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LASER ASSISTED NEW ATTACHMENT PROTOCOL:

A 12-MONTH OUTCOME STUDY

by

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A thesis submitted to the Faculty of the
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ABSTRACT

LANAP: A 12-MONTH OUTCOME STUDY

Sean P Farrell, DDS, 2023

Thesis directed by: Caitlin D Darcey, Program Director, NPDS Periodontics

Background: Laser Assisted New Attachment Procedure (LANAP) is a trademarked protocol for the treatment of periodontal disease. However, there are limited controlled clinical studies reporting on outcomes associated with LANAP and the improvement of periodontal disease. Purpose: The purpose of this 12-month, single-center study is to evaluate the effect of LANAP therapy on periodontal disease. The primary objective of this report is to calculate the change in subject-reported outcomes reported within 6 months post LANAP therapy.

Methods: Eight subjects with periodontal disease were enrolled and underwent LANAP treatment. Clinical examinations were performed at baseline and with follow-up examinations scheduled for 12-months. Changes in clinical parameters of periodontal disease will be evaluated via clinical attachment levels, probing depth, plaque score, gingival bleeding on probing, gingival purulence, gingival recession, tooth mobility, fremitus, and furcation involvement. Subject-reported outcomes were evaluated at baseline and 6 months with scheduled follow-up for 12 months assessing the healing course and oral health quality of life post LANAP via visual analog pain scale (VAS) and oral health impact profile questionnaires (OHIP-14), respectively.

Results: VAS pain scores ranged from 0-7 starting from the first day post-operatively. The average rate of decline in post-operative VAS pain score was 1.19±1.13 for the left-side and 1.31±1.74 for the right-side. Comparisons of baseline and 6-month OHIP-14 data demonstrated significant improvements in physical pain (Δ_{score}= -1.5; -0.5) psychological discomfort (Δ_{score}= -1.5; -0.5), and psychological disability (Δ_{score}= -1.5; -0.5) categories.

Conclusions: Subjects demonstrated clinically significant reductions in post-operative pain and improvements in quality-of-life measurements post LANAP therapy. Such findings validate continuing the study to completion in order to further evaluate LANAP's effect on clinical outcomes. This study will add to the limited published data assessing clinical healing from LANAP treatment. Additionally, this is the first clinical study to investigate subject-reported outcome measures of LANAP treatment.

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LIST OF ABBREVIATIONS

BOP	Bleeding On Probing
BID	Taken Twice Daily
CAL	Clinical Attachment Level
DDS	Doctor of Dental Surgery
Er:YAG	Erbium: Yttrium Aluminum Garnet laser
GI	Gingival Index
LANAP	Laser Assisted New Attachment Protocol
LAPIP	Laser Assisted Peri-Implantitis Protocol
OHIP-14	Oral Health-Related Impact Profile-14 Questionnaire
Nd:YAG	Neodymium-doped: Yttrium Aluminum Garnet laser
Nd:YAP	Neodymium-doped: Yttrium Aluminum Perovskite laser
PD	Probing Depth
PI	Plaque Index
PRN	As Needed
RDH	Registered Dental Hygienist
VAS	Visual Acuity Score

CHAPTER 1: Introduction

Periodontitis is defined as "an inflammatory disease of the supporting tissues of the teeth caused by specific microorganisms or groups of microorganisms, resulting in progressive destruction of the periodontal ligament and alveolar bone with increased probing depth formation, recession, or both" (Wolff , 1994). According to a 2012 study authored by the Centers for Disease Control and Prevention (CDC) Periodontal Disease Surveillance workgroup, between 2009 and 2010 an estimated 47.2% or 64.7 million American adults had mild, moderate, or severe periodontitis, accounting for approximately 1 out of every 2 Americans aged 30 and over (Dye, 2007). In the same study, periodontal disease prevalence increased to 70.1% in adults over age 65. On a global scale, between 1990 and 2010, periodontal disease was estimated to affect 20-50% of persons, with severe periodontitis ranking as the sixth most prevalent condition affecting approximately 744 million individuals (11%) (Kassebaum et al., 2014).

Within the oral cavity, periodontitis manifests as the transformation of junctional epithelium to pocket epithelium containing a dense inflammatory infiltrate within the connective tissues, large-scale collagen breakdown with apical migration of the junctional epithelium to maintain an intact barrier into areas of depleted collagen, and eventual osteoclastic resorption of alveolar bone. (Page & Schroeder, 1976). Although localized to the oral cavity, periodontitis is shown to have a cumulative detrimental effect on an individual's life years. Marcenes et al. in 2013 estimated that between 1990 and 2021, disability adjusted life-years (DALYs) due to severe periodontitis represented a substantial lose in life-years due to disability (Marcenes et al., 2013). Furthermore, severe periodontitis was considered the primary cause of DALYs in the 35 to 59-year-old age

group, accounting for more than five million DALYs globally, and estimated as a mean loss of 108 healthy life years per 100,000 people from a preventable disease (Marcenes et al., 2013).

This notion of preventability is linked to the underlying etiology of periodontal disease, which is a physiologic and histochemical response to the preventable attachment of pathogenic plaque in a susceptible host (Löe, 1965; Socransky, 1998; Löe 1986) In a study regarding the progression of gingivitis, regular abstaining from oral hygiene practices resulted in a shift in oral microbiota quantity and quality (Löe et al., 1965). Community ordination studies demonstrated the importance of the bacterial complex quality as specific oral bacterial complexes were significantly associated with clinical disease parameters of periodontitis (Socransky et al., 1998). In the absence of preventative oral hygiene habits, an estimated 81% of individuals in an untreated population will progress moderately and 8% will progress rapidly to periodontitis (Löe et al., 1986). However, a hallmark study indicates that all subjects who had developed gingivitis re-achieved gingival health upon resuming normal oral hygiene (Löe et al., 1965).

In order to achieve optimal periodontal health, a major focus of periodontal treatment is the removal of pathogenic microbial biofilms typically through mechanical means of scaling and root planning (SRP). While SRP aims to reduce periodontal pocket depth and restore clinical gingival attachment through effective removal of pathogenic plaque, calculus, and toxic non-cellular substances from the teeth and root surfaces, as a therapeutic modality SRP is not without limitation. The foremost limitation relates to provider instrumentation adaptability. Several anatomic factors contribute to this

difficulty such as furcation invasions, adjacent root proximity, developmental grooves and root concavities. In one study, 58% of molars contained furcations where the entrance diameter was 0.75 mm or less, narrower than the average width of instrumentation used for SRP, resulting in limited overall access (Bower, 1979). In other instances, such as aggressive case presentations, specific infectious organisms can evade host defenses and invade host tissues rendering SRP as a monotherapy clinically ineffective (Kornman & Robertson, 1985). Due to these inherent limitations, adjunctive therapies involving systemic antibiotics and antimicrobials delivered locally have been adopted (American Academy of Periodontology, 2006), and alternative modalities utilized, such as laser periodontal therapy, to improve upon traditional SRP limitations.

While the idea of utilizing lasers in dentistry may seem ground-breaking and innovative even by current practice standards, dental laser technology has been in development for over sixty years. In 1960, ruby lasers were developed and subsequent reports by Stern and Sognnaes in 1965 demonstrated their potential to vaporize enamel, but also their propensity to damage dental pulp due to their thermal effects. Accordingly, other wavelengths and media were studied for tissue application over the following decades (Cobb, 2006). As early as 1990, practitioners and researchers began to find clinical oral soft tissue uses for medical-grade CO_2 and Nd:YAG lasers in dentistry (Pohlhaus, 2015).

Dental lasers are based on stimulated emission of radiant energy in which stimulation of an active medium generates the release of photons in a beam of uniform wavelength specific to that medium. The term “laser” is an acronym for Light Amplification by Stimulated Emission of Radiation and is differentiated from visible

light by two distinct characteristics. The first characteristic is that all laser-emitted energy is of a singular uniform wavelength (i.e., monochromatic). The second characteristic is that each generated wavelength is identical in both size and shape, allowing for multiple coherent photon waves in step with one another. Due to these two properties, the generated photons can be collimated into a focused beam with the capability of interacting with a target tissue (Fasbinder, 2008).

Laser light energy incident upon a target tissue denser than air, such as oral tissue, will interact in one of four ways. *Transmission* describes the beam entering the tissue, without any interaction between the incident beam and the tissue, and then emerging unchanged. *Scatter* describes interaction of the beam and tissue but insufficient to cause complete attenuation. Beam diminution and ray distortion proceed in an uncontrolled direction through the tissue with a degree of backscatter (associated mostly with shorter wavelengths, such as diode and Nd: YAG lasers). Another interaction is *reflection* wherein the density of the tissue, or angle of incidence being lesser than the refractive angle, results in beam redirection. Lastly is *absorption*, where incident light energy is attenuated by the tissue and converted into another form (Parker, 2007).

Absorption provides lasers with their primary and beneficial effect as used in dentistry. The goal of dental laser surgery is optimization of photobiologic effects, primarily via photothermal means wherein light energy is converted into heat energy. As tissue temperature gradually increases, a spectrum of observed effects occurs with laser-tissue interaction. Below is a summary of biological effects by gradated temperatures (Coluzzi, 2008).

- Above 37^{o}C: Tissue hyperthermia occurs.

- At 50°C: Non-sporulating bacteria are inactivated.
- ~60°C: Proteins begin to denature and coagulation occurs, allowing for the removal of granulation tissue without tissue vaporization.
- 70-80°C: Adherence between tissue layers occurs due to the unfolding of helical molecules of collagen and their intertwining with adjacent segments (i.e., tissue welding or anastomosis).
- At 100°C: Tissue ablation and soft tissue excision due to water vaporization.
- At 200°C: Tissue necrosis.

Due to this range of tissue effects laser selection is largely dependent on the desired target tissue.

A laser's operation mode also dictates its applicability. Lasers have two basic modes of emission, continuous-wave and free-running pulsed. In continuous-wave emission, energy is constantly emitted while the laser is in its active state, as seen with CO_2 and diode lasers. A variation on this mode is the inclusion of gating or super-pulsing via an electronic or mechanical shutter, which works to reduce unwanted residual thermal damage associated with continuous-wave emission. Alternatively, free-running pulsed emission exhibits energy pulses that are emitted in succession on the order of ten-thousandths of a second, as seen with Nd:YAG and Er:YAG lasers (Coluzzi, 2008).

Applying these principles for use on dental soft tissue yields numerous desirable results. The photo-thermal effect of laser on tissue allows for evaporation or ablation of soft tissue directly (CO_2 and Erbium lasers) or incisions with coagulation and vaporization via refraction at the tip end (Nd:YAG and diode lasers). Additionally, thermal side effects from deeply-penetrating type Nd:YAG lasers result in a thick

coagulation layer on lased soft tissue, demonstrating strong hemostatic properties (Aoki et al., 2015). A laser's photo-thermal effect is also bactericidal in nature via evaporation or denaturation, resulting in bacterial devitalization and inactivation. This creates a disinfected treatment field that promotes wound healing. Furthermore, the Nd:YAG laser specifically exhibits selective absorption in pigments, suggesting a potential mechanism for combating pigmented bacteria such as *P. gingivalis*. In this way, laser irradiation of the root surface may provide an antimicrobial effect inhibiting bacterial attachment and subsequent colonization, beneficial byproducts for treating and healing periodontal pockets.

The abovementioned effects are due to high-level laser therapy aimed at tissue ablation. A unique approach to promoting periodontal wound healing is low-level laser therapy that incorporates reversible stimulation of tissues and cells, known as biostimulation or photobiomodulation. Often low and high-level laser modalities can be used simultaneously with the dissipating energy from high-level therapy resulting in low-level therapy in adjacent tissues (Aoki et al., 2015). These attributes become extremely advantageous in non-surgical pocket therapy. Not only must pathogenic bacterial plaque, calculus, and bacterial endotoxin be removed to restore biocompatibility, but the dense, impenetrable biofilm must be mechanically interrupted to decontaminate diseased root surfaces (Eick et al., 2004).

Root surface decontamination may not always be attained with conventional mechanical therapy and may be more readily accomplished via Nd:YAG laser therapy. Due to the Nd:YAG laser's inherently thin flexible fiber delivery, soft-tissue wall debridement or gingival curettage can be performed more effectively than with use of

conventional instruments. Additional benefits from Nd:YAG laser usage include periodontal pocket decontamination and pocket-lining epithelium vaporization without underlying connective tissue necrosis or carbonization (Aoki et al., 2015).

The US Food and Drug Administration (FDA) has approved several nonsurgical procedures designed to produce "cementum-mediated periodontal ligament new attachment to the root surface in the absence of long junctional epithelium" (Aoki et al., 2015). Typically, this attachment type is regarded as true regeneration and is considered desirable as it mimics the original anatomical form of the periodontium relative to the more non-ideal post-treatment healing observed with a long junctional epithelium. However, regeneration is difficult to validate since it requires histological analysis for definitive proof. Currently, one single manufacturer (Millennium Dental Technologies) and protocol has been able to demonstrate human histologic evidence and has trademarked their technique as the Laser-Assisted New Attachment Procedure (LANAP®) (Aoki et al., 2015). The LANAP protocol involves three sequential procedures combined into one appointment:

1. Nd:YAG laser is directed laterally and apically (settings = 4.0W, 1965 MJ/mm2, 100msec pulse duration, 20Hz) in order to de-epithelialize entire pocket, kill bacteria, and spare connective tissue while providing access for instrumentation to the level of the alveolar crest.
2. SRP with the piezoelectric ultrasonic scaler.
3. Nd:YAG laser applied in a coronal direction from the apical extent to gingival margin (settings = 4.0W, 650µs duration, 20Hz) with the goal of creating a blood

clot to provide surgical closure and epithelial exclusion for the regeneration of new attachment.

Two publications have demonstrated the efficacy of the LANAP protocol as well as histological evidence of new clinical attachment. Yukna and colleagues in 2007, reported the treatment of six pairs of single-rooted teeth diagnosed with chronic periodontitis (Yukna et al., 2007). All teeth had notable subgingival calculus, which was marked by notching at the clinical and radiographic extent of calculus. All teeth underwent scaling and root planing with ultrasonic and hand scalers. Meanwhile, one tooth from each pair received LANAP treatment with an Nd:YAG laser. Three months later, teeth were then extracted via en-bloc resection for histologic processing. Clinically, teeth treated by LANAP demonstrated greater gains in clinical attachment level and greater reduction of probing depths relative to the control teeth. Histologically, all LANAP-treated specimens exhibited new cementum and connective tissue attachment, whereas a majority of control teeth healed by long junctional epithelium without new attachment or regeneration. In a later study by Nevins et al. 2012, twelve periodontal defects were evaluated in eight subjects with advanced periodontal disease (Nevins et al., 2012). An initial examination was performed, and in a similar fashion to Yukna et al, a notch was made at the expected apical extent of calculus on the study teeth and was measured from the cemento-enamel junction (CEJ). LANAP therapy was implemented with an Nd:YAG laser in one visit on both arches at diseased sites. En-bloc biopsies of the test teeth were completed at 9 months. High-resolution micro computed tomography (micro-CT) imaging was used to scan the biopsied teeth, and ground sections were stained and analyzed by light and scanning electron microscopy. Laser surgical therapy in

the twelve periodontal defect areas demonstrated a mean postoperative probing depth reduction of 5.4mm (sd = 2.64mm), clinical attachment level gain of 3.8mm (sd = 2.38mm), and recession of 2.7mm (sd = 1.61mm). Wound healing coronal to the notch placed in the treated teeth demonstrated periodontal regeneration (n = 5), new attachment (n = 1) and healing via a long junctional epithelium (n = 4). The LANAP procedure in this limited population was shown to be a safe technique for performing minimally invasive therapy, resulting in regeneration in approximately half of the subjects as supported by the histologic evidence seen in micro-CT, light, and scanning electron microscopy (Nevins et al., 2012). While these studies show promising results, sample sizes were small and warrant further investigation to substantiate their findings.

There have been several reports of the Nd:YAG laser therapy showing positive, beneficial effects for the treatment of chronic periodontitis. However, few have evaluated subjects treated with the LANAP protocol. Therefore, the aim of this prospective cohort study was to quantify the long-term (12 months) clinical effects associated with LANAP therapy as measured by changes in plaque index (PI), gingival index (GI), probing depth (PD), and clinical attachment level (CAL). However, due to time constraints associated with a periodontics residency program, at this time we are unable to address this study's primary objectives. Accordingly, the aim of this thesis is to evaluate the secondary outcomes of the study which include an assessment of trends in postoperative pain and oral-health related quality of life measurements through an interim analysis of currently enrolled study subjects.

CHAPTER 2: Materials and methods

SUBJECT ENROLLMENT & SELECTION

The study population included individuals undergoing treatment within the Periodontics department at the Naval Postgraduate Dental School (Bethesda, MD). Screenings involved as assessment of a potential subject's medical, surgical, family, and social history; current medications used; pain level; and contraindications to planned treatment. Subjects were required to be 18 years or older with a diagnosis of generalized stage II-IV periodontitis (grade A, B, or C) (Tonetti et al., 2018). Inclusion criteria consisted of at least five teeth per quadrant, at least four sites per quadrant with PD ≥ 4 mm with bleeding on probing (BOP), ability to complete full mouth LANAP therapy within one month, and available for incremental follow-up visits for one-year. Exclusion criteria included currently pregnant and/or lactating females, a history of active periodontal surgical treatment within the last 12 months or SRP within the last 3 months, dental implants, acute periodontal infections (including but not limited to periodontal abscess, necrotizing gingivitis, necrotizing stomatitis, perio-endo lesions, acute herpetic gingivostomatitis) at time of enrollment, history of systemic steroid or antibiotic use within the last 3 months prior to enrollment, and a documented allergy to the post-operative medications in the treatment protocol. All enrolled subjects (n = 8) provided informed consent and subjects who declined enrollment were treated with the recommended LANAP therapy per their existing treatment plan.

CLINICAL AND RADIOGRAPHIC EVALUATION

Clinical and radiographic evaluations were performed at baseline and 12 months. Baseline clinical evaluations consisted of a full mouth periodontal examination, which included plaque score; full mouth PD, CAL, BOP; presence of purulence; and recession at six sites per tooth utilizing a UNC-15 probe. Tooth mobility (Miller mobility classification), fremitus (presence/absence), and furcation involvements (Glickman classification) were assessed and recorded. Radiographic evaluations consisted of a full mouth series of radiographs (to include an updated panoramic x-ray if none present within the last three years) and a complete set of vertical bitewings and periapical radiographs if none present within the last six months. The 12-month evaluation consisted of repeated baseline measurements and updated full mouth radiograph series. Subject-reported outcomes were recorded at baseline, 6 months, and 12 months, and consisted of oral health impact profile questionnaires collected at each follow-up interval, and a daily record of post-operative pain level utilizing a visual analog scale for the first seven days post treatment.

CLINICAL PROCEDURES

For a comprehensive overview of the protocol treatment timeline, refer to Table 1. LANAP surgical appointments (L1, L2) included the following procedures. Local anesthesia was delivered to the maxillary and mandibular quadrants of the side receiving treatment, with or without conscious sedation. Pre-treatment medications included a 30-second rinse with 0.12% chlorhexidine (CHX) and 800mg ibuprofen. Bone sounding measurements from the free gingival margin to the crest of the alveolar bone were made at six sites per tooth for the calculation of a safe range of total energy output (12-17 J/mm). A 360 μm-diameter laser fiber was cleaved, and the MVP-7 Periolase laser was

set to the following parameters: 100-650 μs pulse duration, 3.6 Watts (W) power, and 20 Hz repetition rate. The Nd:YAG laser was directed laterally and apically to de-epithelialize the periodontal pocket, thermally destroy bacteria, and spare connective tissue while providing access for instrumentation to the level of the alveolar crest. SRP with a piezo-electric ultrasonic scaler and hand curettes was conducted using P-, Ball-, and PS-tips in succession and irrigated with 0.03% CHX.

A second application of the Nd:YAG laser was performed in a coronal direction from the apical extent to gingival margin (3.6W, 550-650μs duration, 20Hz) to create a blood clot, provide surgical closure, and to exclude potential epithelial regrowth in order to promote regeneration of new attachment. Gingival tissues were compressed against each instrumented tooth surface for approximately 3 minutes, followed by highspeed occlusal adjustment to balance occlusal contacts in maximum intercuspation and create ideal lateral/anterior excursive mandibular movements. A Coe-Pak periodontal dressing was used for any current smokers and/or areas with non-approximated tissues. Standardized post-operative instructions were discussed verbally and provided in writing. Post-operative medication consisted of analgesic medications (Ibuprofen 800 mg – 1 tablet q6-8h PRN; Acetaminophen 325 mg – 1-2 tablets q4h PRN), antibiotics (24 tablets of amoxicillin 500 mg – 1 tablet q8h or clindamycin 300 mg – 1 tablet q8h), and an antimicrobial mouthrinse (0.12% CHX) 15mL BID for 13 days post-operatively . Post-operative diet was limited to soft foods for 1-week, and mechanical oral hygiene was contraindicated for 1-week. Subjects completed a visual analog score (VAS) pain questionnaire at discharge. LANAP therapy conducted on contralateral side within 7-28 days of initial LANAP therapy.

Follow-up Care and Oral Health-Related Impact

Post-operative assessments occurred at 1 week, 2 weeks, 1, 2, 3, 6, and 9 months. One- and two-week follow-ups consisted of extraoral and intraoral examinations during which study personnel noted healing patterns and any treatment complications, verified and adjusted occlusion (PRN attending periodontist), and received completed daily VAS questionnaire forms. One-month follow-ups included impressions for an occlusal guard and full mouth supragingival polishing with prophy cup and paste. The two-month follow-up included occlusal adjustment, as needed, and delivery of the occlusal guard. The 3-, 6-, 9-month follow-up appointments consisted of periodontal maintenance and oral hygiene instruction. Oral Health-Related Impact Profile-14 (OHIP-14) Questionnaires were completed at baseline and at 6- and 12-month follow-up appointments.

Statistical Analysis

An a priori power analysis calculated a required sample size of 30 subjects. Considered parameters included an effect size of 0.7mm, acceptable probability of committing a type I error of 5%, and a required probability of avoiding type II error at 80%. Initial sample size calculations approximated a sample of size 23. However, to account for 25% attrition, an overall sample size of 30 was determined.

Although not reported in this thesis, significant differences between baseline, 6-, and 12-month clinical outcomes (e.g., probing depth, clinical attachment level, gingival bleeding on probing, plaque score, gingival purulence, gingival recession, tooth mobility, fremitus, and furcation involvement) will be determined using a Students t-test or repeated measures analysis of variance (ANOVA) and chi-square analysis for continuous

and categorical outcomes, respectively. Subject-reported OHIP-14 outcomes were compared between baseline, 6-, and 12-month evaluations.

CHAPTER 3: Results

Eight subjects underwent right-side and left-side LANAP treatment. Two subjects completed the 12-month follow-up; six are currently in the process of completing the protocol follow-up timeline. All subjects demonstrated evidence of healing with no adverse effects observed.

BASELINE DATA

Baseline demographic data is listed in Table 2. Mean age was 51.3 years and ranged from 43 to 58 years. Baseline mean probing depth was 3.37 ± 0.46mm, mean clinical attachment level was 2.83 ± 0.31mm, and BOP was 39.4%.

OHIP-14 QUESTIONNAIRE DATA

OHIP-14 questionnaire summary data is listed in Table 3 with negative score changes ($-\Delta_{score}$) signifying beneficial perception adjustments. Comparing 6-month to baseline response data, the change in OHIP-14 scores ranged from 0 to -2. Questionnaire categories that demonstrated improved perceptions were Physical Pain ($\Delta_{score} = -1.5$), Psychological Discomfort ($\Delta_{score} = -1.5$), Psychological Disability ($\Delta_{score} = -1.5$), Physical Disability ($\Delta_{score} = -1.0$) , and Social Disability ($\Delta_{score=} -0.5$). Functional Limitations and Handicap categories experienced no changes ($\Delta_{score=} 0$).

VAS PAIN SCORES

For left- and right-side treatment, VAS post-operative pain scores ranged from 0 (none) to 7 (severe). The mean pain score per each post-operative day following left-side treatment was 3.67, 2.33, 1.00, 0.50, 0.5, 0.167, and 0.167 for post-operative days 1 to 6,

respectively. (**Figure 1**) Overall, the mean VAS pain score was 1.19 ± 1.32 for the left-side. The mean pain score per each post-operative day following right-side treatment was 4.5, 3.00, 0.83, 0.50, 0.5, 0.167, and 0 for post-operative days 1 to 6, respectively. (**Figure 2**) Overall, the mean VAS pain score was 1.31 ± 1.74 for the right-side. There was no significant differences in mean VAS pain scores between right- and left-sided data ($p = 0.8880$).

PERIODONTAL CLINICAL FINDINGS

Two subjects completed the full 12-month study course and were insufficient to conduct trend analysis.

CHAPTER 4: Discussion

The purpose of this 12-month, single-center study was to evaluate the effect of LANAP therapy on periodontal disease. Due to this study's interim status, the primary objective of this report was to analyze the change in subject-reported outcomes within 6 months post LANAP therapy. Subjective subject-reported outcomes demonstrated mild VAS pain scores of 1.19 ± 1.32 and 1.31 ± 1.74 on average for the left and right sides, respectively, with overall pain scores diminishing to a rating of <1.00 by day 2 post-operatively. Subjects noted significant perception improvements in physical pain, physical disability, psychological discomfort, psychological disability, and social disability.

The subject-reported outcomes in this study are commiserate with studies assessing similar outcomes. Sun et al. in 2020 evaluated differences in reported post-operative pain following conventional periodontal regeneration surgery with and without the addition of combined Nd:YAP laser therapy (Sun et al., 2020). In their findings, significantly lower post-operative VAS pain levels were demonstrated in the Nd:YAP group at 24 hours (2.44±0.28 vs. 4.27±0.19) and 72 hours (1.30±0.14 vs. 2.52±0.23) respectively. Comparatively, the average reported pain level in this study was similar and even slightly less than that reported by Sun et al. 2020, and although subjects ranged up to as high as a pain score of 7.0 on the day of LANAP therapy, on average post-operative pain levels were mild to none in all cases within 48 hours of treatment.

Regarding improvements in oral health perception, similar findings are demonstrated in the literature following periodontal therapy. In a study by Sonnenschein et al. 2018, subjects who were fully adherent to their periodontal maintenance programs

demonstrated improved OHIP-14 scores relative to partially-adherent, insufficiently adherent, and non-adherent subjects (Sonnenschein et al., 2018). Additionally, in their study, the categories of 'physical pain' and 'psychological discomfort' demonstrated the highest change in scores, which corresponds to the data found in the current study. In another study by Brauchle et al. 2013, the impact of periodontal disease and therapy on oral-health related quality of life was similarly evaluated. Subjects with PD >7mm had significantly higher baseline OHIP-14 scores (OHIP-14 score =14) relative to a non-periodontitis control group (OHIP-14 score = 2) and periodontitis subjects with PD up to 7mm (OHIP-14 = 6) (Brauchle et al., 2013). This finding is furthered supported by the change in OHIP seen following therapy; in subjects with PD up to 7mm, overall OHIP-14 scores decreased by 2; meanwhile, subjects with PD >7mm at baseline experienced a decrease in OHIP-14 score by 8 points overall.[23] This case severity dependent post-operative change in OHIP-14 scores as reported by Brauchle et al. was similarly demonstrated in the current study, suggesting that there is an association between disease severity status and a subject's perception of their oral health-related quality of life. Accordingly, treatment impact was expected (and seen) to be linearly associated with disease severity at diagnosis. The more severe the disease presentation, the greater the expected impact on subject post-operative OHIP-14 scores.

The findings in this study were limited by the current matriculation quantity. The sample size in this report included 8 subjects in various stages of the 12-month treatment protocol, less than half of intended study population size. Continued subject enrollment will resolve issues associated with the currently limited sample size.

Another potential limitation towards reaching the goal of 30 subjects was the inclusion and exclusion criteria. Regarding inclusion criteria, LANAP is an inherently strict protocol that requires the subject to be able to complete full-mouth therapy within 1 month and remain available for follow-up visits and a final re-examination appointment at 12 months. As such, acceptance of an ideal study candidate might be declined simply based on a lack of long-term availability for care. Furthermore, availability is difficult to guarantee and project out for an active-duty military, retiree, and dependent-based subject population. Likewise, the exclusion criteria also limited potential subject enrollment since subjects that received periodontal surgery within the last 12 months, non-surgical periodontal therapy within the last 3 months, and those with dental implants or acute periodontal infections were excluded from participation. Typically, subjects with a known diagnosis of generalized stage II-IV periodontitis are likely to be already receiving regular or even sporadic periodontal care, which in the confines of this study excluded their participation. Partially edentulous subjects receiving implant replacement therapy, which is a commonly selected treatment option (Elani et al., 2018), were also excluded from the study.

Although the current inclusion and exclusion criteria restricted and continues to restrict the size of this study's recruitment population, full evaluation of the LANAP protocol necessitates the inclusion and exclusion criteria as prescribed. LANAP is a prescribed protocol and must be strictly followed in order to achieve internal reliability and to maximize treatment outcomes. In order to parse out the true effect of LANAP on treatment outcomes, subjects were required to be available for all follow-up assessments

and outside the treatment window of conventional surgical and non-surgical periodontal therapy.

Favorable future results of the current study have potentially far-reaching treatment effects in favor of LANAP therapy. Conventional quadrant-based osseous surgery for the treatment of periodontal disease requires up to four separate surgical appointments, with 3-4 weeks of healing in between each, for a total of 3-4 months of active therapy. Whereas the use of LANAP allows for complete full-mouth periodontal surgical treatment within 1 month and as quickly as within 2 weeks (excluding follow-on maintenance appointments). Additionally, the loss of attachment due to periodontal disease results in an unpredictable hard and soft tissue topography which may require several different treatment modalities, to include non-surgical therapy, pocket reduction surgery, and guided tissue regeneration. Conventionally, these may require separate appointments since the methodologies can not to be combined into a single procedure, leading to multiple surgical interventions. LANAP combines components of all these treatments within its treatment protocol, allowing for multimodal therapy in a single intervention and eliminating the need for multiple procedures.

Since this study population was limited to active-duty service members, military retirees, and dependents, it is therefore pertinent to discuss the direct impacts LANAP therapy could have on this specific population. Two items of discussion inherent to this population are the potential for inconsistent dental care due to assignment location changes and the military's dental readiness classification scheme. Dental care and the provision of definitive treatment for service members can be adversely affected by the perpatetic nature of the military. Coupled with this is the requirement that members must

be in a dental health status that indicates no active dental disease. Considering these factors, LANAP therapy could allow for the provision of definitive surgical periodontal therapy over a significantly shortened treatment timeline, expanding access to care fleetwide and increasing overall dental health leading to increased member readiness for global deployment.

CHAPTER 5: Conclusions

This report examined subject reported data following LANAP therapy over a treatment period of 12 months. Subject-reported outcomes revealed minimal post-operative pain over the course of the week immediately following each side of treatment respectively, along with continued improvements in subjects' subjective perceptions of oral health as measured by OHIP-14 data.

Table 1. 12-month LANAP Therapy Timeline

Appointment	Events
1st Appt (E1)	Initial evaluation, periodontal charting, x-rays (FMX), Treatment plan presentation, enrollment of subject in study Subject fills out baseline OHIP-14 form (at home)
2nd Appt (L1) - Day 0: LANAP surgery	First half mouth LANAP therapy, Subject given 1st VAS questionnaire to take home
3rd Appt (P1) - 7-14 days s/p L1	Post-op for first side half mouth, Occlusal adjustment first side, 1st VAS questionnaire collected
4th Appt (L2) - Day 7-28: LANAP surgery	Second half mouth LANAP therapy (can be concurrent with P1) Subject given 2nd VAS questionnaire to take home
5th Appt (P2) - 7-14 days s/p L2	Post-op and occlusal adjustments, 2nd VAS questionnaire collected
6th Appt (P3) - 1 month s/p L2	Supragingival polish, Possible occlusal adjustment, Impressions for nightguard
7th Appt (P4) - 2 months s/p L2	Supragingival polish, Possible occlusal adjustment, Nightguard delivery
8th Appt (P5) - 3 months s/p L2	Perio maintenance (RDH), Possible occlusal adjustment (DDS)
9th Appt (P6) - 6 months s/p L2	Perio maintenance (RDH), Possible occlusal adjustment (DDS), Subject fills out 6-month POT OHIP-14 form (at home)
10th Appt (P7) - 9 months s/p L2	Perio maintenance (RDH), Possible occlusal adjustment (DDS)
11th Appt (E2/P8) - 12 months s/p L2	Periodontal re-evaluation, charting, Perio maintenance (RDH), Possible occlusal adjustment (DDS), Subject fills out 12-month POT OHIP-14 form (at home)

Table 2. Study Demographics

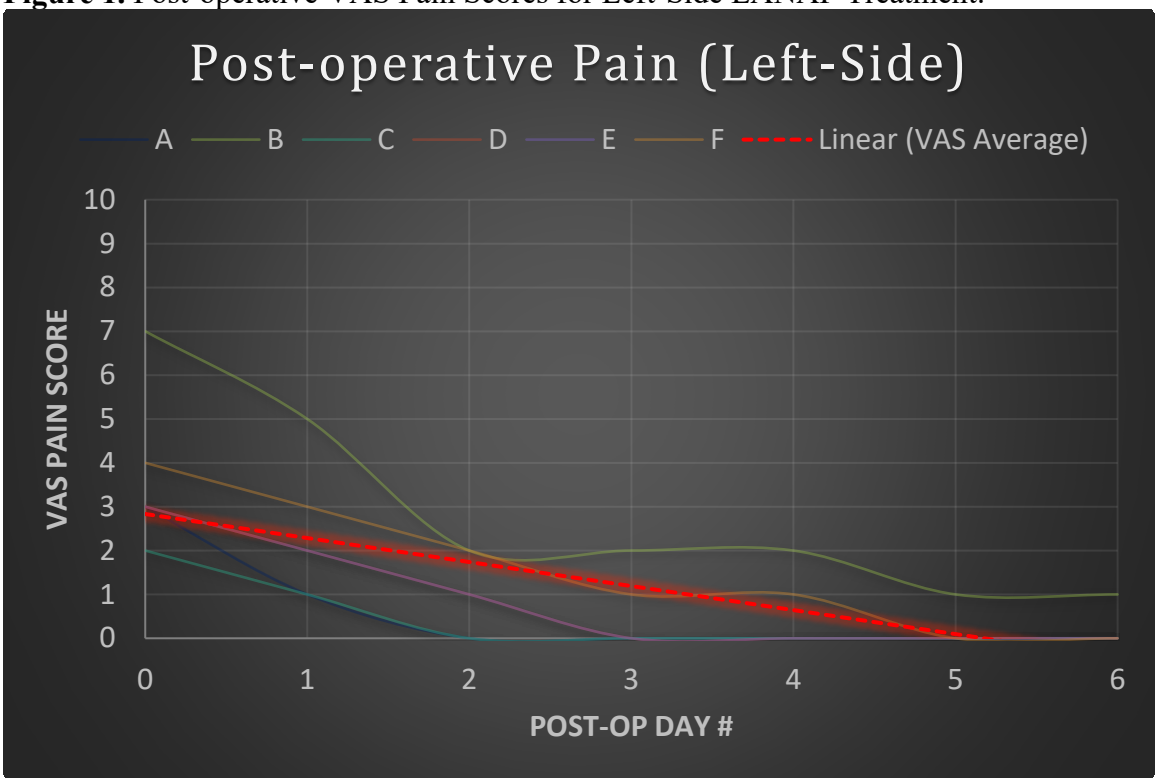
Age	**Mean**	**(SD)**
	51.25	(5.2)
	N	**(%)**
Sex		
Male	6	(75%)
Female	2	(25%)
Race		
Caucasian	5	(63%)
African American	2	(25%)
Asian	1	(13%)
Smoking		
Never	6	(75%)
Minimal	1	(13%)
Former	1	(13%)
Diabetic Status		
Not Diabetic	7	(88%)
Type I	1	(13%)
BMI		
Normal	6	(75%)
Overweight	2	(25%)

No subject reported inflammatory bowel disease, osteoporosis, bisphosphonate use, or any form of arthritis.

Table 3. Average change in OHIP-14 Scores between Baseline and 6-months

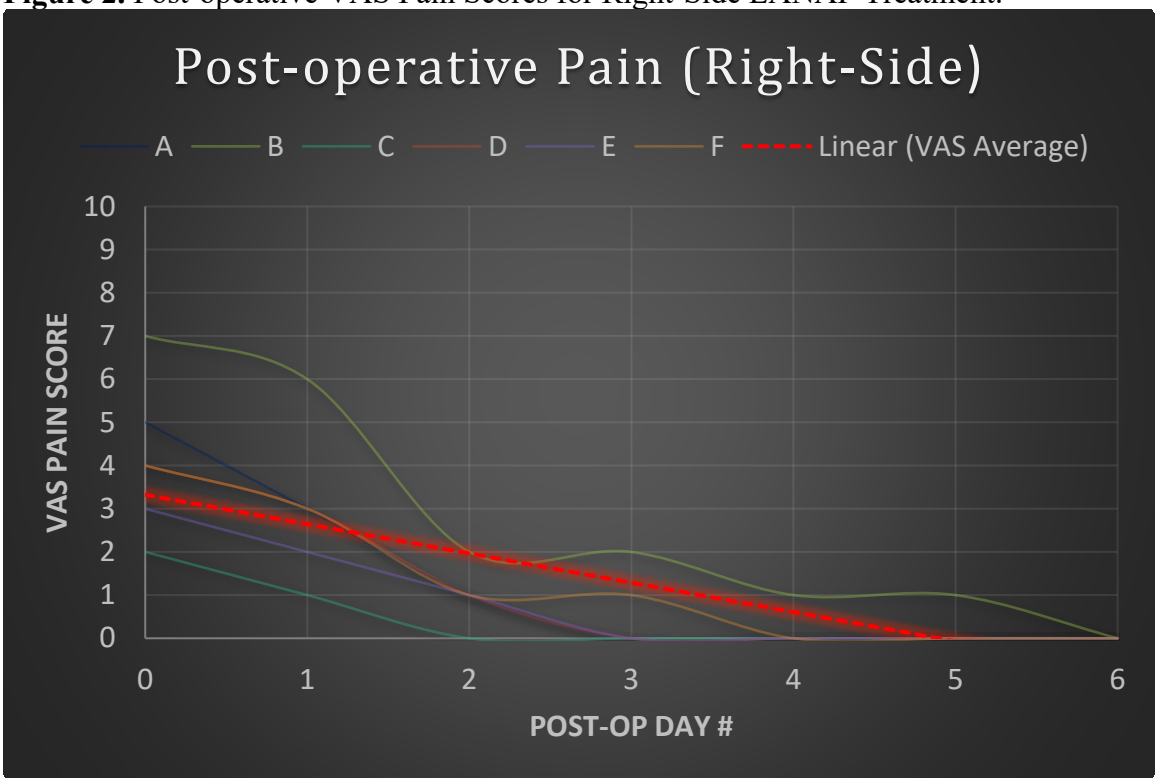
Question Category	Question Topic	Δ in OHIP-14 score at 6 months
Physical Pain	*Painful aching in mouth?*	-1.5
	Uncomfortable to eat?	-0.5
Psychological Discomfort	*Self-conscious teeth/mouth?*	-1.5
	Felt tense because of oral problems?	-0.5
Psychological Disability	*Difficult to relax because of oral problems?*	-1.5
	Embarrassed because of oral problems?	-0.5
Physical Disability	*Had to interrupt meals because of oral problems?*	-1.0
	Diet unsatisfactory because of oral problems?	-0.5
Social Disability	*Irritable with other people because of oral problems?*	-0.5
	Difficulty in doing usual jobs because of oral problems?	-0.5
Functional Limitations	*Trouble pronouncing words?*	-
	Sense of taste worsened?	-
Handicap	*Life less satisfying because of oral problems?*	-
	Unable to function because of oral problems?	-

Figure 1. Post-operative VAS Pain Scores for Left-Side LANAP Treatment.



VAS pain scale: 0= none; 1-3= mild; 4-6= moderate; 7-10= severe. Daily post-operative pain assessments are plotted for days 1-6 post-operative. Letters A through F represent study subjects and the dotted red line represents a linear regression of pain scores. Pain decreased linearly from day 1 to 6.

Figure 2. Post-operative VAS Pain Scores for Right-Side LANAP Treatment.



VAS pain scale: 0= none; 1-3= mild; 4-6= moderate; 7-10= severe. Daily post-operative pain assessments are plotted for days 1-6 post-operative. Letters A through F represent study subjects and the dotted red line represents a linear regression of pain scores. Pain decreased linearly from day 1 to 6.

APPENDIX A

Figure A1. Baseline Oral Health-Related Impact Profile Questionnaire (OHIP-14)

OHIP-14 FORM (Baseline) **Patient #_____**	**Please circle one number for each question.** **Scale:** 0 = never, 1 = hardly ever, 2 = occasionally, 3 = fairly often, 4 = very often				
Functional limitations					
Have you had trouble *pronouncing any words* because of problems with your teeth, mouth or dentures?	0	1	2	3	4
Have you felt that your *sense of taste* has worsened because of problems with your teeth, mouth or dentures?	0	1	2	3	4
Physical pain					
Have you had *painful aching* in your mouth?	0	1	2	3	4
Have you found it *uncomfortable to eat any foods* because of problems with your teeth, mouth, or dentures?	0	1	2	3	4
Psychological discomfort					
Have you been *self-conscious* because of your teeth, mouth, or dentures?	0	1	2	3	4
Have you *felt tense* because of problems with your teeth, mouth or dentures?	0	1	2	3	4
Physical disability					
Has your *diet been unsatisfactory* because of problems with your teeth, mouth, or dentures?	0	1	2	3	4
Have you had to *interrupt meals* because of problems with your teeth, mouth, or dentures?	0	1	2	3	4
Psychological disability					
Have you found it *difficult to relax* because of problems with your teeth, mouth, or dentures?	0	1	2	3	4
Have you been a bit *embarrassed* because of problems with your teeth, mouth, or dentures?	0	1	2	3	4
Social disability					
Have you been a bit *irritable with other people* because of problems with your teeth, mouth, or dentures?	0	1	2	3	4
Have you had *difficulty doing your usual jobs* because of problems with your teeth, mouth, or dentures?	0	1	2	3	4
Handicap					
Have you felt that life in general was *less satisfying* because of problems with your teeth, mouth, or dentures?	0	1	2	3	4
Have you been *totally unable to function* because of problems with your teeth, mouth, or dentures?	0	1	2	3	4

Figure A2. 6-month Oral Health-Related Impact Profile Questionnaire (OHIP-14)

OHIP-14 FORM (6 mos. POT) **Patient #_____**

Please circle one number for each question.

Scale: 0 = never, 1 = hardly ever, 2 = occasionally, 3 = fairly often, 4 = very often

Functional limitations					
Have you had trouble *pronouncing any words* because of problems with your teeth, mouth or dentures?	0	1	2	3	4
Have you felt that your *sense of taste* has worsened because of problems with your teeth, mouth or dentures?	0	1	2	3	4
Physical pain					
Have you had *painful aching* in your mouth?	0	1	2	3	4
Have you found it *uncomfortable to eat any foods* because of problems with your teeth, mouth, or dentures?	0	1	2	3	4
Psychological discomfort					
Have you been *self-conscious* because of your teeth, mouth, or dentures?	0	1	2	3	4
Have you *felt tense* because of problems with your teeth, mouth or dentures?	0	1	2	3	4
Physical disability					
Has your *diet been unsatisfactory* because of problems with your teeth, mouth, or dentures?	0	1	2	3	4
Have you had to *interrupt meals* because of problems with your teeth, mouth, or dentures?	0	1	2	3	4
Psychological disability					
Have you found it *difficult to relax* because of problems with your teeth, mouth, or dentures?	0	1	2	3	4
Have you been a bit *embarrassed* because of problems with your teeth, mouth, or dentures?	0	1	2	3	4
Social disability					
Have you been a bit *irritable with other people* because of problems with your teeth, mouth, or dentures?	0	1	2	3	4
Have you had *difficulty doing your usual jobs* because of problems with your teeth, mouth, or dentures?	0	1	2	3	4
Handicap					
Have you felt that life in general was *less satisfying* because of problems with your teeth, mouth, or dentures?	0	1	2	3	4
Have you been *totally unable to function* because of problems with your teeth, mouth, or dentures?	0	1	2	3	4

Figure A3. 12-month Oral Health-Related Impact Profile Questionnaire (OHIP-14)

OHIP-14 FORM (12 mos. POT) **Patient #_____**

Please circle one number for each question.

Scale: 0 = never, 1 = hardly ever, 2 = occasionally, 3 = fairly often, 4 = very often

Functional limitations					
Have you had trouble *pronouncing any words* because of problems with your teeth, mouth or dentures?	0	1	2	3	4
Have you felt that your *sense of taste* has worsened because of problems with your teeth, mouth or dentures?	0	1	2	3	4
Physical pain					
Have you had *painful aching* in your mouth?	0	1	2	3	4
Have you found it *uncomfortable to eat any foods* because of problems with your teeth, mouth, or dentures?	0	1	2	3	4
Psychological discomfort					
Have you been *self-conscious* because of your teeth, mouth, or dentures?	0	1	2	3	4
Have you *felt tense* because of problems with your teeth, mouth or dentures?	0	1	2	3	4
Physical disability					
Has your *diet been unsatisfactory* because of problems with your teeth, mouth, or dentures?	0	1	2	3	4
Have you had to *interrupt meals* because of problems with your teeth, mouth, or dentures?	0	1	2	3	4
Psychological disability					
Have you found it *difficult to relax* because of problems with your teeth, mouth, or dentures?	0	1	2	3	4
Have you been a bit *embarrassed* because of problems with your teeth, mouth, or dentures?	0	1	2	3	4
Social disability					
Have you been a bit *irritable with other people* because of problems with your teeth, mouth, or dentures?	0	1	2	3	4
Have you had *difficulty doing your usual jobs* because of problems with your teeth, mouth, or dentures?	0	1	2	3	4
Handicap					
Have you felt that life in general was *less satisfying* because of problems with your teeth, mouth, or dentures?	0	1	2	3	4
Have you been *totally unable to function* because of problems with your teeth, mouth, or dentures?	0	1	2	3	4

Figure A4. Visual Acuity Pain Score (Left Side)

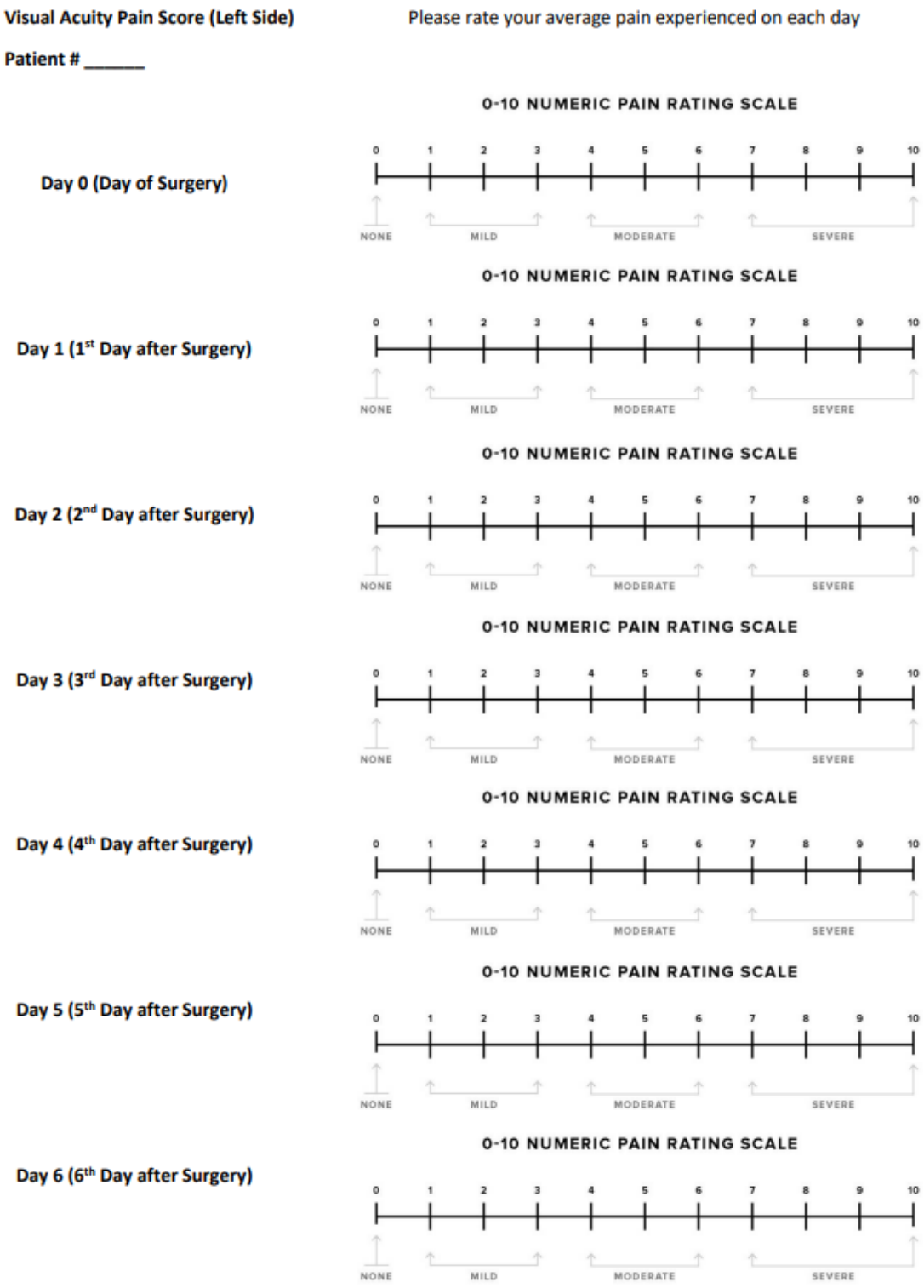


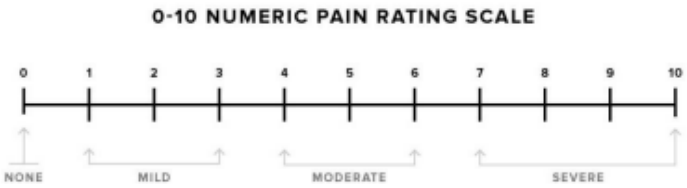
Figure A5. Visual Acuity Pain Score (Right Side)

Visual Acuity Pain Score (Right Side)

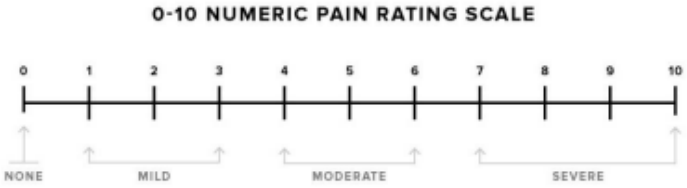
Please rate your average pain experienced on each day

Patient # _____

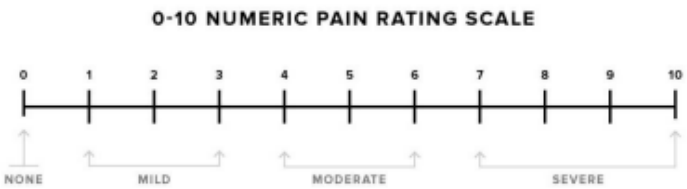
Day 0 (Day of Surgery)



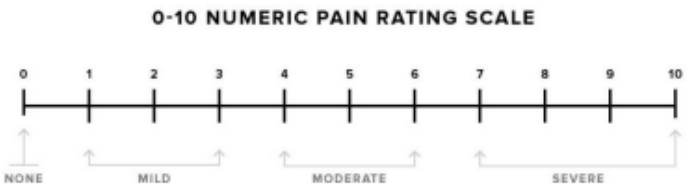
Day 1 (1st Day after Surgery)



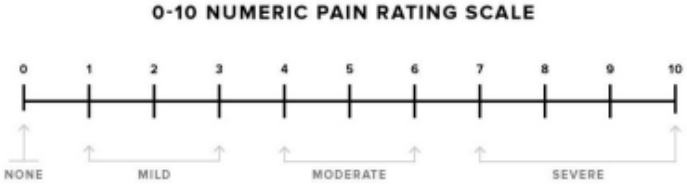
Day 2 (2nd Day after Surgery)



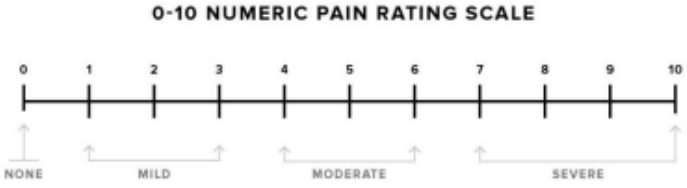
Day 3 (3rd Day after Surgery)



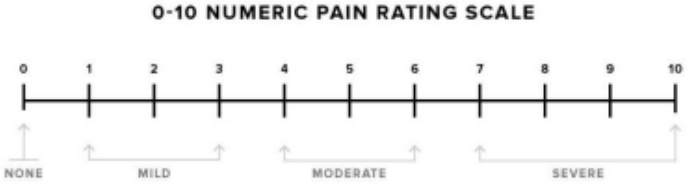
Day 4 (4th Day after Surgery)



Day 5 (5th Day after Surgery)



Day 6 (6th Day after Surgery)



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