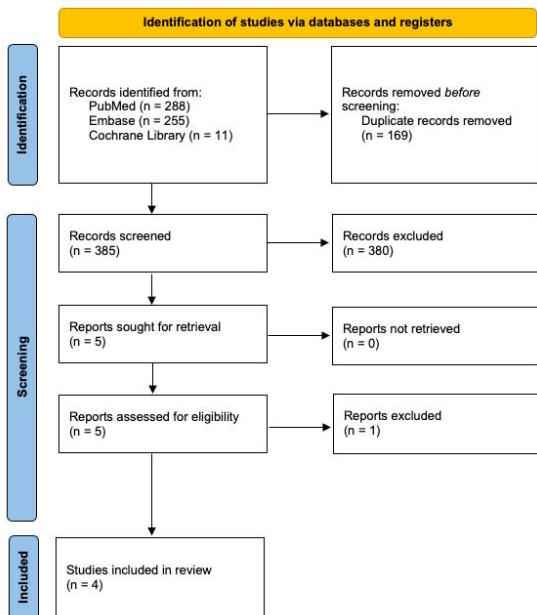


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Innovating Literature

## BACKGROUND

Labral reconstruction and augmentation are novel procedures to restore the anatomic and functional integrity of the hip joint in patients with a deficient labrum or irreparable labral tear. Our purpose is to systematically review studies comparing outcomes of labral reconstruction or augmentation using allograft vs. autograft.

## METHODS



## RESULTS

Author	Graft Type Compared	Revision	Conversion to THA
Cooper et al (2021)	ITB Allograft: 55 ITB Autograft: 150	Allo: 13 (23.6%) Auto: 11 (7.3%)	Allo: 5 (9.1%) Auto: 9 (6%)
Maldonado et al (2019)	Hamstring Allograft: 17 Hamstring Autograft: 12	Allo: 1 (5.9%) Auto: 1 (8.3%)	Allo: 3 (17.6%) Auto: 1 (8.3%)
Maldonado et al (2022)	Hamstring Allograft: 15 Hamstring Autograft: 15	Allo: 3 (20%) Auto: 1 (6.7%)	Allo: 3 (20%) Auto: 1 (6.7%)
Kocaoglu et al (2022)	Tibialis Anterior Allograft: 22 ITB Autograft: 20	Allo (0) Auto (0)	Allo (0) Auto (0)

Allograft correlated with increased revision rates (OR = 2.72; 95% CI, 1.35-5.48; P = 0.005) compared to autograft, with the data also showing low heterogeneity (P = 0.48, I<sup>2</sup> = 0%).

No significant differences in terms of rates of conversion to THA between allograft or autograft (OR = 1.68; 95% CI, 0.76-3.72; P = 0.20), with the data also showing low heterogeneity (P = 0.95, I<sup>2</sup> = 0%).

## RESULTS

Postoperatively there were no significant differences (P > 0.05) in any PRO between those receiving an allograft or autograft across all studies except in patient satisfaction in the study by Maldonado et al (2019) (Allograft vs. Autograft, 8.8 ± 2.1 vs. 6.6 ± 3.3, P = 0.03).

3 studies reported whether there were significant increases (P < 0.05) preoperatively to postoperatively in PROs (all but Cooper), and all 3 studies reported significant increases (P < 0.05) in all PROs, except for the mHHS in the autograft group in study by Maldonado et al (2019) (P = 0.064).

A meta-analysis to determine whether there were significant differences in PROs between those receiving allograft or autograft showed no significant difference (P > 0.05) in mHHS, HOS-SSS, NAHS, or VAS, but did show a significant difference (P = 0.04) in patient satisfaction, with higher satisfaction correlated with receiving allograft.

## KEY FINDINGS

- Allograft correlated with increased revision rates
- No difference in terms of rates of conversion to THA
- Allograft correlated with higher patient satisfaction
- Significant increase in majority of PROs with no significant differences in mHHS, HOS-SSS, NAHS, or VAS between allograft and autograft groups
- Though low heterogeneity between studies, it is difficult to conclude whether allograft or autograft is superior. There is a need for more studies



# Utilizing Deep Learning for Glaucoma Detection in Fundus Images

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California Northstate University<sup>1</sup>, California University of Science and Medicine<sup>2</sup>, Eastern Tennessee State University<sup>3</sup>



## ABSTRACT

Glaucoma, a prevalent ocular disease with significant implications for global health, requires accurate and timely detection to ensure effective management. This study aimed to develop a glaucoma detection model utilizing machine learning algorithms and retinal images obtained from Kaggle.com. Leveraging Google's Collaboration Platform, a dataset of over 1196 retinal images encompassing glaucoma-positive and normal cases was employed for model development. The achieved model demonstrated promising performance metrics, with an average precision of 73% and recall value of 82%. Sensitivity and specificity values were calculated as 73% and 84%, respectively. The overall accuracy of the model reached 78.5%, highlighting its potential as a valuable tool for glaucoma detection using retinal images. Further validation studies and research endeavors are necessary to assess the model's generalizability and integration into clinical practice, paving the way for early glaucoma detection and improved management strategies.

## INTRODUCTION

Glaucoma is a significant ocular disease posing a global health challenge, characterized by progressive damage to the optic nerve and potentially leading to irreversible vision loss if left untreated. It stands as the leading cause of irreversible blindness worldwide. With an estimated 76 million people affected globally, glaucoma presents a substantial burden on individuals and healthcare systems [1-2]. The urgency for early detection and intervention is paramount in managing glaucoma and preserving visual function. Timely diagnosis enables the implementation of effective treatment strategies, preventing further damage and enhancing patient outcomes. However, the complexity and silent nature of glaucoma often contribute to delayed diagnosis and subsequent vision impairment. While traditional screening methods, such as intraocular pressure measurement and visual field tests, have proven valuable, their limitations necessitate the exploration of innovative approaches. By leveraging these imaging modalities and employing advanced data analytics, machine learning algorithms, and artificial intelligence (AI) techniques, novel opportunities arise to enhance glaucoma detection and monitoring. An AI-powered glaucoma detection model holds the potential to augment the diagnostic accuracy, efficiency, and consistency of healthcare professionals. Furthermore, this technology could be particularly impactful in resource-limited regions lacking access to specialized ophthalmologists and comprehensive eye care facilities. By providing a standardized and objective tool, the AI-based model can aid in early detection, facilitate timely referral for treatment, and support effective glaucoma management on a global scale. Through continued research and development, embracing the potential of AI in glaucoma care, we strive to transform the landscape of glaucoma diagnosis and improve patient outcomes. By harnessing the power of technology and collaborative efforts, we aim to mitigate the global burden of glaucoma and safeguard vision for millions of individuals worldwide.

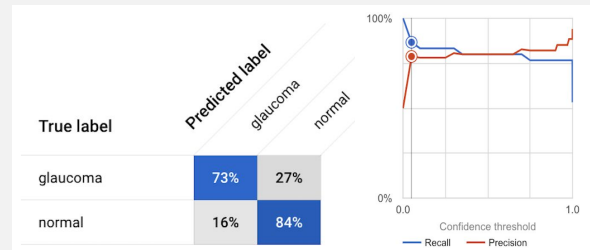
## METHODS

The study aimed to develop a glaucoma detection model utilizing retinal fundus images obtained from publicly available datasets. A dataset consisting of a large number of retinal images, including both glaucoma-positive and normal cases, was used for model development. The images were in digital format and labeled accordingly. Preprocessing steps involved organizing the glaucoma and normal images into separate folders and visually inspecting each image for labeling accuracy and quality. No additional preprocessing techniques were applied, such as image resizing or augmentation. For model development, Google's Collaboration Platform was utilized. A deep learning algorithm, employing CNN methods, was trained to recognize patterns and features associated with glaucoma-positive retinal images using the labeled dataset. The training set comprised 80% of the images, with 10% used for model validation and another 10% for testing. The assignments were randomized to avoid bias. No external datasets were incorporated. The trained model was evaluated using a separate test set of retinal images. Performance metrics, including accuracy, precision, recall, and a confusion matrix, were calculated to assess the model's effectiveness. The model was developed using software tools supported by Google, Python, and deep learning frameworks like TensorFlow and PyTorch.

## RESULTS



The glaucoma detection model developed using Google's Collaboration Platform exhibited promising performance. The model achieved an accuracy of 78.5%, along with an area under the curve (AUC) of 0.897, indicating its ability to accurately classify glaucoma-positive and normal retinal images. The precision value was measured at 73%, reflecting the model's ability to correctly identify glaucoma cases, while the recall value of 82% demonstrates its effectiveness in capturing glaucoma cases. It's important to consider the potential limitation of a high recall, which could imply overfitting and the model merely memorizing images rather than learning patterns, compromising its reliability in predicting future occurrences.



To further evaluate the performance of the glaucoma detection model, sensitivity, specificity, and overall accuracy statistics were calculated using the provided values. The sensitivity, or true positive rate, was determined to be 73%, indicating that the model correctly identified 73% of actual glaucoma-positive cases. The specificity, or true negative rate, was measured at 84%, reflecting the model's proficiency in correctly classifying normal cases. Furthermore, the overall accuracy of the model was determined to be fairly high, representing the proportion of all cases, both glaucoma-positive and normal, that were correctly classified by the model. These results highlight the model's effectiveness in distinguishing between glaucoma and normal retinal images. It is important to note that the experiments were conducted using Google's Collaboration Platform. These findings demonstrate the model's high sensitivity in identifying glaucoma-positive cases and its specificity in recognizing normal cases. The achieved accuracy underscores the model's overall performance in accurately classifying glaucoma cases.

## CLINICAL IMPLICATIONS

Early diagnosis of glaucoma is crucial for initiating appropriate treatment and preventing vision loss [11]. The development of accurate and reliable glaucoma detection models can support healthcare professionals in making timely and informed decisions, especially in resource-limited settings where access to specialized ophthalmologists may be limited. Integrating these models into clinical workflows has the potential to enhance glaucoma control programs and improve patient outcomes. The application of machine learning algorithms to retinal images shows promise in advancing glaucoma diagnosis. Collaborative efforts among researchers, clinicians, and policymakers are necessary to fully harness the potential of these models in combating glaucoma and reducing its global impact.

## Key Findings

The results obtained from this study highlight the potential of machine learning and deep learning algorithms in the field of glaucoma detection. Retinal imaging is a widely accessible and cost-effective diagnostic tool for glaucoma, making it an ideal modality for training and evaluating detection models. The high accuracy of the model, as reflected in the overall accuracy of 78.5%, suggests its potential for aiding in the early detection of glaucoma. Early diagnosis is crucial for initiating timely treatment and preserving vision [9]. The model exhibited high precision, recall, sensitivity, specificity, and overall accuracy, suggesting its utility in distinguishing between glaucoma-positive and normal cases. Early diagnosis of glaucoma is crucial for initiating appropriate treatment and preventing vision loss [11].

## CONCLUSIONS

This study highlights the potential of machine learning and deep learning algorithms in improving glaucoma diagnosis using retinal images. The developed glaucoma detection model demonstrated high accuracy and performance metrics, showcasing its ability to effectively classify glaucoma-positive and normal cases. The integration of such models into clinical practice has the potential to enhance early detection, facilitate prompt treatment initiation, and improve glaucoma management. However, further research, validation, and implementation efforts are necessary to ensure the model's generalizability and efficacy in diverse populations and real-world clinical settings. Collaborative efforts between researchers, clinicians, and policymakers are crucial to harnessing the full potential of these technological advancements in combating glaucoma and reducing its global impact.

## ACKNOWLEDGEMENTS

The authors express their gratitude to the individuals cited in this review for their valuable contributions to the advancement of science. No other acknowledgments are necessary at this time.



# Utilizing Deep Learning for Glaucoma Detection in Fundus Images

Rakesh Kumar<sup>1</sup>, Kartik Goswami<sup>1</sup>, Rajesh Kumar<sup>1</sup>, Sanjeev Goswami<sup>1</sup>

Stockton Pulmonary Associates<sup>1</sup>



## ABSTRACT

Tuberculosis (TB) remains a significant global health challenge, necessitating accurate and timely detection for effective management. This study aimed to develop a TB detection model using chest X-ray images obtained from Kaggle.com, utilizing Google's Collaboration Platform. Over 1196 chest X-ray images, comprising both TB-positive and normal cases, were employed for model development. The model achieved an average precision of 0.934, with precision and recall values of 94.1% each, indicating its high accuracy in classifying TB-positive and normal cases. Sensitivity and specificity values were calculated as 96.85% and 91.49%, respectively. The F1 score was also calculated to be 0.941. The overall accuracy of the model was found to be 94%. These results highlight the potential of machine learning algorithms for TB detection using chest X-ray images. Further validation studies and research efforts are needed to assess the model's generalizability and integration into clinical practice, ultimately facilitating early detection and improved management of TB.

## INTRODUCTION

Tuberculosis (TB) is a significant global health challenge caused by *Mycobacterium tuberculosis*, primarily affecting the lungs and causing severe illness and mortality if untreated [2-3]. Prior to the COVID-19 pandemic, TB ranked highest among infectious diseases in terms of mortality. In 2019 alone, TB resulted in 1.4 million deaths and 10 million new cases worldwide. However, reduced access to care has led to an increase in TB deaths, with 2020 seeing the first year-over-year rise since 2005 [6]. Early detection is crucial for effective disease management and prevention of transmission. Traditional diagnostic methods have limitations, but recent advancements in medical imaging, particularly chest X-ray imaging, have provided valuable insights. However, the subjective interpretation of these images by human experts poses challenges. To address this, we aimed to develop a TB detection model using machine learning algorithms and artificial intelligence (AI) technology. Such a model has the potential to revolutionize TB diagnosis, offering a standardized and objective tool for healthcare professionals. It could enable early detection, prompt treatment initiation, and implementation of effective control measures, especially in resource-limited regions lacking access to expert radiologists and healthcare resources. By leveraging AI, we strive to enhance the accuracy and efficiency of TB diagnosis, contributing to global efforts in combating this persistent infectious disease.

## METHODS

Tuberculosis (TB) is a significant global health challenge caused by *Mycobacterium tuberculosis*, primarily affecting the lungs and causing severe illness and mortality if untreated [2-3]. Prior to the COVID-19 pandemic, TB ranked highest among infectious diseases in terms of mortality. In 2019 alone, TB resulted in 1.4 million deaths and 10 million new cases worldwide. However, reduced access to care has led to an increase in TB deaths, with 2020 seeing the first year-over-year rise since 2005 [6]. Early detection is crucial for effective disease management and prevention of transmission. Traditional diagnostic methods have limitations, but recent advancements in medical imaging, particularly chest X-ray imaging, have provided valuable insights. However, the subjective interpretation of these images by human experts poses challenges. To address this, we aimed to develop a TB detection model using machine learning algorithms and artificial intelligence (AI) technology. Such a model has the potential to revolutionize TB diagnosis, offering a standardized and objective tool for healthcare professionals. It could enable early detection, prompt treatment initiation, and implementation of effective control measures, especially in resource-limited regions lacking access to expert radiologists and healthcare resources. By leveraging AI, we strive to enhance the accuracy and efficiency of TB diagnosis, contributing to global efforts in combating this persistent infectious disease.

## RESULTS



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To further evaluate the model's performance, statistics of sensitivity, specificity, and overall accuracy were calculated using the provided values. The values were calculated by finding the True Positive, True Negative, False Positive, and False Negative from the Confusion matrix in Figure 4. The sensitivity, also known as the true positive rate, was determined to be 96.85%. This indicates that the model correctly identified 96.85% of actual TB-positive cases. The specificity, or true negative rate, was calculated to be 91.49%, reflecting the model's proficiency in correctly classifying normal cases. Furthermore, the overall accuracy of the model was determined to be 94%. This value represents the proportion of all cases, both TB-positive and normal, that were correctly classified by the model. These results highlight the model's effectiveness in distinguishing between TB and normal chest X-ray images. It is important to note that the experiments were conducted using Google's Collaboration Platform on May 22. These results demonstrate the model's high sensitivity in identifying TB-positive cases and its specificity in recognizing normal cases. The achieved accuracy underscores the model's overall performance in accurately classifying TB cases.

## CLINICAL IMPLICATIONS

To further evaluate the model's performance, statistics of sensitivity, specificity, and overall accuracy were calculated using the provided values. The values were calculated by finding the True Positive, True Negative, False Positive, and False Negative from the Confusion matrix in Figure 4. The sensitivity, also known as the true positive rate, was determined to be 96.85%. This indicates that the model correctly identified 96.85% of actual TB-positive cases. The specificity, or true negative rate, was calculated to be 91.49%, reflecting the model's proficiency in correctly classifying normal cases. Furthermore, the overall accuracy of the model was determined to be 94%. This value represents the proportion of all cases, both TB-positive and normal, that were correctly classified by the model. These results highlight the model's effectiveness in distinguishing between TB and normal chest X-ray images. It is important to note that the experiments were conducted using Google's Collaboration Platform on May 22. These results demonstrate the model's high sensitivity in identifying TB-positive cases and its specificity in recognizing normal cases. The achieved accuracy underscores the model's overall performance in accurately classifying TB cases.

## Key Findings

The TB detection model developed using Google's Collaboration Platform exhibited promising performance. The model achieved an area under the curve (AUC) of 0.934, indicating its ability to accurately classify TB-positive and normal chest X-ray images. Both precision and recall values were found to be 94.1%, highlighting the model's high accuracy in correctly identifying TB cases. The model demonstrated a sensitivity of 96.85%, correctly identifying 96.85% of actual TB-positive cases. The model showed a specificity of 91.49%, reflecting its proficiency in correctly classifying normal cases. The overall accuracy of the model was determined to be 94%, indicating its effectiveness in distinguishing between TB and normal chest X-ray images. These results highlight the model's high sensitivity in identifying TB-positive cases and its specificity in recognizing normal cases. The experiments were conducted using Google's Collaboration Platform on May 22, providing insights into the model's performance on that specific date. O

## CONCLUSIONS

This study highlights the potential of machine learning and deep learning algorithms in improving tuberculosis (TB) diagnosis using chest X-ray images. The developed TB detection model demonstrated high accuracy and performance metrics, showcasing its ability to effectively classify TB-positive and normal cases. The integration of such models into clinical practice has the potential to enhance early detection, facilitate prompt treatment initiation, and improve TB control measures. However, further research, validation, and implementation efforts are necessary to ensure the model's generalizability and efficacy in diverse populations and real-world clinical settings. Collaborative efforts between researchers, clinicians, and policymakers are crucial to harnessing the full potential of these technological advancements in combating TB and reducing its global impact.

## ACKNOWLEDGEMENTS

The authors express their gratitude to the individuals cited in this review for their valuable contributions to the advancement of science. No other acknowledgments are necessary at this time.



# Evaluation of Anesthesia Utilization in Surgical Management of Diabetic Macular Edema



Sarah Yee • Akshay J. Reddy • Allen Dang • Muhammad S. Ghauri • Yui Seo • Neel Nawathey • Alex Bachir • Telak Brahmhatt • Rakesh Patel

## ABSTRACT

Diabetes-related macular edema is a fast spreading condition that has damaged the lives of countless people throughout the globe. The current incorporation of subthreshold micropulse laser has indicated the precedence of laser therapy in the treatment of diabetic macular edema. However, vitreoretinal surgery in conjunction with anesthetics correlates with early mitigation of damage to the fovea. Surgery is a delicate procedure that necessitates careful consideration of the types and locations of anesthetics used. Depending on the individual being treated, various drugs and methods may be necessary. For example, some individuals may be allergic to conventional anesthetics, resulting in more severe consequences. According to our statistical analysis, in the surgical treatment of diabetic macular edema, topical anesthetic was utilized more frequently than subconjunctival anesthetic. The examined literature indicated that topical lidocaine was the most commonly employed anesthetic for vitreoretinal surgery; however, alternatives to lidocaine exist, and their effects should be investigated. Consequently, we would want to highlight the impacts of each of the several surgical medications and anesthetics used to treat diabetic macular edema.

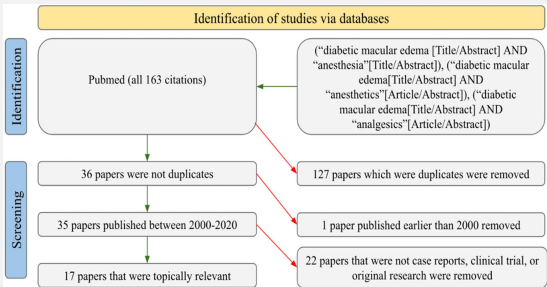
## INTRODUCTION and BACKGROUND

Diabetic macular edema (DME), defined as the leakage of fluids from blood vessels in the retina, is a common diabetic eye disease and the main cause of vision loss in developed nations [1]. In 2019, nearly 750,000 cases of diabetic retinopathy alone were documented in the United States [1]. When diabetic macular edema is left untreated, extra fluid in the retina causes swelling in the macula's surrounding tissue, resulting in permanent damage to the fovea [2]. DME symptoms can range from hazy vision and lack of contrast to total blindness. Due to the prevalence of DME, numerous novel therapeutic methods have been created. Integration of subthreshold micropulse lasers (SML) into laser therapy has been the most significant improvement in treating DME [2]. SML fulfills the same function as traditional continuous-wave lasers, but without the associated negative side effects [2]. Although laser therapy is extensively used and significant advancements have been made in the field, the use of sophisticated anesthetics in vitreoretinal surgery has been found to correspond with more rapid DME intervention [2]. Anesthetics such as lidocaine (LC) is popular due to reduction in blood flow to the eye and consequent minimization of possible blood leakage within the retina [3]. In the case of DME, earlier surgery can minimize macula damage and avoid subsequent foveal degeneration. It is vital to consider the anesthetics used in these surgeries, as one of the key goals of healthcare providers is to minimize patient injury. In this review, we aim to survey a variety of papers and examine the utilization and placement of anesthetics during DME surgical procedures.

## CONCLUSIONS

Diabetic macular edema may become a more prominent condition in the future, given the current and increasing prevalence patients suffering from diabetes. When combating this disease, it is vital to consider the numerous treatment choices and their short- and long-term impacts on individuals. Surgery is one of the therapeutic options for DME, and its effects can vary depending on the anesthetic used. Although lidocaine is the most predominantly utilized anesthetic in DME surgery, it may not be the most effective and safe anesthetic in the future given the promising research and outcomes of cooling anesthesia. Literature appears to support the assumption that the anesthetic for this technique should be given topically and triamcinolone acetonide should be the primary pharmacological injection for conventional DME treatment. Possibly, future studies will demonstrate that non-medicated anesthetic treatments are more successful than the current standard of care.

## METHODS



## REVIEW RESULTS

Table 1: Summary of previous clinical studies of surgical procedures to treat diabetic macular edema <sup>1,2,3,4</sup>						
Author (year)	Area(s) of applied Anesthetic	Type(s) of anesthetic	Number of anesthetic used	Concentration of major anesthetic used	Drugs in injection	Sample Size (N)
Beech (2003) [5]	Subconjunctival	C/A, LC	1	3.0%	APBSP	48
Shen Lingsi (2000) [5]	Topical	SC	1	1%	APB	18
Shen Lingsi (2000) [5]	Topical	SC	1	1%	APB	18
Arora (2000) [7]	Topical	LC	1	20 mg	SC	24
Arora (2000) [7]	Topical	LC	1	20 mg	SC	2 (case report)
Kawachi (2000) [5]	Subconjunctival, Topical	LC	1	4%	TA	36
Kawachi (2000) [5]	Topical	LC	1	4 mg	TA	2 (case report)
Rago (2000) [10]	Topical	LC	1	40 mg	TA	29
Rago (2000) [10]	Subconjunctival	LC	1	4.0 mg	TA	2 (case report)
Lin (2001) [11]	Topical	LC	1	0.5%	TA	13
Maeda (2000) [4]	Subconjunctival	LC	1	4 mg	TA	11
Chakraborty (2010) [12]	Topical	LC	1	40 mg	TA	40
Widder (2010) [14]	Topical	FLX, TC, PB	3	N/A	APBSP	100
Shindani (2014) [17]	Topical	LC	1	2.5, 5, 7.5, 10%	APBSP	389
Sheng (2010) [18]	Topical	SC	1	4 mg	TA	38
Wider (2000) [10]	Subconjunctival, Topical	LC	1	40 mg	TA	49
Sheng (2010) [18]	Subconjunctival, Topical	FLX, LC, TC	3	N/A	TA	70

## LITERATURE REVIEW

Throughout the past two decades, numerous people with diabetic macular edema have had surgical treatment to eradicate this condition. The surgery is an invasive procedure that removes the vitreous around the posterior hyaloid detachment. Additionally, peeling removes any epiretinal and internal limiting membranes. Historically, detachment of the posterior vitreous has been associated with more rapid resolution of DME. Moreover, vitrectomy has been reported to ameliorate DME symptoms via multiple biological pathways [2]. These processes include enhanced retinal oxygenation, enhanced clearance of vascular endothelial growth factor (VEGF) loads, and the release of aberrant vitreomacular adhesions [2]. Previous research has shown that surgery is a highly effective treatment for diabetic macular edema. In order to reduce patient injury, it is necessary to evaluate the application and utilization of anesthetic during these procedures. There are two primary locations of the eye where anesthetics are administered during surgery to eliminate this condition. During DME surgery, the anesthetic is typically used topically or subconjunctivally [1-30]. Although some physicians use both topical and subconjunctival anesthetic [3-6], the vast majority of healthcare professionals only use topical anesthetics [7-17]. While subconjunctival anesthesia is known to reduce patient harm more than topical anesthetics, it has been demonstrated to increase the risk of subconjunctival bleeding [4]. This is likely why the majority of surgical treatments involving DME only employ topical anesthetic and not subconjunctival anesthesia.

DME is treated surgically with injections of medications that counteract the disease's symptoms. In an effort to prevent damage to the patient's fovea, medication administration specifically targets the swelling of the macula [2]. In addition, surgical injections [18] aim to address the rupture of the blood-retinal barrier and the elevation of retinal vascular leukostasis. Triamcinolone acetonide (TA) is the most commonly used medication by ocular surgeons for this surgery. This is perhaps because TA is a well-established anti-inflammatory in medical treatments [19]. Due to the anti-inflammatory actions of TA on the macula, it is one of the most effective treatments for alleviating the previously mentioned difficulties produced by DME. In the majority of research analyzed in Table 1, it was found that TA is the most frequently administered intravitreally during DME surgical treatments. Although TA is the most often used medication for this surgery, it is not the standard medication. This is most likely related to the fact that TA is a relatively new medicine on the pharmaceutical market and anti-vascular endothelial growth factor (AVEGF) is the usual drug for this surgery [20]. While both TA and AVEGF are anti-inflammatory drugs, TA has been shown to reduce central thickness and improve best-corrected visual acuity better [19]. In post-clinical trials, it has been demonstrated that TA has more lasting positive effects on patients' vision than AVEGF [19]. As additional clinical and translational research is conducted, it is possible that TA will replace AVEGF as the new standard of therapy. In order for surgeons to administer TA injections to patients with DME, the patients must first be anesthetized to prevent pain during surgery. Therefore, it is essential to evaluate the type of anesthetics while contemplating DME treatment.





# Surgical Mindfulness: A Patient Centered Model for the Management of Acute Perioperative Pain and Anxiety

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## ABSTRACT

The experience of pain is two-fold, comprised of both physical and mental aspects. There is the physiologic stimulus, such as an injury or healing surgical wound, paired with the neurologic perception of that stimulus. Pertaining to perioperative medicine in particular, adequate pain control is one of the major limiting factors in postoperative healing and hospital discharge. Tapping into the mental component of pain perception and management, anxiety and mental catastrophization have been shown to significantly augment not only the amount of pain a postoperative patient may experience, but also the analgesic requirement. Given the robust research supporting mindfulness meditation as a valid coping mechanism for chronic pain, we propose the application of these same techniques to the perioperative environment as to help patients mitigate their acute postoperative pain.

## INTRODUCTION

Mindfulness was first introduced into the clinical sphere by Jon Kabat-Zinn, PhD in 1979. He pioneered the application of Mindfulness Based Stress Reduction (MBSR) - a program involving a combination of guided meditation, deep breathing, and a self-aware but non-judgemental acknowledgement of the present - as a way to help patients manage their responses to stressors in life. In 1982, Kabat-Zinn applied these practices toward patients dealing with chronic pain through a 10-week guided MBSR course and found that 65% of participants experienced more than a 33% reduction in pain - some as high as 50%.<sup>1</sup> Furthermore, patients also noted positive mood and behavioral developments accompanied by a heightened sense of self-awareness and capacity to cope with stress.<sup>1</sup> Since then, mindfulness has increasingly become an expanding area of research as a way of understanding and even as a method of mediating stress, anxiety, and pain. Additionally, a 2015 study<sup>2</sup> established a stronger link between mindfulness-based meditation, greater pain relief, and the activation of distinct neural pathways compared to placebo analgesia or sham mindfulness techniques. Given the diverse applications of mindfulness, the next frontier is the perioperative environment and implementing these techniques in the setting of acute surgical pain. A recent 2019 study<sup>3</sup> concluded that preoperative patients predisposed towards mindfulness were more likely to overall have decreased postoperative pain - suggesting that mindfulness can be directly targeted as another possible form of pain management.

## PROBLEM

A sizeable component of the pain experience is shaped by both cognitive and emotional factors - two aspects that have historically been ignored. Current literature suggests a predictive association between preoperative anxiety, catastrophization, and the development of chronic postoperative pain.<sup>4</sup> Through our proposed methods, we are hoping to target these specific, aforementioned factors through a combination of pain education, perioperative expectation management, and mindfulness practice.

## APPROACH

- Patient identification
  - Which patient population stands to benefit the most?
  - Elective surgery with acute pain expected to play significant role in recovery
  - Total Knee Arthroplasty (early ambulation improves recovery while reducing VTE risk)
- Pain Education
  - Mechanism of pain transmission and modulation
  - Understanding pain as normal physiology with a role in recovery
- Introduction to mindfulness
  - What is mindfulness and how does it apply to pain?
  - Mindfulness modulates the pain experience centrally, hypothesized to be similar to endogenous opioidergic mechanisms which have been demonstrated during placebo produced analgesia
- Application of mindfulness
  - This can be applied successfully in any way, as long as it encourages patients to address their pain constructively with reasonable expectations
  - Addressing the contextual meaning of pain allows central modulation of pain transmission and experience



## CLINICAL IMPLICATIONS

Despite improvements, there will always be an inherent risk to invasive or pharmacologic anesthesia potentiative of causing patient harm or other complications. For example, neuropathy after regional anesthesia was found at an incidence rate of 3.78/10,000 after spinal anesthesia.<sup>5</sup> On average, 70% of patients experience postoperative pain.<sup>6</sup> Thus, finding methods for pain alleviation is imperative to improving patient outcomes. There is substantial evidence present within the current literature that suggests that meditation has the potential to reduce patient harm and post-surgery pain.<sup>7</sup> Recent studies have demonstrated that engaging patients with a meditation course lessened the chronic pain perceived pre- and post-operatively.<sup>8</sup> This is most likely explained by how the pain perception pathway can be enhanced or diminished by an individual's awareness or perception of said pain. There is evidence present within the current literature that advocates for the potential of meditation in reducing acute pain postoperatively; however there has been no cohesive study that has sufficiently explored this concept.<sup>9</sup> The authors have submitted documentation for institutional review board approval and intend to investigate the link between surgical mindfulness and acute pain. Acute pain is intended to be measured via pain perception scores, anxiety scores, mood scores, and sense of locus of control. If the findings of this future study - which involves showing patients a five-video-series about pain perception as a means to reduce anxiety and pain before and after surgery - is significant, it may lay groundwork for the discovery of a potentially cost-effective method of improving patient outcomes. Further research could verify the validity of these claims.

## References

1. Kabat-Zinn J. An outpatient program in behavioral medicine for chronic pain patients based on the practice of mindfulness meditation: theoretical considerations and preliminary results. *Gen Hosp Psychiatry*. 1982 Apr;4(1):33-47. doi: 10.1016/0163-8343(82)90026-3. PMID: 7042457.
2. Zedran F, Emerson NM, Farris SR, et al. Mindfulness Meditation-Based Pain Relief Employs Different Neural Mechanisms Than Placebo and Sham Mindfulness Meditation-Induced Analgesia. *J Neurosci*. 2015;35(46):15307-15325. doi: 10.1523/JNEUROSCI.2542-15.2015.
3. Weston E, Rakar C, Huang D, Parker A, Robison K, Mathews C. The Association between Mindfulness and Postoperative Pain: A Prospective Cohort Study of Gynecologic Oncology Patients Undergoing Minimally Invasive Hysterectomy. *J Minn Invasive Gynecol*. 2020;27(5):1119-1126.e2. doi: 10.1016/j.jmig.2019.08.023/Singer C, Carvensson M. Recent advances in the technology of anesthesia. *F1000Res*. 2020 May 18;9:F1000 Faculty Rev-375. doi: 10.12688/f1000research.24059.1. PMID: 32494358. PMCID: PMC7236591.
4. Theunissen M, Peters ML, Bruce J, Gramke HF, Marcus MA. Preoperative anxiety and catastrophizing: a systematic review and meta-analysis of the association with postoperative pain. *Clin J Pain*. 2012;28(8):819-841. doi: 10.1097/AJP.0b013e31826a5486.
5. Gottschall A, Van Aken H, Zenz M, Stand T. Is anesthesia dangerous? *Dtsch Arztezt*. 2011 Jul 8. PMID: 21814522. PMCID: PMC3147285.
6. Pyatt S, Gan TJ. Perioperative pain management. *CNS Drugs*. 2007;21(3):185-211. doi: 10.2165/00022012-200721030-00002. PMID: 17385892.
7. Benjamin R, Trexler AM, Datta S, Buenaventura R, Adlari R, Sengul N, Glaser SE, Vallego R. Opioid complications and side effects. *Pain Physician*. 2008 Mar;11(2 [Suppl]):S105-20. PMID: 18443635.
8. Yam MF, Loh YC, Tan CS, Khadijah Adam S, Abdul Manan M, Basir R. General Pathways of Pain Sensation and the Major Neurotransmitters Involved in Pain Regulation. *Int J Mol Sci*. 2019 Jul 24;19(8):2164. doi: 10.3390/ijms19082164. PMID: 30942373. PMCID: PMC67121522.
9. Packiasabapathy S, Suresha AT, Mueller A, Patil M, Gaasangdy DV, O'Gara B, Shaefi S, Marcantonio ER, Yeh GY, Subramanian B. Guided meditation as an adjunct to enhance postoperative recovery after cardiac surgery: study protocol for a prospective randomized controlled feasibility trial. *Trials*. 2019 Jan 11;20(1):38. doi: 10.1186/s13063-019-3103-8. PMID: 30635954. PMCID: PMC6339114.
10. Zedran F, Vago DR. Mindfulness meditation-based pain relief: a mechanistic account. *Ann N Y Acad Sci*. 2016 Jun;1373(1):114-27. doi: 10.1111/nyas.13153. PMID: 27398643. PMCID: PMC4941786.

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# Clinical Wide-Field Retinal Image Deep Learning Classification of Exudative and Non-Exudative Age-Related Macular Degeneration

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## ABSTRACT

Age-related macular degeneration (AMD) is a disease that currently affects approximately 196 million individuals and is projected to affect 288 million in 2040. As a result, better and earlier detection methods for this disease are needed in an effort to provide a higher quality of care. One way to achieve this is through the utilization of machine learning. A deep neural network, specifically a convoluted neural network (CNN) can be trained to differentiate between different types of AMD images given the proper training data. In this study, a CNN was trained on 420 Optos wide-field retinal images for 70 epochs in order to classify between exudative and non-exudative AMD. These images were obtained and labeled by ophthalmologists from the Martel Eye Clinic in Rancho Cordova, CA. After completing the study, a model was created with 88% accuracy. Both the training and validation loss started above 1 and ended below 0.2. Despite only analyzing a single image at a time, the model was still able to accurately identify if the individual had AMD in both eyes or one eye only. The model had the most trouble with bilateral non-exudative AMD. Overall the model was fairly accurate in the other categories. It was noted that the neural network was able to further differentiate from a single image if the disease is present in left, right, or both eyes. This is a point of contention for further investigation as it is impossible for the artificial intelligence (AI) to extrapolate the condition of both eyes from only one image. This research fostered the development of a CNN that was able to differentiate between exudative and non-exudative AMD, as well as determine if the disease is present in the right, left, or both eyes with a relatively high degree of accuracy. The model was trained on clinical data and can theoretically be used to classify other clinical images it has never encountered before.

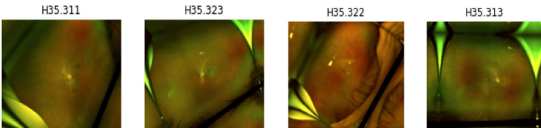
## INTRODUCTION

Age-related macular degeneration is a chronic disease occurring in the central retina that affects 196 million people worldwide [1]. As the disease progresses, it leads to a loss of the visual field. This disease has a range of symptoms such as visual distortions and reduced central vision [1]. Typically, visual loss occurs in the later stages of the disease due to neovascularization and geographic atrophy [2]. As a result, age-related macular degeneration (AMD) can be further classified into exudative (wet) and non-exudative (dry). Wet AMD occurs when the choroidal neovascular membranes under the retina leak fluid and blood. If wet AMD is caught in the early stages it can be treated with anti-vascular endothelial growth factor (anti-VEGF) shots [3]. This, in turn, damages the retina. Dry AMD occurs when the retina and choroid degrade due to atrophy or detachment of the retinal pigment epithelium [3]. In the field of ophthalmology, machine learning has been extensively utilized for classifying diseases such as glaucoma and diabetic retinopathy with high degrees of success [4-5]. Even with the utilization of teleophthalmology, machine learning has the potential to vastly improve the quality of care provided [6]. Convoluted neural networks (CNNs) composed of convolutional layers are primarily used for visual applications. This can be a form of a deep neural network as there are often times many hidden layers. This study was conducted in order to develop a deep learning model that is able to differentiate between exudative and non-exudative AMD through analyzing wide-field images from a clinical setting.

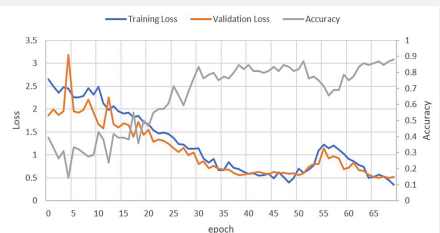
## METHODS

This was a retrospective cohort study of individuals diagnosed with exudative or non-exudative macular degeneration. Retinal fundus images from patients and diagnoses by ophthalmologists were obtained from the Martel Eye Clinic in Rancho Cordova, CA. Images used were wide-field Optos images collected from 2017 to 2021. Images collected were initially filtered to remove low-quality images from the dataset. They were then labeled based on the respective side they were taken on (left or right) and ICD-10-CM diagnostic codes (H35.313, H35.322, H35.321, H35.312, H35.311, or H35.35). The images labeled with H35.35 were labeled to "final". From an initial pool of 957 images, 20% of the images and their labels were randomly sampled and separated into the validation set. The remaining images were randomly sampled until each category had a total of 50 images each. This created a training set of 350 images and a validation set of 70 images for a total of 420 images used. The patient sample size for this study was 210. The machine-learning CNN algorithm was run on a Windows computer with an Nvidia RTX 3090 24GB. A batch size of four images was used with an initial learning rate of  $1 \times 10^{-3}$ . Batch image augmentations were applied along with resizing of the images to 1950 x 1535 pixels. The CNN was run for a total of 70 epochs taking about three minutes and ~20s for each epoch.

## RESULTS



A sample batch of four images with transformations applied along with their ICD-10 diagnostic code. These images after the transformations are the ones that are used to train the model. Since these images were obtained from a clinical setting there is a significant variation in the quality of images. This increased the difficulty of training the model requiring more images in order to compensate for the variations in each image. Image augmentations allow for new data to be created by modifying the original image in order to make an image the model has not been trained on.



It was determined that the CNN model had a final accuracy of 88%. Overall there was a general trend of decreasing loss for both the validation and training set as the number of epochs increased. This trend was opposite to accuracy as it increased as the number of epochs increased. There was a dip in accuracy around epoch 56. This may be due to the model getting stuck in local minimum.

	#	12	0	0	0	0	0	0
Actual \ Predicted								
Nonexudative AMD (R)	0	12	0	0	1	0	0	0
Nonexudative AMD (L)	0	8	0	0	0	0	0	0
Nonexudative AMD (B)	0	2	3	16	0	0	0	2
Exudative AMD (R)	0	0	0	0	12	0	0	0
Exudative AMD (L)	0	0	1	1	0	9	0	0
Exudative AMD (B)	0	0	0	0	0	0	0	5

The confusion matrix that displays the category and predicted category of the validation dataset. This is the result of testing the model on the validation dataset. Overall, the model predicted accurately when compared to the actual diagnosis. The model had relatively little difficulty when determining if the image was a right or left side image when compared to bilateral images.

## CLINICAL IMPLICATIONS

This technology can improve the accuracy and efficiency of AMD diagnosis, enabling early detection and intervention to prevent vision loss. The AI software has the potential to enhance accessibility and efficiency in diagnosing AMD, particularly in teleophthalmology settings. It can serve as a screening tool, supporting healthcare professionals in triaging patients and providing targeted care. Additionally, the AI software can aid in research and discovery, uncovering new patterns and contributing to advancements in understanding ocular diseases. Overall, AI technology holds promise for improving patient outcomes, expanding access to care, and assisting healthcare professionals in delivering more accurate diagnoses and treatment plans in the field of ophthalmology. Furthermore, the study highlights the potential of AI technology to assist in the diagnosis of other ocular diseases, complementing the existing capabilities of healthcare professionals. By leveraging machine learning algorithms, clinicians can benefit from more efficient and reliable analysis of retinal images, leading to faster and more accurate diagnoses. This can ultimately enhance patient care, optimize treatment strategies, and alleviate the burden on healthcare systems by improving workflow and resource allocation.

## Key Findings

- The deep learning model, based on a convolutional neural network (CNN), achieved an accuracy of 88% in differentiating between exudative and non-exudative AMD.
- The model showed high accuracy in determining AMD in the left eye (100%) and in both eyes (69.6%).
- Accuracy was lower for AMD in the right eye, with 81.8% for exudative AMD and 92.3% for non-exudative AMD.
- The model also demonstrated accurate identification of cases that did not fall into any of the AMD categories, with 100% accuracy.
- The study suggests that there may be more obvious signs of exudative AMD in retinal scans, leading to higher accuracy in its detection compared to non-exudative AMD.
- The AI software was able to detect bilateral cases of AMD with surprising accuracy, indicating potential differences between bilateral and unilateral AMD.
- The study highlights the potential of AI software in assisting physicians with AMD diagnosis, especially in cases where access to proper medical care is limited.
- Further research is needed to increase the accuracy and generalizability of the AI model by incorporating larger and more diverse datasets.

## CONCLUSIONS

The authors in this investigation developed a CNN algorithm that is able to differentiate between exudative and non-exudative macular degeneration from ultrawide field Optos images. On the validation dataset, the model was calculated to be 88%. The model was able to differentiate from analyzing a single image if AMD is present in the left eye, right eye, or both eyes. Being able to identify if AMD is present in both eyes from an image of a single retina. AMD needs to be caught early on in order to prevent further patient complications, therefore, it is quintessential for physicians to continue developing tools and methods that facilitate diagnosis. Further research is required to verify and explain the possibility of extrapolating the fact that a patient has AMD in both eyes when only looking at one retinal scan. The results from this exploration demonstrate that AI has the potential to have a significant impact on diagnostics and the overall quality of care in the healthcare industry.

## ACKNOWLEDGEMENTS

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# Revolutionizing Brain Tumor Diagnosis: Leveraging Artificial Intelligence for Accurate Brain Tumor Detection

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## ABSTRACT

Accurate and timely detection of brain tumors plays a crucial role in their diagnosis and treatment. In this study, we aimed to evaluate the performance of an artificial intelligence (AI) model for the presence or absence detection of brain tumors based on magnetic resonance imaging (MRI). Specifically, we assessed the average precision, precision, and recall metrics of the model. **Methods:** A dataset of 228 MRI images, consisting of 182 training images, 23 validation images, and 23 test images, was utilized for training and evaluating the AI model. The model employed advanced deep learning techniques to learn discriminative features from the MRI images and classify them as either tumor-positive or tumor-negative. Precision, recall, and average precision were calculated to assess the model's performance. **Results:** The AI model achieved an average precision of 0.977, indicating a high degree of accuracy in discriminating between tumor-positive and tumor-negative MRI images. The precision metric, representing the proportion of correctly identified tumor-positive cases out of all predicted tumor-positive cases, reached 87%. Similarly, the recall metric, representing the proportion of correctly identified tumor-positive cases out of all actual tumor-positive cases, also reached 87%. **Conclusion:** Our findings demonstrate that the developed AI model for brain tumor detection based on MRI exhibits excellent performance, as evidenced by high precision, recall, and average precision values. These results suggest that the model holds promise as a reliable tool for assisting clinicians in diagnosing brain tumors; however, further validation studies and integration into clinical workflows are warranted to evaluate the model's performance in real-world settings and its potential impact on patient outcomes.

## INTRODUCTION

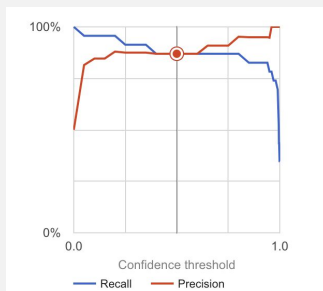
With the rising cost of healthcare, and the increasing stress placed on the medical personnel's shoulders, it is important to consider potential of Artificial intelligence (AI) in the space. Many of the deficiencies in healthcare will continue to be unearthed when our healthcare system is placed under stress, such as with the Covid pandemic [1]. One of those deficiencies was the unequal access to the highest levels of care and diagnosis by those who are unable to pay for it [1]. Utilizing AI can present a window of opportunity to deliver high levels and more efficient methods of care for all [1]. The primary method of diagnosing a tumor in the brain currently is through MRI based on its appearance [2]. AI can be trained through learning models to identify the presence of abnormalities or a tumor [3]. There have been small scale trials of AI being able to replicate the diagnoses of radiologists with 15 years of experience [3]. Additionally some alternate factors that may be important in diagnosing a tumor are genetic risk, age, exposure risk to certain environments and material [2]. These factors can be included in the learning machinery of the AI in the future as it grows to further expand its ability to predict tumor type, and potential malignancy.

## METHODS

Using Kaggle.com, an MRI dataset of 228 images were used to train an AI on Google's Collaboration Platform through machine learning. The MRIs were labelled as either "Tumor" or "NoTumor," and they were divided into three subsets: 80% for training, 10% for validation, and 10% for testing. This ensured for proper testing of the AI trained to detect tumors within the skull.

## RESULTS

The performance of the tumor detection model developed using Google's Collaboration Platform showcased promising outcomes. The model attained an area under the curve (AUC) value of 0.977 on March 24th, 2023, indicating its ability to accurately distinguish between brain MRIs with tumors and those without. Both precision and recall metrics demonstrated an 87% accuracy rate, affirming the model's capability in correctly identifying tumor cases, as illustrated in Figure 1.



To further assess the model's performance, key statistical measures such as sensitivity, specificity, and overall accuracy were calculated using the provided data. These values were derived by analyzing the True Positive (TP), True Negative (TN), False Positive (FP), and False Negative (FN) obtained from the Confusion matrix, as presented in Figure 2. Sensitivity, also referred to as the true positive rate, was determined to be 93%, indicating the model's ability to correctly identify 93% of actual tumor-positive cases. Specificity, representing the true negative rate, was calculated at 78%, highlighting the model's proficiency in accurately classifying cases as normal. These results emphasize the model's heightened sensitivity in detecting tumor-positive cases and its specificity in recognizing normal cases.

True label	Predicted label	
	Tumor	NoTumor
Tumor	93%	7%
NoTumor	22%	78%

## CLINICAL IMPLICATIONS

The integration of AI models in clinical practice has the potential to enhance diagnostic accuracy. By assisting radiologists in detecting brain tumors, AI algorithms can aid in identifying subtle or complex tumor characteristics that may be overlooked by human interpretation alone. Improved diagnostic accuracy can lead to early detection, timely intervention, and better patient outcome/treatment decision-making processes. By providing reliable and consistent tumor classification, the AI model can assist clinicians in determining appropriate treatment strategies. This may include selecting optimal surgical approaches, planning radiation therapy, or guiding the administration of targeted therapies. The model's ability to generate precise and actionable information can lead to more personalized and effective treatment plans. Inter-observer variability is a common challenge in radiological interpretations. AI models offer a standardized and consistent approach to brain tumor detection, reducing variability among different radiologists. By providing objective and reproducible results, AI can enhance the reliability of diagnoses and facilitate better communication among healthcare professionals involved in patient care.

## Key Findings

Inter-observer variability is a common challenge in radiological interpretations. - AI models offer a standardized and consistent approach to brain tumor detection, reducing variability among different radiologists. - AI provides objective and reproducible results, enhancing the reliability of diagnoses. - AI facilitates better communication among healthcare professionals involved in patient care. - AI improves the accuracy of brain tumor detection, leading to more effective treatment planning. - The use of AI reduces the dependence on individual expertise and minimizes errors in brain tumor diagnosis. - AI models can process large amounts of data quickly, leading to faster and more efficient diagnoses. - Incorporating AI into radiological interpretations improves overall efficiency and workflow in healthcare settings.

## CONCLUSIONS

In most cases, AI was able to determine the presence or confirm the absence of a tumor. The AI model often falsely predicted the presence of a tumor, and to a lesser degree falsely confirmed its absence. The accuracy and capabilities of the AI continues to evolve with exposure, and with time will allow us to provide equal access to the highest levels of care. Further criteria besides image can be implemented in the future to aide in the accurate diagnosis and categorization of the tumor.

## ACKNOWLEDGEMENTS

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# Atypical Manifestation of Cytomegalovirus Infection and Retinitis in an Immunocompetent Individual

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## ABSTRACT

Cytomegalovirus retinitis most commonly presents in immunosuppressed patients or the immunologically immature neonatal group. Yet evidence from several studies suggest that occurrence of Cytomegalovirus retinitis may appear even with no systemic immune dysfunction. Due to the lack of literature published on the immunocompetent population, we wish to present a case report with a review of the present research. A middle-aged, otherwise healthy and immunocompetent female presented with femoral thrombus, fever, blurring of vision, and documented cytomegalovirus infection. Core DNA positivity for active CMV infection was obtained, and with antiviral treatment, the patient ultimately regained full vision. CMV retinitis triggered from an isolated systemic condition such as hypertension is not common and suggests that other factors should be considered. We wish to highlight the importance of considering CMV diagnosis even in those who are immunocompetent.

## INTRODUCTION

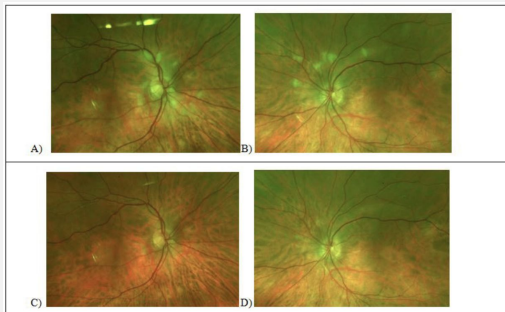
Cytomegalovirus (CMV) comprises one of nine herpesviruses. Infection is very common and mostly asymptomatic in healthy patients with proper immune function. The virus can be spread through the saliva, bodily excretions, infected blood transfusions, or through placental transfer. Once infected, the virus becomes latent by avoiding detection and immune elimination until an opportunistic event occurs. Symptomatic illness in the host indicates either reactivation of the dormant virus or reinfection with a different strain. Complications of this disease can affect many organ systems with consequential morbidity and mortality. Ocular involvement may cause devastating vision loss. It was originally thought that patients only manifested with symptoms during a compromised state. Prior reports of systemic CMV infection in the immunocompetent have focused on organ systems other than the eye, such as the gastrointestinal and central nervous systems [1]. We report an otherwise healthy patient who presented with a femoral thrombosis and was subsequently noted to develop CMV retinitis. Thrombosis is a well corrected complication in patients with CMV infection [2]. We wish to detail this case and focus on the factor of immunosenescence and its relation to CMV infection and reactivation.

## METHODS

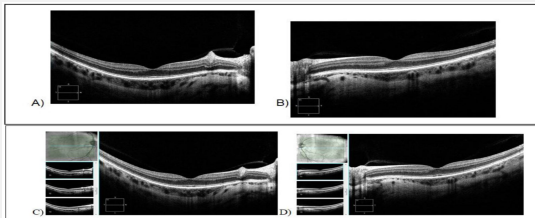
A literature search of articles published between 1976 and 2017 using PubMed was performed using the keywords "CMV," "cytomegalovirus," "retinitis," and "immunocompetent." Cases that included infants, existing history of intravitreal injections or eye surgeries, eye trauma, immunodeficiency, recurrent or chronic infections, and patients who tested negative for CMV infection or that were not confirmed were not included. Titles and abstracts were reviewed to ensure patients were not in a compromised state prior to diagnosis of CMV infection. Only articles in English were incorporated into our analysis.

## RESULTS

Fundoscopic imaging of the right (A) and left (B) eye, taken during the first outpatient visit, 1 week after appearance of ocular symptoms. Cotton wool spots were seen in both eyes, concerning of choroidal lesions and retinal ischemia. There is significant venous engorgement noted in the right eye. Fundoscopic imaging of the right (C) and left (D) eye, taken post-treatment, two and a half weeks after first outpatient encounter for comparison. Nerves and vessels were within normal limits, edges were sharp without swelling OU. There was complete resolution and disappearance of cotton wool spots.



Using the keywords as specified in the "Methods" section, our search yielded a total of 80 publications. A total of 11 articles describing 18 patient cases of CMVR met our search criteria. Information extracted from each report were age, gender, diagnostic confirmation of CMV infection, and co-existing medical history. The average age of immunocompetent patients selected for our review was 63 years old, with diabetes (44%) as the most common co-existing medical diagnosis and hypertension (28%) as the second (Table 1). There were more reported cases of CMVR in men (67%) than women (33%).



## CLINICAL IMPLICATIONS

As T cells play a critical role in controlling infections in immunocompetent patients, changes to the cellular population explains the vulnerability to CMV. Alteration to T cell phenotype has been documented in the older population where repetitive T cell stimulation with CMV antigen is a driving force for immunosenescence. The consequence of committing increased amounts of resources to manage CMV is the impaired overall function of the immune system. Immunosenescence is seen clinically as decreased efficacy of vaccination in the elderly (influenza, tuberculosis) due to deficient immune cell recruitment. The aged immune response is not as effective in controlling viral reactivation. Immunocompetent patients with a history of inflammatory bowel disease who develop CMV colitis have frequently elevated levels of cytokines (tumor necrosis factor-alpha and interferon-gamma). As of 2020, of the 3116 articles involving CMV retinitis on PubMed, only two reviews of literature have been made regarding CMV retinitis in immunocompetent patients which shows that this is an extraordinarily rare phenomenon. Using data from recent studies, it is estimated that the incidence rate of immunocompetence in individuals with CMV retinitis is 1.32/100 person decades.

## Key Findings

The immunocompetent female in the case study was confirmed to have CMV through serological testing. The vision and general health of the patient was improved after two weeks of treatment with valgancyclovir (treatment was for three weeks total). Fundoscopic images taken two and a half weeks after the start of treatment showed complete resolution when compared to initial images before treatment. CMV DNA QNT, CRP, and ESR all returned to normal limits after treatment. More reported cases of CMVR in men than women. Prevalence is inversely correlated to the country's socioeconomic status, increases with age, and differs between race and ethnicity, with the highest incidence in Mexican Americans. Recent studies have noted common non-immunological factors that may weaken the immune system enough for viral appearance of CMV such as: age over 60 years, malignancy, local immunosuppression therapy, and diabetes mellitus. In immunocompetent patients, primary CMV infection runs its course like an undifferentiated viral syndrome or is manifested by a mononucleosis like syndrome, "fever and myalgia." The most common CMV ocular presentations in decreasing frequency are: retinitis, vasculitis, retinal hemorrhages, keratic precipitates, anterior chamber cells, and vitritis.

## CONCLUSIONS

Complications from CMV infection in those who are deemed immunocompetent may not be as rare as we thought. It is important for physicians to consider cytomegalovirus infection in their differential diagnosis in patients presenting with fever and malaise even though they are in the low-risk group. Although use of gancyclovir therapy is not conclusive in the immunocompetent host, our patient showed improvement after treatment and may serve as confirmation in future cases to avoid ocular sequelae. The patient was not HIV positive, diabetic, nor were they on any medication that alters the immune system. It still remains an enigma how this condition occurred in an immunocompetent host and only affected their eyes, especially when considering the severity of the condition. Perhaps with more immunological analysis, the variability of the T-cell response across the human body may be better understood.

## ACKNOWLEDGEMENTS

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# Deep Learning Classification of TB Chest X-rays

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## ABSTRACT

Tuberculosis (TB) remains a significant global health challenge, necessitating accurate and timely detection for effective management. This study aimed to develop a TB detection model using chest X-ray images obtained from Kaggle.com, utilizing Google's Collaboration Platform. Over 1196 chest X-ray images, comprising both TB-positive and normal cases, were used for model development. The model achieved an average precision of 0.934, with precision and recall values of 94.1% each, indicating its high accuracy in classifying TB-positive and normal cases. Sensitivity and specificity values were calculated as 96.85% and 91.49%, respectively. The F1 score was also calculated to be 0.941. The overall accuracy of the model was found to be 94%. These results highlight the potential of machine learning algorithms for TB detection using chest X-ray images. Further validation studies and research efforts are needed to assess the model's generalizability and integration into clinical practice, ultimately facilitating early detection and improved management of TB.

## INTRODUCTION

Tuberculosis (TB) is a significant global health challenge caused by *Mycobacterium tuberculosis*, primarily affecting the lungs and causing severe illness and mortality if untreated [2-3]. Prior to the COVID-19 pandemic, TB ranked highest among infectious diseases in terms of mortality. In 2019 alone, TB resulted in 1.4 million deaths and 10 million new cases worldwide. However, reduced access to care has led to an increase in TB deaths, with 2020 seeing the first year-over-year rise since 2005 [6]. Early detection is crucial for effective disease management and prevention of transmission. Traditional diagnostic methods have limitations, but recent advancements in medical imaging, particularly chest X-ray imaging, have provided valuable insights. However, the subjective interpretation of these images by human experts poses challenges. To address this, we aimed to develop a TB detection model using machine learning algorithms and artificial intelligence (AI) technology. Such a model has the potential to revolutionize TB diagnosis, offering a standardized and objective tool for healthcare professionals. It could enable early detection, prompt treatment initiation, and implementation of effective control measures, especially in resource-limited regions lacking access to expert radiologists and healthcare resources. By leveraging AI, we strive to enhance the accuracy and efficiency of TB diagnosis, contributing to global efforts in combating this persistent infectious disease.

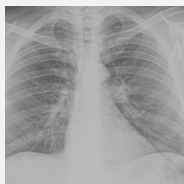


Figure 1: TB X-ray



Figure 2: Normal chest X-ray

## METHODS

This study aimed to develop a tuberculosis (TB) detection model using chest X-ray images obtained from datasets on Kaggle.com [9]. A dataset of over 1196 chest X-ray images, including 633 TB-positive Chest X-rays and 563 normal cases, was utilized for model development. The images were in digital format (e.g., JPEG, PNG) and were labeled accordingly.

To preprocess the data, the TB and normal images were organized into separate folders. Each image was visually inspected to ensure proper labeling and quality. No additional preprocessing, such as image resizing or augmentation, was performed.

For model development, Google's Collaboration Platform was employed. The deep learning algorithm, using CNN methods, was trained to learn the patterns and features associated with TB-positive X-rays using the labeled chest X-ray dataset (seen in Figure 1) by using 80% of the images to train the model, 10% of the images to validate the model, and another 10% of the images to test the model. The assignments in this study were all randomized. No external datasets were used in this study.

The trained model was evaluated using a separate test set of chest X-ray images. Its performance was assessed based on its ability to accurately identify TB-positive X-rays and distinguish them from normal X-rays, seen in Figure 2. Evaluation metrics, including accuracy, precision, recall, and confusion matrix, were calculated to quantify the model's performance.

The model was constructed using a software tool supported by Google. The software tools used included Google's Collaboration Platform, Python, and deep learning frameworks such as TensorFlow and PyTorch.

## RESULTS

The TB detection model developed using Google's Collaboration Platform exhibited promising performance. The model achieved an area under the curve (AUC) of 0.934, indicating its ability to accurately classify TB-positive and normal chest X-ray images. Both precision and recall values were found to be 94.1%, highlighting the model's high accuracy in correctly identifying TB cases as seen in Figure 3. Although a possible limitation from a high recall means that the model could be overfitting, where the machine learning algorithm memorizes the data rather than learning from patterns. This could lead to recall rates near 100 which would mean the model is just memorizing the pictures and is not able to reliably predict future occurrences since it did not learn.

To further evaluate the model's performance, statistics of sensitivity, specificity, and overall accuracy were calculated using the provided values. The values were calculated by finding the True Positive, True Negative, False Positive, and False Negative from the Confusion matrix in Figure 4. The sensitivity, also known as the true positive rate, was determined to be 96.85%. This indicates that the model correctly identified 96.85% of actual TB-positive cases. The specificity, or true negative rate, was calculated to be 91.49%, reflecting the model's proficiency in correctly classifying normal cases.

Furthermore, the overall accuracy of the model was determined to be 94%. This value represents the proportion of all cases, both TB-positive and normal, that were correctly classified by the model. These results highlight the model's effectiveness in distinguishing between TB and normal chest X-ray images.

It is important to note that the experiments were conducted using Google's Collaboration Platform on May 22. These results demonstrate the model's high sensitivity in identifying TB-positive cases and its specificity in recognizing normal cases. The achieved accuracy underscores the model's overall performance in accurately classifying TB cases.

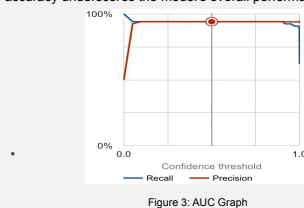


Figure 3: AUC Graph

True label	Predicted label	
	Normal	TB
Normal	91%	9%
TB	3%	97%

Figure 4: Confusion Matrix

## CONCLUSIONS

This study highlights the potential of machine learning and deep learning algorithms in improving tuberculosis (TB) diagnosis using chest X-ray images. The developed TB detection model demonstrated high accuracy and performance metrics, showcasing its ability to effectively classify TB-positive and normal cases. The integration of such models into clinical practice has the potential to enhance early detection, facilitate prompt treatment initiation, and improve TB control measures. However, further research, validation, and implementation efforts are necessary to ensure the model's generalizability and efficacy in diverse populations and real-world clinical settings. Collaborative efforts between researchers, clinicians, and policymakers are crucial to harnessing the full potential of these technological advancements in combating TB and reducing its global impact.

## CLINICAL IMPLICATIONS

- The results obtained from this study highlight the potential of machine learning and deep learning algorithms in the field of TB detection. Chest X-ray imaging is a widely accessible and cost-effective diagnostic tool for TB, making it an ideal modality for training and evaluating detection models.
- The high accuracy of the model, as reflected in the overall accuracy of 94%, suggests its potential for aiding in the early detection of TB. Early diagnosis is crucial for initiating timely treatment and curbing the transmission of the disease [9].
- The model exhibited high precision, recall, sensitivity, specificity, and overall accuracy, suggesting its utility in distinguishing between TB-positive and normal cases.
- Early diagnosis of TB is crucial for initiating appropriate treatment and preventing the transmission of the disease [11].
- The development of accurate and reliable TB detection models can support healthcare professionals in making timely and informed decisions, particularly in resource-limited settings where access to expert radiologists may be limited. The integration of such models into clinical workflows has the potential to enhance TB control programs and improve patient outcomes.
- The application of machine learning algorithms to chest X-ray images shows promise for advancing TB diagnosis.
- Collaborative efforts between researchers, clinicians, and policymakers are necessary to realize the full potential of these models in combating TB and reducing its global impact.

## REFERENCES

- Zaman K. Tuberculosis: a global health problem. *Journal of health, population, and nutrition*. 2010; 26:111-113.
- Altamirano, Dine ZW, Seid C, et al. Tuberculosis in individuals who recovered from COVID-19: A systematic review of case reports. *PLoS One*. 2022;17(11):1-11. doi:10.1371/journal.pone.0278707
- Luke E, Swafford K, Shirazi G, et al. TB and COVID-19: An Exploration of the Characteristics and Resulting Complications of Co-infection. *Front Biosci (Schol Ed)*. 2022; 14(8):1-13. doi:10.1093/fbs/abz006
- Global tuberculosis report. (2022;2022). <https://www.who.int/publications/item/978924061929>
- Dye C. (2008). *Global Epidemiology of Tuberculosis*. The Lancet, 367, 938-940. -References - Scientific Research Publishing. [www.scirp.org](http://www.scirp.org). Accessed May 25, 10.1016/S1473-6566(06)86384-0
- Pai M, Kasana T, Swaminathan S. Covid-19's Devastating Effect on Tuberculosis Care — A Path to Recovery. *New England Journal of Medicine*. Published online January 5, 2022.
- Kaufmann SHE. How can immunology contribute to the control of tuberculosis? *Nature Reviews Immunology*. 2001; 1:20-30.
- Fenton EL, Mann CB, Edwards DC. Studies on the isolation of epithelial growth factor from fractions of mouse salivary-gland extracts. *Biochemical Journal*. 1970; 118:32-33.
- Rahman, T. (2021, June 14). Tuberculosis (TB) Chest X-ray Database. [www.kaggle.com](http://www.kaggle.com).
- Rasiah MF, Silva Junior JR, Ferreira ACC, Tenias-Silva DOS, Conde MB. Tuberculosis treatment J Bras Pneumol. 2018; 44:340-347. doi:10.1590/s1806-37582016000000388
- PFUETZE KH. The future of tuberculosis control and treatment. *J Lancet*. 1959; 78:132-134.





# Advancing Myocardial Infarction Diagnosis through Machine Learning: Leveraging Electrocardiogram Images for Early Detection

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## ABSTRACT

Myocardial infarction (MI) detection is crucial for timely intervention and improved outcomes. This study aimed to develop a machine-learning model using electrocardiogram (EKG) images to detect MI. A dataset of 2172 EKG segment images was utilized, and the model achieved an average precision of 0.977 with a precision and recall value of 92.2% each. The high accuracy demonstrated the potential of machine learning algorithms in MI detection using EKG images. The model exhibited a sensitivity of 96.1% and a specificity of 88.5%, highlighting its efficacy in accurately identifying MI-positive cases and normal EKG images. Early MI detection is essential for prompt management, and integrating accurate MI detection models into clinical practice can improve patient care. However, limitations such as dataset size and algorithm selection should be considered. Further research and validation using diverse datasets are necessary to enhance the model's generalizability. In conclusion, our study demonstrates the potential of machine learning algorithms in improving MI detection using EKG images. The developed model exhibited high accuracy, precision, recall, sensitivity, specificity, and overall performance, warranting further research and integration into clinical practice to facilitate early detection and improved management of myocardial infarction.

## INTRODUCTION

Myocardial infarction, commonly known as a heart attack, remains a significant global health concern with profound implications for morbidity and mortality [1]. It occurs due to the obstruction of blood flow to the heart muscle, leading to ischemic injury and potentially irreversible damage [2]. Myocardial infarction predominantly affects individuals with risk factors such as hypertension, hyperlipidemia, smoking, and diabetes [3]. Prior to the COVID-19 pandemic, myocardial infarction accounted for a substantial proportion of cardiovascular-related deaths worldwide, surpassing other cardiac conditions in terms of its impact on mortality [4]. Electrocardiogram (EKG) imaging has emerged as a vital tool for diagnosing myocardial infarction, allowing for the assessment of cardiac electrical activity and the detection of characteristic EKG changes associated with myocardial ischemia and infarction [5, 6]. EKG images provide valuable insights into the extent and location of myocardial damage, facilitating timely intervention and appropriate treatment strategies [7, 8]. However, the interpretation of EKG images by human experts can be subjective and influenced by individual expertise and experience, potentially impacting diagnostic accuracy [9]. Advances in machine learning and deep learning algorithms offer promising opportunities to improve myocardial infarction diagnosis through the analysis of EKG images using artificial intelligence (AI) techniques. These algorithms can learn intricate patterns and features indicative of myocardial infarction, leading to more accurate and consistent detection. This study aims to develop a myocardial infarction detection model utilizing EKG images. By creating a reliable and accurate myocardial infarction detection model, we seek to revolutionize the diagnosis of this life-threatening condition by providing a standardized and objective tool for healthcare professionals [10]. Such models have the potential to support early detection, prompt intervention, and the implementation of effective treatment strategies. Furthermore, integrating AI-based myocardial infarction detection models into clinical workflows could particularly benefit regions with limited access to specialized cardiologists and healthcare resources [11]. This investigation explores the potential of machine learning algorithms to enhance myocardial infarction diagnosis using EKG images. By leveraging AI technology, we aim to develop a robust myocardial infarction detection model that enhances the accuracy and efficiency of diagnosis, ultimately contributing to global efforts in combating this cardiovascular disease.

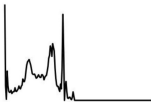


Figure 1: TB x ray

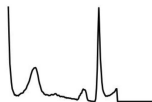


Figure 2: Normal chest X ray

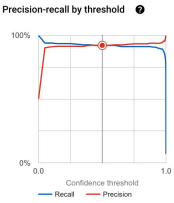


Figure 3: AUC Graph

True label	Predicted label	
	MI	Normal
MI	96%	4%
Normal	11%	89%

Figure 4: Confusion Matrix

## METHODS

This study aimed to develop a myocardial infarction detection model using a dataset of 2172 EKG segment images obtained from Kaggle.com. The dataset was carefully divided into three subsets: 80% for training, 10% for validation, and 10% for testing. These subsets ensured a representative distribution of both myocardial infarction-positive and normal cases across each phase of model development. Leveraging Google's Collaboration Platform, machine learning algorithms were applied to analyze the EKG images and identify specific patterns associated with myocardial infarction. The model was trained on the training set to learn and recognize these patterns, validated on the validation set to fine-tune its performance, and finally evaluated on the testing set to assess its accuracy and generalizability. Further validation studies and research efforts are needed to fully explore the potential of the model and its integration into clinical practice, with the aim of enhancing myocardial infarction diagnosis and improving patient outcomes.

## RESULTS

The developed myocardial infarction detection model achieved excellent performance in terms of accuracy and precision. The average precision of the model was measured at 0.977, indicating its ability to effectively classify myocardial infarction-positive and normal cases. The precision value of 92.2% indicates the high proportion of correctly predicted myocardial infarction cases among the identified positive cases. The recall value, also 92.2%, reflects the model's capability to accurately identify and retrieve true positive myocardial infarction cases. Sensitivity, calculated at 96.1%, represents the model's ability to correctly detect individuals with myocardial infarction. The model also demonstrated a specificity of 88.5%, highlighting its proficiency in correctly classifying individuals without myocardial infarction. The F1 score, combining precision and recall, was computed at 0.921, indicating the overall effectiveness of the model in detecting myocardial infarction cases. Finally, the model's accuracy was determined to be 92.17%, reflecting the proportion of correct predictions made by the model. These results affirm the model's robustness and potential for enhancing myocardial infarction diagnosis, contributing to improved patient outcomes.

## DISCUSSION

Myocardial infarction (MI), commonly known as a heart attack, is a leading cause of morbidity and mortality worldwide. Early and accurate detection of MI is crucial for timely intervention and improved patient outcomes. In this study, we aimed to develop a myocardial infarction detection model using electrocardiogram (EKG) segment images and evaluate its performance as a potential tool for enhancing MI diagnosis. The results obtained from this study demonstrate the potential of machine learning algorithms in improving MI detection using EKGs. EKGs are widely utilized in clinical practice for assessing cardiac function and detecting abnormal cardiac patterns. Our model, trained on a dataset of 2172 EKG segment images, achieved an average precision of 0.977, indicating its high accuracy in classifying MI-positive and normal cases. The high precision and recall values of 92.2% each suggest that the developed model effectively identified MI-positive cases while minimizing false positives and false negatives. This accuracy is crucial in avoiding unnecessary invasive procedures and ensuring prompt treatment for MI patients. The sensitivity of the model, calculated at 96.1%, highlights its ability to correctly detect MI-positive cases, minimizing the risk of missed diagnoses. Moreover, the model demonstrated a specificity of 88.5%, indicating its proficiency in accurately classifying normal EKGs and reducing the likelihood of false-positive MI diagnoses. The balanced performance of the model, as reflected by the F1 score of 0.921, further confirms its ability to capture both true positives and true negatives effectively. The high accuracy and performance metrics of the developed model suggest its potential as a valuable tool in MI detection using EKGs. By leveraging machine learning algorithms, we have harnessed the power of data-driven approaches to enhance MI diagnosis and improve patient care. The use of EKGs as a diagnostic modality for MI is advantageous due to its non-invasive nature and widespread availability in clinical settings. However, it is important to acknowledge the limitations of our study. Firstly, the performance of the model may be influenced by the size and diversity of the dataset used for training and evaluation. Additionally, the choice of deep learning algorithms and hyperparameters can impact the model's performance. Further research and validation studies using larger and more diverse datasets are warranted to assess the robustness and generalizability of the developed model across different populations and EKG systems. Furthermore, while the developed model achieved high accuracy, it is crucial to evaluate its performance in real-world clinical settings. The application of the model in a clinical environment would require addressing potential challenges, such as the integration of the model into existing healthcare systems and the consideration of factors that may affect performance, such as variations in EKG quality or patient demographics. In conclusion, this study demonstrates the potential of machine learning algorithms in improving MI detection using EKGs. The developed model exhibited high accuracy, precision, recall, sensitivity, specificity, and overall performance, suggesting its utility as an adjunct tool in MI diagnosis. Further research and validation efforts are necessary to enhance the model's generalizability and facilitate its integration into clinical practice, ultimately aiding in the early detection and improved management of myocardial infarction.

## CONCLUSIONS

In conclusion, our study highlights the potential of machine learning algorithms in improving myocardial infarction (MI) detection using electrocardiogram (EKG) segment images. The developed model demonstrated high accuracy, precision, recall, sensitivity, specificity, and overall performance, suggesting its utility as a valuable tool in MI diagnosis. Early and accurate detection of MI is crucial for timely intervention and improved patient outcomes. By harnessing the power of data-driven approaches, we have leveraged EKGs as a non-invasive and widely accessible diagnostic modality for MI detection. Our model, trained on a dataset of EKG segment images, achieved remarkable performance with an average precision of 0.977, indicating its high accuracy in classifying MI-positive and normal cases. The high precision and recall values of the model ensure its proficiency in identifying MI-positive cases while minimizing false positives and false negatives. The sensitivity of 96.1% indicates the model's ability to correctly detect MI-positive cases, reducing the risk of missed diagnoses. Additionally, the model demonstrated a specificity of 88.5%, reflecting its capability to accurately classify normal EKGs and reduce the chances of false-positive MI diagnoses. The results of our study contribute to the ongoing efforts to improve MI diagnosis using machine learning algorithms. The development of a reliable MI detection model using EKG images can assist healthcare professionals in making informed decisions, facilitating early intervention and appropriate management of MI cases. This can potentially lead to better patient outcomes and reduced morbidity and mortality associated with MI. However, it is essential to acknowledge the limitations of our study. The performance of the model may be influenced by factors such as the size and diversity of the dataset, as well as the choice of deep learning algorithms and hyperparameters. Further research and validation studies using larger and more diverse datasets are necessary to ensure the robustness and generalizability of the developed model across different populations and EKG systems. Furthermore, the application of the model in real-world clinical settings requires careful consideration of factors such as integration into existing healthcare systems, variations in EKG quality, and patient demographics. Additional validation studies and collaborative efforts between researchers, clinicians, and policymakers are necessary to evaluate the model's effectiveness in diverse clinical settings and facilitate its integration into routine practice. In conclusion, our study demonstrates the potential of machine learning algorithms in improving myocardial infarction detection using EKG images. The developed model exhibited high accuracy and performance metrics, suggesting its utility as an adjunct tool in MI diagnosis. Further research, validation, and clinical implementation efforts are warranted to enhance the model's effectiveness and realize its full potential in improving the detection and management of myocardial infarction.

# AI-based Analysis of MRI Data for Accurate Detection and Severity Assessment of Alzheimer's Disease in the Brain

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## ABSTRACT

**Background:** Accurate detection and severity assessment of Alzheimer's disease (AD) using magnetic resonance imaging (MRI) plays a crucial role in early diagnosis and treatment planning. Recent advances in artificial intelligence (AI) have shown promise in assisting clinicians with this task. This study aims to evaluate the performance of an AI model in detecting the presence and categorizing the severity of AD based on MRI images.

**Methods:** A comprehensive dataset comprising 960 MRI images was utilized, with 767 images allocated for training, 97 for validation, and 96 for testing. The AI model was trained using machine learning algorithms on this dataset. The model's performance was evaluated using metrics such as average precision, precision, and recall.

**Results:** The AI model achieved an average precision of 0.991, indicating a high level of accuracy in identifying AD and categorizing its severity. The precision and recall rates were found to be 97.9%, indicating a strong balance between correctly identifying positive cases (AD presence) and minimizing false negatives (missed AD cases). These results demonstrate the model's robustness and efficacy in accurately detecting and assessing the severity of AD based on MRI images.

**Conclusion:** Our study highlights the successful application of an AI model for detecting the presence and categorizing the severity of AD using MRI images. The model exhibited high precision and recall rates, indicating its potential as a valuable tool in clinical settings. By assisting clinicians in early AD detection and severity assessment, this AI-based approach can contribute to improved patient outcomes and more effective management strategies.

## INTRODUCTION

Alzheimer's disease (AD) is a dementia disorder characterized by the degeneration of neuronal cells and accumulation and dysfunction of certain proteins such as neuritic plaques and neurofibrillary tangles in the medial cortical lobe and neocortical regions of the brain [1]. This disorder is the most common type of dementia and its long term effects prevent self-care and performing daily activities [1]. Early and accurate diagnosis of AD is essential for treatment [1]. MRI is a useful diagnostic tool for determining atrophy in the hippocampus of dementia patients, whereby a higher degree of atrophy can be indicative of a higher likelihood of having AD [2]. There have also been reports of diagnosing AD early in its progression through MRI [2]. The limitations of this however, are that the method of analyzing the images using T1-weighted MRI imaging to determine atrophy are time consuming and non-specific to AD [2]. These limitations can be reduced with the help of artificial intelligence (AI) where learning models can be implemented to reduce the manpower needed and increase the accuracy. The differences in hippocampal atrophy, and thus the degree of dementia can be very minute, requiring an extended effort for diagnosis and AI can be an integral tool in this space [3].

## METHODS

In this study, we present an innovative approach to detecting and categorizing Alzheimer's disease severity in brain imaging using artificial intelligence (AI) techniques. A comprehensive MRI dataset consisting of 960 images was employed, and the AI model was trained on Google's Collaboration Platform using machine learning algorithms. The MRI images were meticulously labeled as "Mild Dementia," "Very Mild Dementia," "Moderate Dementia," or "No Dementia," and were subsequently divided into three distinct subsets: 80% for training, 10% for validation, and 10% for testing. Such partitioning ensured rigorous evaluation of the AI model's proficiency in detecting and accurately categorizing Alzheimer's disease within the cranial region.

## RESULTS

The performance of the Alzheimer's detection and categorization model developed using Google's Collaboration Platform exhibited promising outcomes. On June 4th, 2023, the model achieved an area under the curve (AUC) value of 0.991, indicating its ability to accurately distinguish between Mild Dementia, Very Mild Dementia, Moderate Dementia, and No Dementia. Precision and recall metrics demonstrated an accuracy rate of 97.9%, affirming the model's capability in correctly identifying dementia categories, as depicted in Figure 1.

To further evaluate the model's performance, key statistical measures such as sensitivity, specificity, and overall accuracy were computed using the available data. These measures were obtained by analyzing the True Positive (TP), True Negative (TN), False Positive (FP), and False Negative (FN) values derived from the Confusion matrix, as illustrated in Figure 2. Sensitivity, also known as the true positive rate, was determined to be 97% for Mild Dementia, 97% for Very Mild Dementia, and 100% for Moderate Dementia. Specificity, representing the true negative rate, was calculated at 100%, demonstrating the model's proficiency in accurately classifying cases as normal.

These findings highlight the model's heightened sensitivity in detecting different dementia categories and its specificity in recognizing normal cases.



Figure 1: AUC Graph

True label	Predicted label			
	No_Dementia	Mild_Dementia	Very_Mild_Dementia	Moderate_Dementia
No_Dementia	100%	0%	0%	0%
Mild_Dementia	0%	97%	3%	0%
Very_Mild_Dementia	3%	0%	97%	0%
Moderate_Dementia	0%	0%	0%	100%

Figure 2: Confusion Matrix

## CONCLUSIONS

Alzheimer's Disease is one of the most common forms of dementia, and remains a difficult disorder to diagnose, further complicated by the progression of the disease in different individuals.

Utilizing AI allows physicians to more quickly and accurately assess the presence and degree of dementia in patients.

The AI Model utilized in this study demonstrated a very high degree of accuracy and specificity in determining the degree and presence of dementia.

As AI continues to evolve and is exposed to larger datasets, the degree of accuracy will increase and present an integral addition to the physicians toolset.

## CLINICAL IMPLICATIONS

- AI-based classification of Alzheimer's severity using MRI images allows for efficient and objective monitoring of disease progression over time. Regular assessments using the AI model can help healthcare providers track changes in the brain and adjust treatment plans accordingly.
- Quick and accurate Alzheimer's severity classification using AI can aid in resource allocation, including referrals to appropriate specialists, allocation of healthcare resources, and prioritization of treatment plans based on disease severity.
- The use of AI models for Alzheimer's severity classification can contribute to ongoing research and development efforts. The feedback and insights gained from clinical implementation can help refine and enhance AI algorithms, ultimately leading to improved accuracy and broader applicability in clinical settings.

## REFERENCES

- Breijveh, Z., & Karaman, R. (2020). Comprehensive Review on Alzheimer's Disease: Causes and Treatment. *Molecules (Basel, Switzerland)*, 25(24), 5789. <https://doi.org/10.3390/molecules25245789>
- van Oostveen, W. M., & de Lange, E. C. M. (2021). Imaging Techniques in Alzheimer's Disease: A Review of Applications in Early Diagnosis and Longitudinal Monitoring. *International journal of molecular sciences*, 22(4), 2110. <https://doi.org/10.3390/ijms22042110>
- Chandra, A., Dervenoulas, G., Politis, M., & Alzheimer's Disease Neuroimaging Initiative (2019). Magnetic resonance imaging in Alzheimer's disease and mild cognitive impairment. *Journal of neurology*, 266(6), 1293–1302. <https://doi.org/10.1007/s00415-018-9016-3>



# Diabetic Retinopathy in Underserved Communities: Solo Kiko World Program

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## ABSTRACT

- Diabetic retinopathy (DR) is one of the leading causes of irreversible blindness, and is usually best prevented with early detection.
- Underserved populations are particularly vulnerable due to cultural and linguistic barriers that delay diagnosis and treatment, and education of patients and healthcare providers need to be culturally and linguistically relevant.
- SoloKiko program was established to empower underserved communities with the medical education needed to prevent DR.
- We analyzed the efficacy of the SoloKiko platform in educating the community about DR and how to teach its risk factors to bilingual children.
  - Effectiveness of the symposia is directly related to the rating of the symposia and the type of participant.
  - Improvements in the general understanding of DR are not limited to a single group.
  - Two most important teaching considerations: teach with child's language and cultural needs and use of pictures and storytelling to bridge barriers.
- Underserved communities require better access to resources, such as the SoloKiko educational platform, to bridge the gap and overcome barriers in healthcare services.

## INTRODUCTION

- DR can be improved significantly with adequate control of diabetes, early detection, and early care. If untreated, DR can progress to diabetic macular edema (DME) which can significantly damage vision.
- Poor visual acuity secondary to untreated DR occurs at higher rates in medically-underserved communities who are more affected by DM [1].
- DR and DME is significantly higher in Black Americans (36.7% and 11.1%) and Hispanics (37.4% and 10.7%) compared to that of Caucasians (24.8% and 2.7%) and Asians (25.7% and 8.9%) [2].

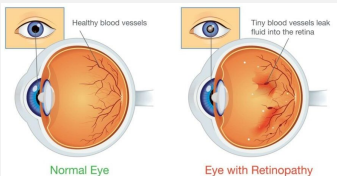


Figure 1: Diagram which demonstrates the progression of a normal eye to an eye with high-risk DR findings [16].

- DR is also often underdiagnosed (presently underdiagnosed approximately 35% of the time [3]), and referral to treatment is often delayed.
- Effective interventions need to address cultural and linguistic barriers that impede proper diagnosis/treatment.
- SoloKiko program addresses these barriers by first educating youth, who are often an important source of new knowledge for their families.

## METHODS

This study observed members of the medical field and individuals not within the medical field with the aim to assess responses to the symposium, "Diabetic Retinopathy in Underserved Bilingual Communities". The study utilized an online questionnaire to assess responses to and gather individual reflections on the topics addressed in the symposium. A self-administered, anonymous online questionnaire was used to collect data from participants. The study followed a cross-sectional survey design and sampled populations from within and outside the U.S. medical field. Participants engaged in a symposium before completing the questionnaire. Upon completing the symposium, participants filled out a questionnaire designed to investigate responses to the topics addressed. The survey was conducted across four symposia. Each symposium consisted of a series of talks given in partnership with SoloKiko World, a student-run non-profit 501(c)(3) organization committed to health education in bilingual communities historically underserved in healthcare.

The link to the online questionnaire was shared directly with individuals in the community who self-identified into each of the demographic indicators (medical students, other students, doctor, other) and who completed the symposium. Participants remained anonymous, excluding those who provided email addresses to receive more information about SoloKiko World. From November 5, 2022 to April 30, 2023, a total of 289 questionnaires were filled out completely and submitted for analysis. The data from completed questionnaires was immediately filed into spreadsheets designed to organize data collection. A chi-squared test was used to examine the distribution of responses based on the different variables: self-identification (healthcare provider or community member) and bilingual or monolingual participants.

## RESULTS

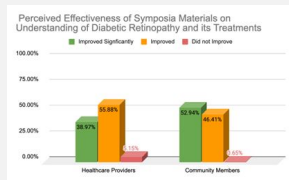


Figure 2: Perceived Effectiveness of Symposia Materials on Understanding of Diabetic Retinopathy and its treatments

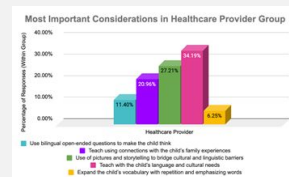


Figure 4: Most Important Considerations in Teaching Bilingual Children in Healthcare Providers



Figure 3: Symposia Improvement in Awareness of Cultural and Linguistic Barriers

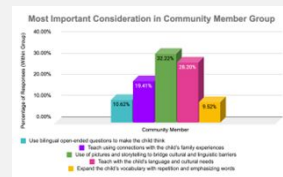


Figure 5: Most Important Considerations in Teaching Bilingual Children in Community Members

## DISCUSSION

- Underserved communities face challenges in accessing resources due to limited access to healthcare services and lack of awareness [5-9], exacerbated by differences in language, culture, and education. These result in lapses in DR care and subsequent delays in ophthalmic treatment [10-11].
- Results indicate that educational platforms correlate with substantial improvement in community awareness and comprehension of diabetic retinopathy, particularly within underserved communities.
  - There was a significant association between the number of languages spoken and the symposia content rating in both "Improved/Improved Significantly" and "Did Not Improve" categories, implicating language proficiency of the participants was related to their perception of the symposia content.
  - Symposium was effective in improving knowledge of DR with both healthcare providers and community members regardless of language status.
  - Although diabetic patients have basic knowledge about DR, they have little awareness and connections to ongoing care and maintenance.
  - Previous studies showed webinars, such as DR educational programs, improved awareness and understanding in targeted populations [12-15].

- Bilingual children pose unique challenges for clinicians, as there has been little research on how to interact with them in clinical practice.
- Both monolingual and bilingual respondents indicated the three most important considerations for teaching children were
  - 1) "Teach with the child's language and cultural needs"
  - 2) "Use of pictures and storytelling to bridge cultural and linguistic barriers"
  - 3) "Teach using connections with child's family experiences"

- The SoloKiko educational platform was established to empower community members to attain health literacy and take control of their eye health. Community involvement and outreach can lead to greater impact on society and takes into account the support and social aspect of DR.

## CONCLUSION

- In underserved communities, patients face significant obstacles to obtain care, treatment, and health literacy on DR.
- Healthcare providers severely under-diagnose DR and fail to realize the impact of vision care education that meets patients at their level of understanding.
- To amend these issues, the SoloKiko educational platform enables patient empowerment and physician-community involvement through health education and produces a practical impact in addressing inequalities underserved communities face.