Official Study Title

Clinical Efficacy of I-PRF, Povidone-Iodine, and Diode Laser asAdjuncts to non-surgical periodontal treatment in Smokers and Non-Smokers periodontitis Patients: A Split mouth RandomizedClinical Trial

Protocol Details:

- Protocol Version: **1.0**
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Ethics Committee Approval:

- Committee: **Comité Local de Protection des Personnes (CLPP), Tunis Military Hospital**
- Decision No.: **176/2026/CLPP/Hôpital Militaire de Tunis**
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CLINICAL RESEARCH PROTOCOL

Clinical Efficacy of I-PRF, Povidone-Iodine, and Diode Laser as Adjuncts to non-surgical periodontal treatment in Smokers and Non-Smokers periodontitis Patients: A Split mouth Randomized Clinical Trial

Plan:

1. Primary Objective
2. Study Design & Methodology
3. Participant Selection
4. Randomization & Allocation
5. Clinical Procedure & Statistical Analysis
6. Expected Results & Clinical Significance
7. Ethical Compliance & Trial Registration

- This study is **a randomized, controlled, split-mouth clinical trial** designed to evaluate and compare the effectiveness of **four different subgingival** adjuncts used along side standard **Scaling and Root Planning (SRP).** This protocol is designed to be a **standardized therapeutic model**. The subgingival adjuncts are standardized, ensuring that the results are not operator dependent and can be replicated across any dental unit.

Primary Objective

- The primary goal of this study is to evaluate the clinical efficacy of three distinct adjunctive strategies: Biological (I-PRF), Antiseptic : Povidone-iodine , Diode-Laser activation, compared to a Saline Control in the initial treatment of stage 2, 3 and stage 4 of the 2018 AAP/EFP periodontal classification.

Key Research Goals:

- **Performance Comparison:** To determine if the **Biological** group (I-PRF), which introduces high concentrations of growth factors and leukocytes, provides superior Probing Pocket Depth (PPD) reduction compared to an **antiseptic group** (Povidone-Iodine) and **photobiomodulation group** (diode laser activation).
- **The Smoking Factor:** To investigate if the regenerative properties of I-PRF can overcome the compromised healing response typically found in the Smoking Subgroup.
- **Healing Quality:** To identify which group shows the fastest reduction in inflammation, measured by Bleeding on Probing (BOP) and Clinical Attachment Level (CAL) gain.

CLINICAL HYPOTHESIS

- We hypothesize that while all adjuncts will improve results over SRP alone, the biological group (I-PRF) will show the most significant gains in the Smoker Subgroup due to its ability to stimulate local angiogenesis and tissue repair in a traditionally poor healing environment.
- By including smokers, this study addresses “the down to reality " challenge in dentistry. Smoking often impairs the blood supply to the gums; this trial investigates:

if a biological approach like I-PRF (which introduces fresh growth factors) or a high-volume Antiseptic irrigation with Povidone-iodine, or a 980nm diode laser activation can overcome these healing barriers.

Study Design & Methodology

- **Split-Mouth Format**: Each participant acts as their own control. The four quadrants of the mouth are randomly assigned to a different treatment, ensuring that individual factors (like genetics or oral hygiene) affect all four groups equally:

    1. Control: Saline irrigation (0.9%).
    2. Biological: I-PRF prepared at a G-force of 60 G for 3 min
    3. Antiseptic: Povidone-iodine irrigation (1%).
    4. Diode-Laser Activation

- **Standardization:** To ensure scientific rigor, all liquid adjuncts are delivered in a standardized volume (5 mL) using a blunt-tip cannula.

- **Outcomes:** The success of the treatments will be measured by a **blinded examiner over 6 months,** tracking the decrease of bleeding on probing (BOP) and the reduction of pocket depths and the clinical attachment gain :

Bleeding on Probing (BOP) : Bleeding on Probing (BOP) will be assessed within 15 seconds after gentle probing at six sites per tooth using a calibrated periodontal probe (The instrument used (UNC-15 periodontal probe). The presence or absence of bleeding will be recorded and expressed as the percentage of bleeding sites per treatment quadrant. Measurements will be obtained by a blinded examiner at baseline, 3 months, and 6 months

Pocket Depth (PPD) : Probing Pocket Depth (PPD) will be measured in millimeters using a calibrated UNC-15 periodontal probe at six sites per tooth (mesiobuccal, midbuccal, distobuccal, mesiolingual/palatal, midlingual/palatal, and distolingual/palatal). Measurements will be performed by a calibrated examiner blinded to treatment allocation at baseline, 3 months, and 6 months.

Clinical Attachment Level (CAL) : Clinical Attachment Level (CAL) will be measured in millimeters using a calibrated UNC-15 periodontal probe at six sites per tooth by measuring the distance from the cementoenamel junction (CEJ) to the base of the periodontal pocket. Assessments will be performed by a blinded calibrated examiner at baseline, 3 months, and 6 months.

Participant Selection

Sample Size : 50 participants (200 total quadrants).
We selected a sample size of 50 participants to ensure a high statistical power (0.80). Based on previous literature, a split mouth design significantly reduces inter-subject variability, allowing us to detect a clinically relevant difference of 0,5 mm in PPD reduction with a confidence level of 95% ($p<0,05$).

This sample size also accounts for a predicted 20% attrition rate and allows for a meaningful sub-group analysis regarding the impact of smoking on healing.

Following the principles outlined by Lesaffre et al. (2007), a sample of 50 participants is sufficient to detect a clinically significant PPD reduction of 0.5 mm (Heitz-Mayfield, 2005) at a 95% confidence interval.

- **Inclusion:** Patients with Stage II-IV Periodontitis; at least one bleeding pocket > 4 mm minimum in every quadrant.

- **Smoking Stratification:** The sample will intentionally include smokers to assess treatment efficiency in compromised healing environments. Smoking status (pack per year) will be recorded as a baseline variable.

- **Exclusion:** patients who:
  - Pregnant /Lactating
  - History of radiotherapy or chemotherapy in the head/neck region.
  - Known hypersensitivity to Iodine or Methylene blue solution
  - Systematic antibiotic use within the last 30 days
  - Long-term use of immunosuppressants or corticosteroids (daily use) - type 1 / 2 diabetes

Randomization & Allocation

To ensure an unbiased distribution of treatments among the maxillary and mandibular quadrants:

- **Randomization:** a computer-generated 4x4 Latin Square design will be used to assign the four treatments to the four quadrants.

- **Allocation Concealment:** The treatment sequence for each participant will be stored in sequentially numbered, opaque, sealed envelopes (SNOSE). The investigator will open the envelope only after the SRP is completed for all quadrants.

- **Blinding:** A calibrated independent examiner, blinded to the treatment allocation, will perform all clinical measurements (PPD, CAL, BOP) at baseline, 6 weeks, 3 months and 6 months.

Clinical Procedure & Statistical Analysis

A. Standardized Clinical Workflow (Single-Session Protocol):

To ensure maximum scientific control and clinical efficiency, the entire mechanical and adjunctive intervention will be completed in a **single appointment** for each participant.

- **Phase I: Baseline Prep (T0):** All 50 participants receive a professional supragingival scaling and **Standardized Oral Hygiene Instructions (OHI)** to ensure a uniform baseline Plaque Index.

- **Phase II: Full-Mouth Mechanical Therapy:** Scaling and Root Planning (SRP) is performed under local anesthesia across all four quadrants.

- **Phase III: Strategic I-PRF Preparation:** Just before the completion of the SRP, 10 mL of venous blood is collected. It is centrifuged at **for 3 minutes** (Low-Speed Concept) to ensure the I-PRF is fresh and in its liquid phase for immediate application.

- **Phase IV: Immediate Local Adjunct Application:** Once scaling is finalized, the quadrants are treated according to the randomization sequence (Group A, B, C, D):

-Biological Arm: Freshly prepared liquid I-PRF is delivered sub-gingivally via a blunt tip cannula until the pocket is saturated.
-Irrigation Arms: Standardized **5 mL** irrigation of Saline, 1% Povidone iodine.

-Photo biomodulation Arm:5ml methylene blue 0.3% solution activated with a diode laser (980nm).

- **Phase V: Longitudinal Follow-up:** Blinded clinical re-evaluations (PPD, CAL, and BOP) occur at **8 weeks (T1), 3 months (T2) and 6 months (T3).**

B. Statistical Analysis Plan:

The objective is to determine if the Biological (I-PRF), or antiseptic (1% Povidone- iodine) or photo biomodulation approach offers superior benefits over the control, particularly in the Smoking Subgroup.

- **Primary Statistical Model:** A Mixed-Design ANOVA will be used to analyze the data. ○ Within Subjects Factor: The treatment modality across the four quadrants. ○ Between Subjects Factor: The smoking status (Smoker vs. Non-smoker).
- **Significance & Validation:**

  ○ The confidence level is set at 95% (p<0,05%) with 80% power. ○ Mauchly's Test will be applied to check for sphericity, and Bonferroni Post- Hoc Corrections will be used for all pair-wise comparisons between the four groups

Expected Results & Clinical Significance

A. Primary Clinical Hypotheses

Based on the biological properties of the materials used, we anticipate the following outcomes:

- **Superiority of I-PRF:** We expect the **Biological (I-PRF)** group to demonstrate the highest reduction in Probing Pocket Depth (PPD) and the greatest gain in Clinical Attachment Level (CAL) at 3 months.

- **The "Smoker" Advantage:** While smokers typically show poor results with standard SRD, we hypothesize that the growth factors in I-PRF (VEGF, TGF) will partially compensate for their impaired microcirculation, showing a significantly better healing curve than the photo biomodulation or Iodine groups in this specific population.

- **Immediate vs. Long-term:** We expect the **Povidone-Iodine** groups to show a rapid decrease in Bleeding on Probing (BOP) within the first month due to the antimicrobial effect, while the I-PRF and the laser disinfected group will show more "stable" long-term tissue regeneration by the third month.

B. Clinical Significance

The findings of this study will contribute to evidence-based dentistry in two major ways:

- **Standardization of Biological Adjuncts:** By using a precise 60g-**force for 3 minutes** protocol, this study will help clarify if the "Low-Speed Concept" is superior to chemical or Laser photo biomodulation adjunct.
- **Personalized Periodontal Therapy:** The results will help clinicians decide if specific patient types (like smokers) should be prioritized for biological therapy (I-PRF) rather than standard antiseptic irrigation or Laser pocket disinfection.

Ethical Compliance & Trial Registration

To ensure full transparency, traceability, and adherence to the **Declaration of Helsinki**, this study will be formally registered and monitored through the following steps:

A. ClinicalTrials.gov Registration

Before the first patient is recruited, the protocol will be registered on **ClinicalTrials.gov**. This provides the study with a unique **NCT Number**

Public Accountability: Registration ensures that the primary outcome (BOP /CAL / PPD reduction) is declared upfront, preventing "selective reporting" of results.

- **Methodological Rigor:** It confirms that the G-force (60g), the sample size (50 patients), and the split-mouth design were established before data collection began.

B. Military Ethics Committee & Institutional Review Board (IRB) Approval

The protocol will be submitted to the **Military Hospital IRB** for review. We will emphasize three key safety protocols:

- **Informed Consent:** Participants will receive a clear explanation that the I-PRF is autologous (their own blood), minimizing the risk of cross-contamination or rejection.
- **Aseptic Protocol:** the preparation of the I-PRF (for 3 min), the delivery of 1% Povidone iodine, Saline irrigation and Laser methylene Blue activation will be performed under strict sterile conditions.

- **Adverse Event Reporting:** A formal mechanism will be in place to record any localized inflammation or hypersensitivity, though risks are minimal given the use of standardized protocols.

C. Data Management

- All clinical data will be anonymized using patient ID codes to maintain confidentiality.
- The raw data and the statistical code used for the **Mixed-Design ANOVA** will be stored in a secure repository to allow for future peer review or meta-analysis.