Success Rate of Full Pulpotomy in Mature Permanent Molars with Irreversible Pulpitis with Apical Periodontitis Detected Using Artificial Intelligence and those without Apical Periodontitis: A Randomized Controlled Trial.

I. Cover Page

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II. Abstract

Statement of problem: Although performing full pulpotomy in mature permanent molars with irreversible pulpitis showed success rates comparable to RCT, there is a growing need for further studies in order to determine the predictability of pulpotomy in teeth with apical periodontitis. **Aim of the study:** The aim of this study is to compare the success rates in cases of moderate pulpitis without apical periodontitis in comparison to cases of severe pulpitis with AI-Detected apical periodontitis. Additionally, the study aims to evaluate the accuracy of a novel AI technology in identifying apical periodontitis from radiographs, comparing its findings to the operator's radiographical and clinical observations. **Subjects and methods:** Patients with mature permanent molars diagnosed with irreversible pulpitis will be selected. The teeth will be divided according to the presence or absence of apical periodontitis into 2 groups. The first group being moderate pulpitis without apical periodontitis to be treated with full pulpotomy and the second group being severe pulpitis with apical periodontitis to be treated with full pulpotomy. Finally, a third control group of teeth with irreversible pulpitis to be treated with conventional root canal treatment will be added. An artificial intelligence software will process the preoperative radiographs to detect the presence of apical periodontitis, and its accuracy will be compared to the blinded operator using clinical and radiographic methods. The patients will be randomly allocated to receive either full pulpotomy or conventional root canal treatment. Full pulpotomy using MTA will be performed for groups 1 and 2, and a final restoration will be placed. While group 3 will receive conventional root canal treatment and a final restoration. Cases will be followed up after 1, 3, and 6 months respectively to assess the clinical and radiographic success.

III. Background

The dental pulp constitutes a distinct and intricate entity susceptible to various thermal, traumatic, microbial, and chemical stimuli. [1] As a result, the dentin-pulp complex experiences a sophisticated immune response, leading to the recruitment of immune cells and inflammation of dental pulp cells at the local level. [2,3,4] Historically, in instances of irreversible pulpitis, the conventional recommendation has been root canal treatment (RCT), based on the belief that the pulp lacked the ability to undergo recovery. [5,6]

Vital pulp therapy (VPT) is an approach focused on minimally invasive measures, aiming to seal the pulpal wound with a bioactive substance subsequent to the removal of infected pulpal tissues. [7,8] Procedures associated with VPT encompass direct and indirect pulp capping, partial pulpotomy, and full pulpotomy. [9] Typically, VPT interventions are carried out to safeguard the radicular pulp in both deciduous and adult immature teeth. [10,11] In accordance with the position statements released by the American Association of Endodontists (AAE) in 2021 and the European Society of Endodontology (ESE) in 2019, full and partial pulpotomy emerge as promising and more conservative alternatives to root canal treatment for managing mature permanent teeth afflicted with irreversible pulpitis and cariously exposed pulps. [10,12] This is also backed by literature since a lot of researches shows that performing full pulpotomy to manage mature permanent molars with irreversible pulpitis is highly successful. [30,31,32,33]

A full pulpotomy entails the complete removal of coronal pulp tissues, succeeded by the application of a biomaterial onto the remaining tissues at the root canal orifices. [12] The utilization of pulpotomy preserves the pulp mechanoreceptors, along with its defensive and developmental functions, including the formation of primary and secondary dentin.[12] Furthermore, pulpotomies are characterized by being less time-consuming, less invasive, and less intricate when compared to root canal treatment. Over the past two decades, numerous studies have indicated that pulpotomy can serve as an effective alternative to root canal treatment for managing irreversible pulpitis in mature permanent teeth.[13,14]

The AAE classification simplifies pulpitis into reversible and irreversible categories. However, the term "irreversible" is questioned as histological evidence shows no clear boundary for irreparability. In 2017, a new classification proposed by Wolters et al [15] eliminated the term "irreversible" and linked symptoms to VPT management strategies. Subsequent research by Careddu and Duncan in 2021 supported the new classification's potential prognostic benefit in partial pulpotomy.

Wolter's classification mainly entitles the following:

1) Initial Pulpitis:

A heightened but not prolonged response to the cold test, insensitivity to percussion, and an absence of spontaneous pain. [15]

2) Mild Pulpitis:

An intensified and extended reaction to cold, warm, and sweet stimuli lasting up to 20 seconds, potentially percussion-sensitive. Histologically, this suggests limited local inflammation confined to the crown pulp. [15]

3) Moderate Pulpitis:

Evident symptoms, strong, heightened, and prolonged response to cold which can last up to several minutes, potentially percussion-sensitive, and spontaneous dull pain that can be partially or completely alleviated with pain medication. Histologically, this indicates extensive local inflammation confined to the crown pulp. [15]

4) Severe Pulpitis:

Severe spontaneous pain and distinct pain response to warm and cold stimuli, often sharp to throbbing, causing difficulty sleeping (exacerbated when lying down). Tooth sensitivity to touch and percussion is pronounced. Histologically, this suggests extensive local inflammation in the crown pulp, possibly extending into the root canals. [15]

Wolter et al indicated that initial and mild pulpitis will only require indirect pulp therapy. [15]

Traditionally, it was hypothesized that a tooth with a periapical radiolucency has a necrotic, infected pulp space. Thus, root canal treatment was the treatment of choice for these teeth.(2) However, it was proven that even in the presence of a large periapical radiolucency, portions of the radicular pulp tissues can maintain their vitality.(3) This suggests that in cases with apical periodontitis, if vital pulp tissues are evident after pulp exposure, pulpotomy can be a viable alternative treatment modality to root canal treatment.(4)

In 2018, Taha et al. aimed to evaluate the outcome of full pulpotomy in mature permanent teeth using Biodentine. Eight of the cases exhibited preoperative periapical rarefaction, and seven of them showed improvement in the periapical index score. Similarly, in a 2016 randomized clinical trial, all of the seven cases with preoperative periapical radiolucencies showed complete resolution of the lesions at the end of the study.(5) Other earlier studies also reported success of pulpotomy procedures in cases with periapical involvement. (34,35,36) However, there is a growing need for further studies in order to determine the predictability of pulpotomy in teeth with apical radiolucencies, and to detect features that can act as negative prognostic factors in these cases.(4)

In 2013, the American Association of Endodontists classified the diagnosis of periapical condition into normal apical tissues, symptomatic apical periodontitis, asymptomatic apical periodontitis, chronic apical abscess, acute apical abscess, and condensing osteitis. The term “apical periodontitis” indicates that the apical periodontal tissues are inflamed. In symptomatic apical periodontitis, the tooth has a painful reaction to palpation, percussion, and biting. Radiographically, the tooth may have a normal periodontium or a periapical radiolucency depending on the stage of the periapical disease. On the other hand, teeth with asymptomatic apical periodontitis do not exhibit pain on palpation or percussion, and they are associated with a periapical radiolucency in the radiograph.(1)

It is well-recognized that the effectiveness of detecting radiographic apical periodontitis is contingent upon the proficiency of the operator(16). Therefore, it has become imperative to develop or employ Artificial Intelligence (AI)-based software solutions that can accurately diagnose periapical radiolucencies. Artificial intelligence (AI) is designed to mimic human intelligence and

address specific challenges. AI contributes to the creation of algorithms that can learn from provided information and make predictions. Machine learning, a subset of AI, constructs algorithms based on data.[17] Among the earliest AI algorithms were neural networks (NNs). Deep learning neural networks are complex structures with multiple layers, while shallow learning neural networks are simpler with fewer layers. Convolutional neural networks (CNNs) are primarily used for analyzing intricate images.[17]

AI technology has arisen as a response to the need for machines to emulate human intelligence, facilitating the provision of more standardized results.[18] For instance, AI-enabled imaging applications in the medical domain exhibit autonomous object detection and image classification capabilities, with numerous studies demonstrating remarkable accuracy and promise in diagnosing pathologies[19], interpreting radiological data[20], and assessing dermatological conditions[21].

From a dental perspective, AI applications can be stratified into several domains, encompassing diagnosis, decision support, treatment planning, and prognosis prediction, with diagnostic capabilities being particularly prominent. AI stands poised to augment diagnostic precision and efficiency, thereby alleviating the professional burden on dentists, who increasingly rely on computerized decision support systems.[18]

Within the realm of endodontics, Anita Aminoshariae et al in 2021 mentioned that AI can currently assist in detection of peri-apical lesions, crown and root fractures, working length determination and even the morphology of root canals and the root canal systems.[23] A systematic review by Agata Ossowska et al in 2022 concluded that AI can also be used in predicting the ability of dental pulp stem cells to survive in some treatments and predicting the success of re-treatment of a failed root canal therapy (RCT).[24] However, it's important to note that AI tended to over-detect lesions while human operators tended to under-detect them.[22]

Duncan et al, in 2022, recommended the use of CBCT as it can detect periapical lesions better than 2-Dimensional X-Rays.[4]In another review by Issa et al in 2023, AI has exhibited an exceptional level of precision in detecting apical periodontitis within periapical radiographs, owing

to its capacity to detect intricate patterns and attributes beyond the detection of human observation.[6]

This, in turn, positions it as an efficient auxiliary diagnostic instrument for dental professionals, simultaneously mitigating the clinical burden and improving the standard of care.[6]

The main goal of this research is to compare cases of moderate pulpitis without apical periodontitis in comparison to cases of severe pulpitis with AI-Detected apical periodontitis. Additionally, the study aims to evaluate the accuracy of a novel AI technology in identifying apical periodontitis from radiographs and to establish the correlation between the utility of AI as a dependable supplementary tool in the decision-making process when contemplating full pulpotomy for mature permanent molars.

In the paper by Duncan et al, even though it was proven that even in the presence of a large periapical radiolucency, portions of the radicular pulp tissues can maintain their vitality, more clinical studies are needed to assess the success rates of cases with severe irreversible pulpitis with apical periodontitis.

The study done by Anita Aminoshariae et al reported that AI can accurately detect peri-apical lesions. However, another study by Cantu et al reported that AI generally tends to over-detect lesions. Thus, it is imperative to compare AI findings to the operator's radiographical observations.

IV. Research Question

PICOTS Question: In patients with mature permanent molars diagnosed with irreversible pulpitis, will teeth diagnosed with severe pulpitis with apical periodontitis and teeth diagnosed with moderate pulpitis without apical periodontitis and treated with full pulpotomy MTA have a similar success rate to teeth treated with conventional root canal treatment after a six-month follow-up period?	
Patient/Problem	Patients with mature permanent molars diagnosed with irreversible pulpitis with or without apical periodontitis
Intervention	Full pulpotomy using MTA in teeth diagnosed with "moderate pulpitis" without apical periodontitis and "severe pulpitis" with apical periodontitis.
Comparator	Conventional root canal treatment
Outcome	Success Rate
Time	After one, three and six months
Setting	MIU Dental Clinic Complex

PICOTS Question: Will the AI software accurately detect the presence of apical periodontitis from preoperative digital 2D radiographs when compared to clinical findings of apical periodontitis?	
Patient/Problem	Accurate detection of apical periodontitis
Intervention	Artificial intelligence software
Comparator	Clinical findings of apical periodontitis
Outcome	Presence/absence of apical periodontitis
Time	One time
Setting	MIU dental clinics complex

V. Aim of the Study, Research Objectives and Clinical Relevance

Aim:

To evaluate the success of MTA full pulpotomy performed in mature permanent molars with moderate or severe pulpitis compared to the success of conventional root canal treatment.

To compare the success rates in cases of severe pulpitis with AI-Detected apical periodontitis in comparison to cases of moderate pulpitis without apical periodontitis. Additionally, the study aims to evaluate the accuracy of a novel AI technology in identifying apical periodontitis from radiographs, comparing its findings to the operator's radiographical observations.

Null Hypothesis:

1) There is no significant difference between the success rate in cases with moderate pulpitis without apical periodontitis and those with severe pulpitis with apical periodontitis and between both of those groups and with teeth treated with conventional root canal treatment.
2) There is no significant difference between the ability of Artificial Intelligence to detect the presence of apical periodontitis compared to operator's radiographical observations.

Objectives:

- To compare the success rate between cases with moderate pulpitis without apical periodontitis, and those with severe pulpitis with apical periodontitis and compare both groups to a control group treated with conventional root canal treatment.
- To evaluate the ability of Artificial Intelligence to detect presence of apical periodontitis compared to operator's radiographical observations.

Outcomes:

	Outcome(s)	Measuring device	Measuring unit
Primary	Success rate after full pulpotomy in cases with and without apical periodontitis	Clinical and radiographic criteria of success and failure	Success/failure
Primary	Accuracy of AI software in detecting apical periodontitis	AI readings on 2D X-Ray	Clinical assessment and radiographic scoring system

Clinical Relevance:

- When treating adult permanent molars with irreversible pulpitis, full pulpotomy is less invasive, less expensive, and less likely to result in iatrogenic mistakes than root canal therapy.
- Understanding prognostic factors would guarantee more predictable pulpotomy results and help with decision-making in cases of adult permanent molars with irreversible pulpitis with and without apical periodontitis.
- By decreasing human error, the use of AI algorithms might improve the detection of apical periodontitis; hence, it can be a valuable addition to the treatment planning of these cases.

VI. Study Design:

☒ **Randomized Controlled Trial**

VII. Subjects and Methods:

1. Study Setting:

The study will be conducted in the Complex Clinics of Misr International University.

2. Sample Type:

☒ **Convenient**

3. Sample Size Calculation:

A power analysis was designed to have adequate power to apply a statistical test of the null hypothesis that there is no association between severity of pulpitis and success rate. By adopting an alpha (α) level of (0.05), a beta (β) level of (0.2) (i.e., power=80%) and an effect size (ω) of (0.407) calculated based on the results of a previous study [25]; the **total** required sample size (n) was found to be (48) cases. Sample size was increased by (20%) to account for possible dropouts during follow-up period to be (58) cases. Sample size calculation was performed using with R statistical analysis software version 4.3.2 for Windows [26].

Selection of samples:

Patients presented to MIU dental clinics complex.

4. **Inclusion Criteria:**

- Presence of vital mature permanent molars diagnosed as severe irreversible pulpitis with apical periodontitis diagnosed clinically and radiographically and cases diagnosed as moderate irreversible pulpitis without apical periodontitis diagnosed clinically and radiographically per Wolter's classification.
- Participants of both genders falling within the age range of 20 to 45 years.
- Confirmation of vital bleeding pulp tissue in all canals following complete pulpotomy.

5. **Exclusion Criteria:**

- Non-vital tooth
- Moderate pulpitis with apical periodontitis
- Teeth with Immature roots
- Uncontrolled pulpal bleeding persisting beyond 10 minutes post-application of sodium hypochlorite as a hemostatic agent.
- Insufficient bleeding post-pulp exposure, indicative of pulp degeneration.
- Cases categorized as initial and mild pulpitis per Wolter's classification.

♦ **Justification for Exclusions**

❖ Exclusion criteria encompass cases displaying pulp necrosis or uncontrollable root canal bleeding as they are not indicated for pulpotomy, and those involving immature teeth as they are not the main goal of this study. Cases with initial and mild pulpitis are excluded, as they are more suitably addressed with indirect pulp therapy. Cases with moderate pulpitis with apical periodontitis are also excluded since they're not one of the aims of the study.

♦ **Intervention and Methodology**

a. Handling Extracted Teeth for Research

N/A

b. Methods

Diagnosis:

Fifty-eight patients possessing mature permanent molars diagnosed with Severe pulpitis with apical periodontitis and moderate pulpitis without apical periodontitis will be referred to MIU dental clinics for treatment.

- Pre-Operative Radiographic assessment of the periapical index (PAI) [27] will be performed by independent evaluators.
- Teeth will be subjected to periodontal diagnosis, categorizing them into two groups based on the Wolter's classification and the presence or absence of apical periodontitis and a third control group. (Blinded to Artificial Intelligence Results mentioned in the next step)
    - Group 1: Teeth with moderate pulpitis without Apical Periodontitis to be treated with full pulpotomy
    - Group 2: Teeth with severe pulpitis with Apical Periodontitis to be treated with full pulpotomy
    - Group 3 (Control group): Teeth with irreversible pulpitis treated with Conventional root canal treatment.
- Then, Artificial intelligence software will analyze radiographs for the presence or absence of apical periodontitis and its results will be blinded to the independent evaluators of the radiographic assessment.
- **Stage I:** Clinical diagnosis will be performed by post-graduate students supervised by PhD holders. Then, the radiographic x-rays taken will be compared to the clinical diagnosis done by the post-graduate students.
- After that, the pulpotomy procedure will be done as explained later.
- **Stage II:** All of the following will be assessed at one, three, and six months:
    A) The success rates (according to the criteria of clinical and radiographic success mentioned later) in cases of moderate pulpitis without apical periodontitis vs severe pulpitis with apical periodontitis vs conventional root canal treatment.
    B) The success rates (according to the criteria of clinical and radiographic success mentioned later) of cases diagnosed by radiograph as having apical periodontitis.
    C) The success rates of cases diagnosed by Artificial Intelligence as having apical periodontitis.
    D) Accuracy of Artificial intelligence in diagnosing apical periodontitis vs human observations using radiographs.

Pulpotomy Procedure (Groups 1 and 2): [28,29]

- All pulpotomy treatments will be performed as part of the routine endodontic requirements executed in the MIU postgraduate endodontic program.
- The operators are well trained in performing full pulpotomy, and they will be working under the supervision of their supervisors (Prof. Dr. Ahmed Ghobashy, Prof. Dr. Nihal Thabet, Prof. Dr. Abeer Hashem and Assoc. Prof. Dr. Amr Bayoumi).
- Operators and outcome assessors will be blinded to radiographic periapical conditions.
- Local anesthesia using 4% Articaine with 1:100,000 Epinephrine will be administered.
- Rubber dam application, crown disinfection with 5% NaOCl, and endodontic access cavity completion will be executed.

- Full pulpotomy will be performed, confirming pulp vitality via bleeding pulp tissue.
- Hemostasis will be achieved with 2.5% Sodium Hypochlorite and repeated as needed for a maximum of 10 minutes. [28]
- MTA placement with a thickness of 2-3mm will be done followed by a wet cotton pellet over the MTA.
- Then a layer of resin modified glass ionomer will be applied and cured for 20 seconds, then a direct composite resin restoration will follow.
- Immediate post-operative periapical radiograph will be taken.

Conventional Root Canal Treatment Procedure (Group 3)

- All root canal treatment procedures will be performed by well-trained operators under the supervision of their supervisors (Prof. Dr. Ahmed Ghobashy, Prof. Dr. Nihal Thabet, Prof. Dr. Abeer Hashem and Assoc. Prof. Dr. Amr Bayoumi).

Post-operative instructions and Follow-up:

- Post-operative instructions will be given to the patient to take analgesic if necessary and to return if the pain persists.
- Patients will receive post-operative instructions and scheduled follow-up visits at 1, 3, and 6 months.
- Coronally restored teeth will be evaluated, and repairs conducted as needed.
- Blinded outcome assessors will review all radiographs.
- The patient will be informed of a specific regimen to follow in case of postoperative pain.
- There will be an emergency team available in MIU every day to manage complications.
- The patient will be provided with the contact number and location of the team. He/she will be instructed to contact the team in case of severe pain or other complications.
- The emergency team will inform the primary investigator with the emergency procedure done.

Methods of Evaluation:

1. **Clinical Success Criteria:**

a) Absence of clinical signs:

- Negative percussion
- Negative palpation
- No sinus tract/ fistula
- No mobility
- Negative periodontal probing
- No swelling

b) Absence of Clinical Symptoms:

- No pain
- No loss of function

2. Radiographic Success Criteria

- Radiographs will be taken at 1,3, and 6 months respectively.
- 2D Periapical X-rays will be used.
- Resolution of old or absence of new periapical lesion or growth of an old lesion evident on the radiograph (Periapical index score [PAI] will be used.)
- No external root resorption.
- No furcal bone loss.
- Absence of canal calcification.
- Absence of internal resorption.

3. Clinical Failure Criteria:

a. Presence of clinical signs:

- Positive percussion
- Positive palpation
- Presence of sinus tract/ fistula
- Presence of mobility
- Positive periodontal probing
- Presence of swelling

b. Presence of Clinical Symptoms:

- Presence of pain
- Loss of function

4. Radiographic Failure Criteria

- Radiographs will be taken at 1,3, and 6 months respectively.
- 2D Periapical X-rays will be used.
- Presence of new periapical lesion or growth of an old lesion evident on the radiograph (Periapical index score [PAI] will be used.)
- Presence of external root resorption.
- Furcal bone loss.
- Presence of canal calcification.
- Presence of internal resorption.

c. The **artificial intelligence software** will be used to process the postoperative radiographs in order to detect the presence of any new or persisting periapical pathosis.

Number of Visits:

After recruitment of the patient in the study, there will be **four** dental visits.

- First visit: The patient will receive either the pulpotomy procedure or conventional root canal treatment.
- Second visit: Follow-up visit using clinical and radiographic assessment **after one month**.
- Third visit: Follow-up visit using clinical and radiographic assessment **after three months**.
- Fourth visit: Follow-up visit using clinical and radiographic assessment **after six months**.

c. Statistical Analysis

Categorical data will be represented as frequencies and percentages and will be analyzed using chi-square test. Numerical data will be explored for normality by checking the data distribution and by using Shapiro-Wilk's test. If the data was found to be normally distributed, it will be presented as mean and standard deviation values and independent t-test will be used for the analysis. If the assumption of normality was found to be violated; the data will be presented as median and range values and will be analyzed using Mann-Whitney U test. The significance level will be set at $p<0.05$ for all tests. Statistical analysis will be performed with R statistical analysis software version 4.3.2 for Windows [26].

d. Randomization

- The patients will be randomly allocated to receive either full pulpotomy or conventional root canal treatment.
- Randomization will be performed using Microsoft excel software (Version 2402 Build 16.0.17328.20124).

e. Blinding

- The patient, main investigator, and statistician will be blinded to the pulpal status by Wolters classification, radiographic caries depth, and the AI findings in order to avoid bias.

7. Ethical Considerations

a. Risks and Discomforts to the Patients

I. Risk of allergy to the local anesthetic agent used.
II. Risk of latex allergy during rubber dam isolation.
III. Risk of allergy to the hemostatic agent or any of the constituents of the repair material used.
IV. Risk of perforations to the pulp chamber floor during access cavity preparation.
V. Risk of post-operative complications such as pain or swelling.
VI. Risk of radiation exposure used during conventional root canal treatment.

b. Minimization of Risk

I. Proper medical history will be obtained from the patient to ensure that there is no allergy to the local anesthetic agent, latex products, hemostatic agent, or repair material.

II. The pulpotomy procedure will be performed by experienced endodontists, and preoperative radiographs will be provided for guidance during access cavity preparation.

III. Management of postoperative complications:

- The patient will be informed of a specific regimen to follow in case of postoperative pain.
- There will be an emergency team available in MIU every day to manage complications.
- The patient will be provided with the contact number and location of the team. He/she will be instructed to contact the team in case of severe pain or other complications.
- The emergency team will inform the primary investigator with the emergency procedure done.

IV. Minimizing the number of X-ray exposures and providing the patients with lead aprons during exposure.

c. Criteria for Discontinuation of Study or Enrollment or Modification of Intervention

- Patients not willing to continue participating in the study.
- Patients with allergy to the local anesthetic agent.
- Severe fracture of the tooth that necessitates its extraction.
- If there is excessive uncontrollable bleeding from the canal orifices after amputation of the coronal pulp tissues, the tooth will be treated with root canal treatment and will be excluded from the study.

d. Benefits to the Patients and to the Community

I. Treating mature permanent molars with irreversible pulpitis with apical periodontitis using pulpotomy instead of root canal treatment will eliminate several

iatrogenic errors such as ledges, strip perforations, canal transportation, and file separation.

II. The community will benefit from applying more conservative alternative treatment options to maintain tooth vitality, which will prolong the restorative cycle of teeth and will improve the general oral health of the population.

III. The study of prognostic factors will allow more predictable application of full pulpotomy in the mentioned cases, which will benefit the community.

IV. The use of artificial intelligence technology can decrease human error and further facilitate the decision-making process in the treatment of mature permanent molars with irreversible pulpitis with apical periodontitis

e. Privacy

I. The dental procedures will be performed in dental units separated with barriers to maintain the privacy of the patient.

II. Patients' personal data, including thoughts, personal identifying information (PII), and personal health information (PHI) will only be known by the PI and will not be disclosed to anyone else.

f. Confidentiality

I. Any information about the patient will be obtained by the principal investigator only and will be handled with secrecy.

II. The information will be stored on a computer with password protection and will only be accessible to the principal investigator and the supervisor.

g. Data Management:

I. Patient records will be stored in the form of hard copies. They will be safely stored in locked storage units inside rooms specified for safekeeping of patient records in MIU.

II. Any patient information in the form of soft copies as radiographs will be stored on the computer of the principal investigator and will be password protected.

III. For legal and research purposes, all data will be safely stored for a minimum period of 1 year.

h. Consent Procedures if Applicable

A written informed consent will be provided by the principal investigator in the MIU diagnostic clinic to be signed by the participants. The consent will clearly state the aim of the study, the procedures to be administered, and criteria for enrollment and discontinuation. It will also clarify all the possible benefits and risks posed by the study.

i. Patient Informed Consent Form

j. Adverse Event Reporting

Adverse Events (AES):

- Adverse events will be reported within 24 hours.
- Possible adverse events in this study include perforating the pulp chamber floor during access cavity preparation.
- The operator will report the incidence in the patient treatment record and to the institutional review board (IRB).
- Management: The operator will seal the perforation using MTA and will follow-up with the patient as needed.

Serious Adverse Events (SAEs):

- Serious adverse events will be reported within 24 hours.
- Serious adverse events include intraoperative severe anaphylactic reactions, as well as postoperative diffuse facial swelling.
- The incidence of these events will be reported immediately.
- In case of severe anaphylactic reactions, the procedure will be discontinued immediately. The patient will be handled by medical specialists, and hospitalization will be done if needed.
- In case of postoperative facial swelling, the PI will prescribe the appropriate medication, and hospitalization will be done if the case is severe. Traditional root canal treatment will be performed, and the patient will be excluded from the study.

Stopping Rules:

- If multiple adverse events occur to a participant, his/her enrollment in the study will be stopped, and proper management of the adverse events will be done.

8. Sample Archiving and Future Use of Specimens

Radiographs obtained from patients will be safely stored for a minimum of one year.

VIII. Research Work Plan and Timetable

Work Plan :

Principle investigator (P.I): Marwan Sherif
Supervisor: Prof. Dr. Ahmed Ghobashy
Co-Investigator: Prof. Dr. Mohamed Mokhtar Nagy

Timetable :

Task	Responsible investigator (Name)	Year1: 2023												Year2: 2024											
		Jan	Feb	Mar	April	May	June	July	Aug	Sep	Oct	Nov	Dec	Jan	Feb	Mar	April	May	June	July	Aug	Sep	Oct	Nov	Dec
Protocol Writing & Plagiarism Check	P.I Supervisor 1 Supervisor 2											*													
Submission to Research Committee	P.I Supervisor 1 Supervisor 2												*												
Research Committee Approval	P.I Supervisor 1 Supervisor 2													*											
Submission to IRB	P.I Supervisor 1 Supervisor 2													*											

IRB Approval																*								
Registration on clinicaltrials.gov (*see last page)*																*								
Teeth Selection/Patient Enrollment*																	*							
Procedures																		*						
Progress Report																								*
Data Entry and Statistical Analysis																								*
Thesis/ Manuscript Writing																								*

IX. Budget

Requirements	**Unit Number**	**Unit Price**	**Total** (Unit Number X Unit Price)	**Funding Source**		
I. Equipment				Self-funded	Available @MIU	MIU Permission Required
1**. Dental operating microscope**	1		0		YES	
2. 2D Radiograph	60		0	0	YES	
3. Phosphoric Plates	2	2,500 EGP	5,000 EGP	YES		
4. AI Software	1	1,100$	1,100$	YES		
5.Film holder	3	1500	45000	YES		
6. Diagnostic Set	60				YES	
7. Metal Syringe	60				YES	
8. Rubber Dam Clamp	60				YES	
9. Rubber Dam frame	60				YES	
10. Rubber Dam Punch	60				YES	
11. Endodontics Explorer	60				YES	

12. Plastic Syringe	60				YES	
13. Excavator	60				YES	
14. Paralleling device	60				YES	
15. Diamond stones	60				YES	
16. Carbide burs	60				YES	
II. Supplies						
1. Sodiom hypochloride irrigation					YES	
2.MTA					YES	
3.Glass Ionomer restoration					YES	
III. Data Analysis			1000EGP	YES		
IV. Others						
1.			0	0		
2.			0	0		
Total Budget			65,500			

X. References

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Ethical Approval Application Form

Section I: Research Details

1. Date of IRB Submission:
2. Study Start Date: February 2023
3. Study End Date: July 2024
4. **Research Source of Funding:** (*check all that applies)* ☒ **Self-Funded** ☐ **MIU** ☐ **Other, Mention**_____

Section II: Applicant Details

1. Applicant (Principle Investigator)	☐ **Undergraduate** ☒ **Postgraduate** ☐ **Staff**
2. Supervisor(s) Name (For students)	**Prof. Dr. Ahmed Ghobashy**
3. Research Type:	☒ **Master** ☐ **Doctorate** ☐ **Other**
4. Approval from IRBs/RECs Other than MIU IRB	☐ **Obtained** *(provide copy)* ☐ ***To be obtained*** *(provide copy when available)* ☒ ***Not applicable***

Section III: List of Attachments:

- ☐ **Complete Protocol**

☐ **Consent Form, English**

☐ **Consent Form, Arabic**

☐ **Study Questionnaires (If applicable)**

☐ **MIU Research Committee Approval &Research Code**

☒ **CV of Principle Investigator (PI)**

☒ **Ethics Training Certificate for PI and Other Research Staff (Valid at least for 1 Years)**

☐ **Advertisements (If applicable)**

☐ **Approval from Other IRBs/RECs (If Applicable)**

☐ **Others**

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I declare that the information given herein is accurate. I have read the ethics policy and will follow the guidelines therein.

Applicant Signature **Marwan**_____

Date / /20

Supervisor Signature (When Applicable) _____

Date / /20

N.B. Protocol after Research Committee approval and completed IRB application should be sent by e-mail to the MIU-IRB: ethical.committee@miuegypt.edu.eg **and MIU-IRB Administrator:** amira.kamal@miuegypt.edu.eg