

**Evaluation of the Clinical and Radiographic Success of Platelet-Rich Fibrin, Chitosan, and Blood Clot as Scaffolds in Regenerative Endodontic Treatment of Molars**

**NCT ID not yet assigned**

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## RESEARCH PROTOCOL

<b>NAME OF THE RESEARCH:</b>	<b>Evaluation of Clinical and Radiological Success of the Platelet-Rich Fibrin, Chitosan and Blood Clot as a Scaffold in the Regenerative Endodontic Treatment of Molar Teeth</b>
<b>CENTER/CENTERS WHERE THE STUDY WILL BE DONE</b>	<b>Inonu University Faculty of Dentistry Department of Pedodontics</b>
<b>BASIS AND JUSTIFICATION OF THE RESEARCH:</b>	Young permanent teeth may become necrotic due to caries or trauma. Root development stops in necrotic teeth, resulting in thin root dentin walls and an open apex. Therefore, appropriate mechanical preparation and subsequent hermetic filling during endodontic treatment becomes difficult, and root canal treatment cannot be performed. Calcium hydroxide apexification and single-session apexification techniques are frequently used, but they cannot ensure continued root development. Teeth with these techniques are prone to fracture due to thin root canal walls. Thus, regenerative endodontic treatments, which provide pulp regeneration, dentin formation, and continued root development after treatment, have become widespread. The terms regenerative endodontics, revascularization, and revitalization have been adopted in the literature. Regenerative endodontics aims to promote continued root maturation by restoring the pulp-dentin complex. (1) A fundamental component of regenerative endodontic treatment is the presence of a scaffold that allows for the adhesion, proliferation, and differentiation of stem cells from the apical papilla. Many studies in the literature have examined various scaffold materials used in regenerative endodontic treatment and compared their success. These studies support the idea that an ideal scaffold material should support the survival and proliferation of apical papilla stem cells, be biocompatible, allow cell migration and vascularization, be biodegradable, and be nontoxic. Several studies have determined that, in the absence of a scaffold, apical papilla stem cells do not adhere to the root canal system and therefore fail to regenerate the pulp-dentin complex (2, 3, 4).

	<p>Although PRF and blood clots are widely used and will be used in this study, chitosan is an important alternative regenerative endodontic treatment material that has achieved successful results in recent years (2). Although there are studies evaluating these three materials together and separately, there are no studies evaluating their clinical and radiological success in molar teeth. Controlled clinical studies are needed, particularly for molar teeth.</p> <ol style="list-style-type: none"> <li>1. Lin, Louis M, and Bill Kahler. "A review of regenerative endodontics: current protocols and future directions." <i>Journal of Istanbul University Faculty of Dentistry</i> vol. 51,3 Suppl 1 S41-S51. 2 Dec. 2017, doi:10.17096/jiufd.53911</li> <li>2. Raddall, Gavin et al. "Biomaterials and Scaffold Design Strategies for Regenerative Endodontic Therapy." <i>Frontiers in bioengineering and biotechnology</i> vol. 7 317. 15 Nov. 2019, doi:10.3389/fbioe.2019.00317</li> <li>3. Trevino, Ernesto G et al. "Effect of irrigants on the survival of human stem cells of the apical papilla in a platelet-rich plasma scaffold in human root tips." <i>Journal of endodontics</i> vol. 37,8 (2011): 1109-15. doi:10.1016/j.joen.2011.05.013.</li> <li>4. Jadhav, Ganesh et al. "Revascularization with and without platelet-rich plasma in nonvital, immature, anterior teeth: a pilot clinical study." <i>Journal of endodontics</i> vol. 38,12 (2012): 1581-7. doi:10.1016/j.joen.2012.09.010</li> </ol>
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<b>AIM OF THE RESEARCH</b>	<p>This study aimed to evaluate and compare, both clinically and radiographically, the treatment and long-term follow-up results of using platelet-rich fibrin, blood clots, and chitosan as scaffolds in molar tooth regeneration.</p>
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<b>RESEARCH METHOD:</b>	<p>The sample group for the planned study will be selected from among patients applying to the Inonu University Faculty of Dentistry Pedodontics Clinic with necrotic pulp and immature apices. Block randomization will be used to determine the material to be applied to the teeth. According to the minimum sample size determined by the power analysis, the study will be conducted on at least 24 teeth. Patients who leave the study early or do not comply with the treatment procedure will be excluded, and new patients will be added in their place. Patients will not undergo additional procedures, appointments, or radiograph requests within the scope of the study. Regeneration treatment is a popular, routinely applied procedure in our clinic and in dentistry faculties. It is also successfully performed by pedodontists and endodontists in private clinics. The protocol stipulates that each study participant will be informed about the nature of the treatment to be administered and the research to be</p>
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conducted. Informed consent will be obtained from the patient's legal guardian. In the initial session, local anesthesia will be administered to the teeth, a rubber dam will be positioned, and the caries will be meticulously removed. Subsequently, the pulp will be meticulously eradicated through the employment of a sterile barnacle. Each canal will undergo irrigation with 20 milliliters of a 2.5% sodium hypochlorite solution. Subsequently, a volume of 20 milliliters of sterile saline will be applied to each canal. Calcium hydroxide paste will be placed as a medicament in the canals that have been dried with paper points and closed with a temporary filling. The patient will be contacted to schedule a second session between one and four weeks later. In the second session, local anesthesia will be administered without the use of a vasoconstrictor. Prior to this, a rubber dam will be placed, and the temporary filling will be removed. The calcium hydroxide paste placed in the canal as a medicament will be removed, and each canal will undergo a gentle irrigation with 20 milliliters of 17% ethylenediaminetetraacetic acid (EDTA). The canals will be dried using paper points. The induction of bleeding will be accomplished through the utilization of an excessive number of instruments, specifically a 20 number K File, which will be inserted 2 mm beyond the apical extent of the canal. Subsequently, platelet-rich fibrin or chitosan (Sigma-Aldrich) will be placed in the canal as a scaffold. In the "control group," where apical bleeding will be used directly as a scaffold, which is mentioned as the gold standard in the literature because it is the most easily accessible material, these will not be used and only bleeding from the apex will be sufficient. MTA (Angelus MTA) will be applied to the canal orifices to prevent oral fluids from leaking into the canal. The MTA will be covered with glass ionomer cement. Dental elements that are deemed suitable for endodontic restoration will undergo treatment with composite fillings. Teeth that are not amenable to restoration with composite fillings due to extensive material loss can be restored with stainless steel crowns. The protocol stipulates that patients are to be contacted for medical checkups at three-month intervals during the first year of the study, and at six-month intervals during the second year. The evaluation of the data will be conducted with the utilization of statistical software and the expertise of subject matter specialists. During the check-ups, the teeth will be evaluated according to the criteria listed below.

**A- CLINICAL**

1. Loss of Tooth
2. Presence of pain

	<ul style="list-style-type: none"> <li>3. Percussion and Palpation Sensitivity</li> <li>4. Presence of Pathological Mobility</li> <li>5. Presence of fistula</li> <li>6. Evaluation of restoration</li> </ul> <p><b>B- RADIOGRAPHIC</b></p> <ul style="list-style-type: none"> <li>1. Pulp Obliteration</li> <li>2. Internal - External Root Resorption</li> <li>3. Apical Radiolucency</li> <li>4. Increase - Decrease in Lamina Dura Width</li> <li>5. Presence of Ankylosis</li> <li>6. Root length</li> <li>7. Root thickness</li> </ul>
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<b>POWER ANALYSIS:</b>	<p>The number of people in the study was decided by a calculation called "power analysis." The G*power 3.1 program was used to calculate the sample size. The sample size was determined to be 24, with 8 teeth for each group. The effect size was set at 0.25, the margin of error at 0.05, the confidence level at 0.95, and the universe representation power at 0.95 Cohen states that the sample size for which power values ranging from 0.90 to 0.99 were calculated should be reached (5).</p> <p>5. Cohen, J, (1988), Statistical Power Analysis for the behavioral sciences, 2. Edition, Taylor &amp; Francis INC, New York, US.)</p>
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<b>END POINT OF THE RESEARCH</b>	<p>The goal of this study is to follow patients over time to see if regeneration treatment works for molar teeth with open apex. We will use three different scaffolds for the treatment. No clinical controlled study has been found in the literature on regeneration with molar teeth. The existing data are in the form of case reports or studies performed on incisors. The goal of the study is to successfully obtain 12-18 months of clinical and radiographic follow-up with at least 24 teeth. We will compare the success rates of the materials used based on the data we get. Since scientists haven't found the perfect material yet, this study will be a big help to researchers when it's finished.</p>
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<b>EXPECTED BENEFITS AT THE END OF THE RESEARCH</b>	<p>The goal is to compare the long-term success of chitosan, a material that has been proven to work in clinical trials, with other materials. This will provide useful data for the scientific literature. Chitosan is used a lot in dentistry because it kills bacteria and helps tissue grow. (6). Studies have shown that it has some benefits. It is a good support structure for a type of tooth cell called apical papilla stem cells. It is also compatible with living tissue and is not very toxic. However, there is limited information about the use of chitosan in literature about other teeth. Since the roots are thin in molars, it is quite difficult to perform root canal treatment with apical plug. Therefore, the regenerative endodontic procedure was developed as an alternative, which is quite advantageous in molars with open apicals. Since many patients come from nearby provinces, the number of molars that need a regenerative endodontic treatment is also increasing in our clinic, where we see a lot of patients. This study aims to provide valuable data to the existing literature by evaluating molar teeth. Comparison of 3 different scaffold materials will contribute to the determination of materials that are advantageous in terms of cost/benefit ratio and will provide support for their clinical use.</p> <p>6) Fakhri, Elaheh et al. "Chitosan biomaterials application in dentistry." <i>International journal of biological macromolecules</i> vol. 162 (2020): 956-974. doi:10.1016/j.ijbiomac.2020.06.211</p> <p>7) Chang, Bei et al. "Injectable scaffolds: Preparation and application in dental and craniofacial regeneration." <i>Materials science &amp; engineering. R, Reports : a review journal</i> vol. 111 (2017): 1-26. doi:10.1016/j.mser.2016.11.001</p>
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**PLANNED DURATION OF THE STUDY:**

Planned Start Date:	10.01.2022
Planned Completion Date:	01.08.2024

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