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EFFICACY OF LOW-LEVEL LASER THERAPY IN TREATMENT OF TEMPOROMANDIBULAR MYALGIA: A RANDOMIZED CONTROLLED TRIAL.

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A mini thesis submitted in partial fulfilment of the requirements for the degree Master of dental surgery in Prosthodontics, Department of Restorative Dentistry, University of the Western Cape.

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KEYWORDS

Chronic Pain Intensity

Interference Score

Jaw Functional Limitation

Low-level laser therapy

Maximum Pain-free Opening

Myalgia

Myofascial Pain Syndrome

Photobiomodulation

Research Diagnostic Criteria for TMD

Temporomandibular Disorder

ABSTRACT

EFFICACY OF LOW-LEVEL LASER THERAPY IN TREATMENT OF TEMPOROMANDIBULAR MYALGIA: A RANDOMIZED CONTROLLED TRIAL.

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MChD Mini-thesis, Department of Prosthodontics, University of the Western Cape.

Background:

Objective: The objective of the study was to compare pain and functional limitation of temporomandibular myalgia patients, before and after low-level-laser treatment (LLLT).

Methods: This was a prospective, randomized, placebo-controlled, triple-blinded clinical study. Patients diagnosed with temporomandibular myalgia according to the DC/TMD protocol were recruited from the TMD clinic of the Mitchell's Plain Oral Health Centre. Treatment was performed using diode laser (Sirolaser, Dentsply Sirona). The 3 regions of the masseter and temporalis muscles were treated bilaterally with a dose of 8J/cm^2 per region. Pain and function were assessed using pain-free opening, numeric rating scales (NRS), Characteristic Pain Intensity Scores (CPIS), Interference Score (IS), and Jaw Functional Limitation Scale (JFLS) at the first and last LLLT and at 4-week recall (intervals 1, 2, 3). Statistical analysis was done by means of explorative categorical principal and multivariate interdependent analysis.

Results: Seventeen (15 females) of the 19 patients completed the LLLT (89% retention). Mean pain-free opening increased for both treatment (A) and placebo (B) group (35.0 mm to 41.2 mm; 34.8 mm to 37.9 mm respectively). This increase was not statistically significant between groups. All patients from group A reported less (n = 7) or similar pain (n = 2) with opening after treatment. For group B, 4 patients reported improvement, 1 no change and 3 worse pain with opening after treatment. Mean CPIS for groups A and B for the 3 time intervals were 69.63, 47.41, 34.07 and 70.42, 55.71, 52.92 respectively. Mean IS were 53.67, 32.22, 25.56 and 49.88, 40.48, 22.88 respectively. Global scores calculated from the JFLS for groups A and B for the 3 time intervals were 4.368, 3.380, 3.189 and 4.760, 4.396, 5.046 respectively. No effect between groups and no effect of time was statistically significant.

Conclusions: Within the limitations of this trial, the laser group reported more improvement in mobility, pain experience and function but these improvements were not statistically significant.

DECLARATION

I declare that "*Efficacy of low-level laser therapy in treatment of temporomandibular myalgia: a randomized controlled trial*'' **is my own work, that it has not been submitted for any degree or examination in any other university, and that all the sources I have used or quoted have been indicated and acknowledged by complete references.**

Name: Neo Eric Netshilindi

Signature: 

Date signed: 27 November 2021

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DEDICATION

- To my late father Bernard Netshilindi (Monye selete sa ha Maimela - Ndou ya Tshilindi). Ndaa.
- To my mother Magauta Netshilindi for your endless prayers and words of encouragement.
- To my sister and brother-in-law, Mapula and Tshifiwa Mahosi for always being one call away.
- To the SANDF for affording me the opportunity to further my studies.

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LIST OF ABBREVIATIONS

ACh	Acetylcholine
ATP	Adenosine triphosphate
CcO	Cytochrome c oxidase
CPI	Chronic Pain Intensity
GCPS	Graded Chronic Pain Scale
IS	Interference Score
JFLS	Jaw Functional Limitation Scale
LLLT	Low-level laser therapy
NIR	Near infrared
NRS	Numeric rating scale
RDC/TMD	Research Diagnostic Criteria for Temporomandibular Disorders
ROS	Reactive oxygen species
TENS	Transcutaneous nerve stimulation
TMD:	Temporomandibular disorder
TMJ	Temporomandibular joint

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CHAPTER 1: LITERATURE REVIEW

1.1 Introduction

Temporomandibular disorders (TMDs) are a group of disorders that affect the temporomandibular joint (TMJ), often presenting as pain and dysfunction related to the masticatory system. Symptoms result as disease processes affect the muscular and or articular components of the TMJ. According to Slade *et al.* (2016), approximately 4% of people experience TMD symptoms yearly. Upon follow up, 49% of those people may have recurrent symptoms.

Myofascial pain syndrome is defined as pain in any skeletal muscle or muscle fascia that involves trigger points (Jafri, 2014). Trigger points are hyper-irritable spots, usually within the firm band of muscle or in the muscle fascia (Gaynor and Muir, 2014). They are painful on compression and may commonly result in referred pain, motor dysfunction, and even autonomic phenomena.

The International Network on Orofacial Pain and Related Disorders Methodology published a classification and developed diagnostic criteria for TMD conditions (DC/TMD) (*Osterlund et al.*, 2018). The DC/TMD protocol is based on a set of validated instruments for clinical and research applications and assists in the diagnosis of the 11 most common TMD conditions. The term "myalgia" is the diagnostic term in the DC/TMD classification that refers to muscle pain. While the term "myofascial pain" in the same classification, is a subtype of myalgia and is defined by the spread of pain beyond the site of palpation but within the borders of the muscle examined (Schiffman, 2014). Sometimes these terms may be interchanged but if we focus on the definitions provided by the DC/TMD it becomes evident that these terms describe different clinical presentations of pain. Nonetheless, these conditions represent the most commonly diagnosed forms of TMD.

Various treatment options have been proposed for the management of myofascial TMD; however, scientific evidence evaluating the efficacy of treatment modalities has been described as being of moderate strength and offers limited confidence to the practitioner (Abrahamsson *et al.*, 2020). Some issues that were raised with regards to previous studies are: heterogeneity, small sample size and high risk of bias. It is therefore advised that conservative methods are practiced in the management of TMDs.

Low-level laser therapy (LLLT) refers to the Class IIIb laser group (less than 600 mW of power); It does not burn the skin or underlying tissue, while the depth of penetration is determined by wavelength (Pandeshwar *et al*, 2016); LLLT is a non-invasive, non-thermal, safe, and biostimulative treatment modality (Melis, Di Giosia and Zawawi, 2012). The exact mechanisms of action are unknown, however, there are numerous proposed mechanisms through which LLLT produces its effects in the treatment of myofascial pain and dysfunction. One suggested mechanism is that LLLT improves local microcirculation, by increasing oxygen supply to the hypoxic cells that are related to the trigger point area (Simunovic, 1996; Kiralp *et al.*, 2006).

According to cell and animal studies, LLLT may produce positive biological effects on the soft tissue after injury through two possible ways: (1) LLLT induced angiogenesis that occurs as a result of increased growth factor secretion and formation of collateral vessels in the injured tissue; and (2) LLLT modulates biochemical inflammatory markers and produces local anti-inflammatory effects in cells and soft tissue (Bjordal *et al.*, 2003).

1.2 Epidemiology

Among patients with orofacial pain, the most frequent diagnoses are: myofascial TMD pain (single or multiple diagnoses) (42%), disc displacement with reduction (32.1%) and arthralgia (30%) (Poveda-Roda *et al.,* 2012). Myofascial TMD, disc displacement, and degenerative disorders were found to occur with greater frequency among populations in the rural area compared to those leaving in urban areas (Balke *et al.*, 2010). Using the RDC/TMD, a meta-analysis that included 21 epidemiological studies with a total of 3,463 subjects experiencing orofacial pain, made the conclusion that the overall prevalence for myofascial TMD pain was 45.3%, whereas the prevalence of disc displacement was 41.1% (Manfredini *et al.*, 2011).

Studies based on general populations including a total of 2,491 subjects, pooled into a systematic review, generated an overall prevalence of 9.7% for myofascial TMD and 11.4% of disc displacement.

Patients with myofascial TMD are known to suffer from numerous other non-related health conditions and represent a group of people who are more likely to have increased use of the healthcare system (Yost *et al.*, 2020). Myofascial TMD was found to be commonly associated with entities, such as headaches (Manfredini *et al.*, 2011). Individuals experiencing myofascial

TMD were more likely to suffer from conditions such as chronic daily migraine and tension-type headache when compared with individuals without TMD pain (Gonçalves *et al.*, 2011).

Prognosis of myofascial TMD was seen to be controversial (Rammelsberg *et al.,* 2003). They reported inconsistent progression of myofascial TMD among subjects in a 5-year longitudinal study. This study included data of 235 patients that were either referred for treatment of active TMD or from a general population initially presented without TMD. The patients received treatment when needed therefore additional data could be collected at treatment follow-up and recall visits. Over the 5 years, about 31% of the cases were found to be persistent, 33% being remittent and 36% recurring . Furthermore, it was found that, significant predictors of persistent vs remitted and recurrent cases were: baseline pain frequency, number of painful palpation sites, and total number of body sites with pain. No predictors that distinguished remission vs recurrence were identified.

The aetiology and pathology of TMD are still under debate. Currently, evidence seems to point at multiple factors acting at the same time. Therefore, the possible factors related to development of myofascial TMD pain are discussed below.

1.3 Aetiology

The exact aetiology of TMDs remains poorly understood. Temporomandibular disorders have been associated with numerous initiating, predisposing, and aggravating factors that are either neuromuscular, biopsychosocial or neurobiological in nature (Demirkol *et al.*, 2015).

Possible causative factors include occlusal abnormalities, orthodontic treatment, bruxism and orthopaedic instability, macrotrauma and microtrauma, joint laxity and exogenous oestrogen. Psychological factors that include stress, mental tension, anxiety or depression have also been suggested to cause TMD (Chisnoiu *et al.*, 2015).

Factors that lead to the onset of symptoms are called Initiating Factors, these are primarily related to trauma and inappropriate loading of the masticatory system. Perpetuating factors may include the following: Behavioural factors, Social factors, Emotional factors and Cognitive factors (Chisnoiu *et al.*, 2015).

Predisposing factors are those that alter the masticatory system, elevating risk of development of TMD. These processes could be either pathophysiological, psychological or structural (Chisnoiu *et al.*, 2015).

For disorders of muscular origin, specifically, several theories of aetiology have been proposed that involve trigger point formation, excessive activity of acetylcholine (ACh) and formation of tout bands, local hypoxia and energy depletion, peripheral and central sensitization (Kalladka *et al,* 2021).

Trigger points are tender spots occurring in taut bands of muscle fibres. These are formed when muscular functional demands exceed muscle adaptation. Trigger points have been identified as initiators of muscular pain in TMDs (Kalladka *et al*, 2021).

Acetylcholine formation has been shown to be upregulated as a result of peripheral sensitisation. Excess availability of ACh leads to prolonged muscle contraction and ultimately the formation of taut bands (Kalladka *et al,* 2021).

Local hypoxia occurs as result of prolonged muscle contraction that leads to restriction of microvascular blood flow. Furthermore, local hypoglycaemia, decrease of ATP production and accumulation of metabolic waste products occur as result of decreased blood flow. These states further prolonging of muscular contraction and feeds into a painful cascade (Kalladka *et al,* 2021).

The role of the nociceptive system in myofascial TMD has been investigated through assessment of trigeminal and extra-trigeminal pain sensitivity in patients with TMJ pain. For such cases, trigeminal hypersensitivity is considered to be a manifestation of peripheral sensitization whereas extra-trigeminal hypersensitivity would be a manifestation of central sensitization (Fernandez-de-las-Penas and Svensson, 2015). Literature exists that supports the idea that both sensitization processes could be implicated in the disease process of myofascial TMD (Sarlani, 2003).

The clinical role of sensitization mechanisms in myofascial TMD has been supported by the fact that two categories of patients with TMD have been identified: a sensitive group and insensitive group. This classification is based on the “Fibromyalgia tender point count” that focuses on the number of tender points used to diagnose fibromyalgia syndrome (Pfau, 2009).

1.4 Clinical features

Temporomandibular disorders are conditions that affect the masticatory muscles, the temporomandibular joint (TMJ) and other associated surrounding structures. The classical clinical features of TMDs are: pain related to the muscles or joint, TMJ sounds and restriction

of movement, deviation or displacement of the mandible on opening and closing movements (Fernandez-de-las-Penas and Svensson, 2015). Patients may complain of spontaneous facial pain or orofacial pain that is felt during mandibular movements.

Patients may experience pain in the masseter muscle that spreads to the temporalis muscle. This is a cardinal symptom of patients diagnosed with myofascial TMD pain; but not exclusive of this condition (Alonso-Blanco *et al.*, 2012). Alonso-Blanco and colleagues managed to determine the anatomical sites of the orofacial region where symptoms would typically occur, in women with myofascial TMD, using patient-based pain drawings. They found the symptoms to be mainly located in the lateral part of the masseter muscle (Alonso-Blanco *et al.*, 2012).

Another typical sign may be tenderness or pain on palpation of the masticatory muscles and joints. Masticatory muscles are easily accessible to manual palpation, and authors have standardized the areas that should be explored, in protocol that aims to solicit pain through application of pressure. The recommended pressures applied during examination are: 1 kg for 2 seconds (applied to the masseter and temporalis muscle) and 0.5 kg to the TMJ (Schiffman, 2014). The sign of (increased pain on palpation) is suggestive of the involvement of sensitization mechanisms and the possible presence of myofascial trigger points (La Touche *et al.*, 2009).

Additionally, the clinical features of myofascial TMD include parafunctional habits, tooth clenching and restricted jaw movement (Poveda Roda *et al.*, 2007). The mandibular movement parameters that are usually clinically evaluated include maximum opening, lateral excursions to both sides, as well as maximum protrusion. However, restricted mandibular movements may not necessarily provide information leading to any specific diagnosis as multiple reasons can be related to impaired movement (e.g., TMJ ankyloses, muscle contracture, Eagle syndrome). Other clinical signs such as TMJ clicking are usually more associated to TMD of joint origin, e.g., displaced discs.

1.5 Diagnoses and classification

The International Network for Orofacial Pain and Related Disorders Methodology published a classification and developed diagnostic criteria for TMD conditions (DC/TMD) (Österlund et al., 2018). The DC/TMD protocol is based on a set of validated instruments for clinical and research applications and assists in the diagnosis of the 11 most common TMD conditions. Diagnosis is based on a complete dental and medical history, extra-oral and intraoral

examination and the Axis I and Axis II instruments incorporated in the DC/TMD protocol (Schiffman *et al.*, 2014).

The Axis I instruments consist of a TMD screening form (validated to detect the most common pain-related TMD), valid diagnostic criteria that characterises the most common symptoms (Schiffman *et al.*, 2014) and a comprehensive examination routine. The Axis II protocol consists of a series of self-assessment instruments. They provide information on pain intensity, pain-related disability, psychological distress, jaw functional limitations and parafunctional behaviours, comorbid pain-conditions and a pain drawing to assess pain locations (Schiffman *et al.*, 2014). These validated instruments allow for the identification of patients with conditions that range from simple to complex TMD presentations (Schiffman *et al.*, 2014).

1.6 Treatment of temporomandibular disorders

Many treatment strategies have been suggested for TMDs. They range from conservative (self-management, occlusal devices, physical, pharmacological and behavioural therapy) to more invasive surgical treatments. List and Axelsson (2010), in their systematic review of the management of TMDs concluded that the available evidence suggested that occlusal appliances, acupuncture, behavioural therapy, jaw exercises, and postural training could all be effective in the reduction of pain related to TMDs. Furthermore, insufficient evidence was found supporting the effect of electrophysical modalities and surgical therapies. Therefore, the first approach to TMD management should focus on conservative non-invasive interventions (List and Axelsson, 2010).

Non-surgical and surgical treatment strategies were further elaborated by Dimitroulis (2018). He stated that over 90% of TMJ patients could be managed through non-surgical techniques and that these techniques are best applied in combination. The non-surgical strategies that have been described include patient explanation and reassurance, patient education and self-care, medication, jaw physical therapies, occlusal appliance therapy, behavioural therapy, psychotherapy and other therapies (such as chiropractic manipulation) (Dimitroulis, 2018).

1.6.1 Multi-disciplinary patient centred approach

Multimodal care of patients with myofascial TMD has been demonstrated through vast clinical and scientific evidence to be most efficient. This may involve several health care professionals, e.g., dentists, orthodontists, medical doctors, physical therapists, and psychologists.

Treatment interventions should be personalized, patient-centred and include passive and active strategies, active listening, empathy, addressing psycho-social issues such as: depression, anxiety, and catastrophizing, based on clinical findings during the history and examination process (Fernandez-de-las-Penas and Svensson, 2015). Patient-centred care involves sharing the decision-making process between clinicians and patient. Therefore, to educate the patient about the nature of their problems, and the explaining the disease mechanism becomes an integral part of compassionate care (Fernandez-de-las-Penas and Svensson, 2015).

The role of sensitization has been discussed previously. In terms of management, current literature suggests that clinical identification of sensitization and classifying as either sensitive (central sensitization) or non- sensitive (peripheral sensitization) may aid in selecting appropriate treatment modalities, or combinations. This is based on the premise that the presence of central sensitization in TMD patients may negatively influence treatment prognosis (Pfau, 2009).

If a patient is identified to have myofascial TMD that is mediated by peripheral sensitization, specific treatment of the affected tissue and application of exercises and functional activities are encouraged. If it is suspected that the myofascial TMD pain is mainly mediated by a central sensitization, a multimodal strategy consisting of, pharmacological, physical and cognitive approaches, is advocated for (Pfau, 2009).

1.6.2 Physical therapies

Several manual therapies have been suggested to be effective in managing myofascial TMD: 1) joint mobilization targeting mandibular accessory ligaments (Cuccia, Caradonna and Caradonna, 2011), 2) manual therapies aiming at muscle tissues, i.e., myofascial trigger points, 3) mobilization interventions that target the cervical spine, and even postural correction have been applied for the management of TMD pain. However, further studies are needed to assess the efficacy of these strategies (La Touche *et al.*, 2009).

Systematic reviews have not produced strong evidence to support the role of manual therapies. According to McNeely *et al*. al, there are few studies investigating the efficacy of manual therapies for the management of TMD, and also, existing studies have been found to be of low methodological quality (McNeely, Olivo and Magee, 2006a). It was further concluded that the use of manual therapies in combination with active exercises may be effective for reducing pain and improving function in TMD, although more high-quality studies are needed (McNeely, Olivo and Magee, 2006a).

1.6.3 Exercises

Therapeutic exercises are prescribed with the aim of addressing specific TMJ impairments and improving the function of the cranio-cervico-mandibular system. Most exercise programs are designed to produce the following effects: improvement of muscle coordination, relaxing clinically tense musculature, increasing range of motion, as well as to increase muscular contraction strength and proprioception (force-generating capacity) (Fernandez-de-las-Penas and Svensson, 2015).

Scientific evidence for this approach is lacking since, in the studies, the therapeutic exercises are not usually applied alone, but in combination with other conservative procedures (Michelotti *et al.*, 2005; Moraes *et al.*, 2013) . Additionally, several aspects of therapeutic exercise programs such as: intensity, repetition, frequency and duration, need to be clarified in the literature.

1.6.4 Other physical therapy modalities

The electro-physical modalities that are being applied in clinical settings include; shortwave diathermy, transcutaneous electronic nerve stimulation, ultrasound, laser. Objectives of electro-physical modalities are: reduction of inflammation, promoting muscular relaxation, and increase of blood flow through altering capillary permeability (Fernandez-de-las-Penas and Svensson, 2015). However, the scientific evidence surrounding these modalities is conflicting. McNeely *et al*. reported that there was no evidence to support the use of electro-physical modalities for pain reduction in TMD (McNeely, Olivo and Magee, 2006; Chang *et al.*, 2014). On the contrary, a separate meta-analysis noted a moderate effect for the application of LLLT (dosages of 780 and 830 nm) on the masticatory muscles or joint capsule for TMD pain (Chang *et al.*, 2014). It was further noted that there is cause for future research to integrate the application of electro-physical therapies within a multidisciplinary treatment program.

Needling therapies

Various needling therapies such as acupuncture, dry needling as well as botulinum toxin type have been generally applied by clinicians for treatment of TMD pain. A meta-analysis study concluded that acupuncture can significantly reduce pain in the short term for patients suffering from TMD of muscle origin (La Touche *et al.*, 2010). A separate meta-analysis study reported that trigger point dry needling exhibit grade A evidence for pain reduction in upper quadrant syndromes, including myofascial TMD pain, at short-term (Kietrys *et al.*, 2013). Finally,

Ernberg *et al. (2011)*, concluded that Botulinum toxin type A was not efficacious as an adjunct to conservative methods for patients with myofascial TMD pain.

Orthopaedics

Various orthopaedic approaches have been proposed to be clinically effective for the management of TMD pain. According to List and Axelsson (2021), the management of TMD with a stabilization appliance that is worn at night is likely to lead to short-term improvements, compared to no treatment, but the effects when compared with placebo were found to be inconclusive. Hard stabilization appliances were found to be more effective at improving TMD pain in comparison to non-occluding appliance and no-treatment control, although the latter comparison did not reach statistical significance (Fricton *et al.*, 2018). Other types of appliances: soft stabilization appliances, anterior positioning appliances, and anterior bite appliances showed to have limited evidence of efficacy (Fricton *et al.*, 2018). However, a meta-analysis study by Ebrahim *et al.* (2012), concluded that the studies evaluating the pain reduction ability of appliance therapy provide evidence of only moderate confidence due to the level of bias in the included trials. The scientific evidence establishing the role of appliances for patients with TMDs may be somewhat promising but future studies will require larger trials with better safeguards against bias.

1.6.5 Psychological approaches

The complicated task of altering the attitudes, lifestyles, social and the physical environment of individuals remains one of the biggest challenges in long term management of patients experiencing myofascial TMD. This is based on the acceptance of the hypothesis that inappropriate cognitions, emotions, and behaviours that include catastrophizing, hyper-vigilance, avoidance behaviour, and somatization may influence pain.

Individuals that suffer from myofascial TMD are known to exhibit some or all of these psychological problems. It is suggested that, in the initial phase of treatment, patients are educated on pain neurophysiology, aiming at conceptualizing pain for individuals who have inappropriate beliefs about their pain symptoms and complaints. If this is not done, a poor understanding of their pain may result in the development of maladaptive attitudes, cognitions, behaviour and subsequently, a poor compliance to any active exercise program.

Psychological therapies that can be applied to patients with myofascial TMD include: patient education, biofeedback, relaxation training, stress management, and cognitive-behavioural therapy. List & Axelsson (2010) had concluded in a systematic review that these methods were

effective in the overall management of TMD . Cognitive behavioural therapy for chronic pain is believed to be useful in reducing the element of pain catastrophizing, improving pain intensity and physical and psychosocial disability (Turner, Mancl and Aaron, 2006).

1.7 Laser

Low level laser treatment, phototherapy or photobiomodulation employs the use of photons at a non-thermal irradiance to alter biological process (Avci *et al.,* 2013). This technique was discovered following the invention of the laser in the 1960s. First the Ruby laser was invented in 1960, followed by the Hellium-Neon (HeNe) laser in 1961. It was in 1967, when Endre Mester, working at Semmelweis University in Budapest, Hungary, discovered that applying laser to the backs of shaven mice, stimulated faster hair growth. Mester further demonstrated that HeNe laser could stimulate wound healing in mice (Mester *et al.*, 1967; Chung *et al.*, 2012). Soon after that, Mester began applying his findings onto human subjects, using HeNe laser to treat non healing skin ulcers. Today, LLLT is increasingly used in therapeutic procedures to reduce inflammation, oedema, and chronic joint disorders, to promote healing of wounds, deeper tissues, and nerves and to treat neurological disorders and pain.

1.7.1 Mechanisms of low-level laser therapy

Low-level laser therapy involves exposure of cells to red and near infrared (NIR) light and is referred to as low level due to the light energy densities being lower compared to other forms of laser therapy that are used for ablation, cutting and thermal coagulation (Avci *et al.*, 2013). Low-level laser therapy is currently used to treat a variety of conditions; however, its therapeutic use remains controversial for two fundamental reasons. First, the underlying biochemical effects remain poorly understood, so its use is to a great extent, empirical. Second, laser exposure parameters such as the wavelength, fluence, power density, pulse structure, and exposure time of the applied light must be considered for each treatment (Mester *et al.*, 1967).

A suboptimal choice of parameters may reduce the therapeutic effectiveness, or even negative therapeutic outcomes. As a result, many of the published results on LLLT report negative results largely because of inappropriate selection of the light source and dosage. This choice is important as there is a specific optimal dose of light for any particular application, and doses higher or lower than the optimal value may have no therapeutic effect. Moreover, LLLT is characterized by a biphasic dose response, meaning that, lower doses of light are often more beneficial than high doses. According to Posten *et al.* (2005), properties of low-level lasers are:

a) Power output of lasers: 0.001- 0.1 Watts.

b) Wave length: 300-10,600 nm.

c) Pulse rate: 0 - 5000 Hertz (cycles per second).

d) Intensity: 0.01-10 W/cm^2

e) Dose: 0.01 - 100 J/ cm^2.

Laws of photobiology state that in order for a low power visible light to exert any effect on a living biological system, the photons must be absorbed via electronic absorption bands belonging to some molecular photo-acceptors, which are called chromophores (Sutherland, 2002).

The exact biochemical mechanism resulting in the therapeutic effects of LLLT are not yet completely understood. It has been observed that LLLT has a wide range of effects at the molecular, cellular, and tissue levels (Posten, 2005). Evidence suggests that, within the cell, LLLT acts on the mitochondria to increase adenosine triphosphate (ATP) production, modulation of reactive oxygen species (ROS), and the induction of transcription factors (Karu, Pyatibrat and Afanasyeva, 2005) (Chung *et al.*, 2012).

- **Mitochondrial respiration and ATP**

Current research into the mechanism of LLLT is centred around processes of the mitochondria. Cytochrome c oxidase (CcO) is a large multicomponent transmembrane protein that contains a binuclear copper centre (CuA) along with a heme binuclear centre (a3-CuB), both of which facilitate the transfer of electrons from water soluble CcO to oxygen. As a terminal enzyme of the electron /transport chain, CcO plays a vital role in the bioenergetics of a cell (Srinivasan and Avadhani, 2012).

Cytochrome c oxidase has been thought to be the main photoacceptor for the red-Near Infrared (NIR) range in mammalian cells as its absorption spectrum obtained in different oxidation states was shown to be similar to the action spectrum for biological responses to light (Capaldi, 1983; Hamblin, 2007). The absorption of photons by CcO leads to electronically excited states, and consequently can speed up the rate of electron transfer reactions (Yu *et al.*, 1997). More electron transport causes increased production of ATP (Passarella et al, 1984). The light induced increase in ATP synthesis combined with a higher proton gradient lead to an increasing activity of the Na^+/H^+ and Ca^{2+}/Na^+ antiporters, and of all the ATP driven carriers for ions, such as Na^+/K^+ ATPase and Ca^{2+} pumps. ATP is the substrate for adenylcyclase, therefore, the

ATP level will determine the level of cAMP. Both Ca^{2+} and cAMP are very important second messengers. Ca^{2+} regulates most process occurring in humans (muscle contraction, blood coagulation, nerves signal transfer, gene expression) (Hamblin, 2006). Therefore, it is the photoactivation of terminal enzymes, like CcO, that contribute to the activation of the diverse biological cascade that are observed subsequently to laser irradiation.

- **Nitric Oxide and low-level laser therapy**

Nitric oxide (NO) inhibits the activity of CcO (Beltrán, 2000). This may be due to competitive inhibition between NO and O_2 for the reduced binuclear centre **(a3-CuB),** of CcO. This reaction is reversible (Antunes *et al*., 2004). However, it has been proposed that laser irradiation could reverse this inhibition through photodissociating NO from its binding sites (Karu, 2005; Lane, 2006). This dissociation by LLLT is possible because of the coordinate binding being much weaker than a covalent bond. The dissociation of NO from CcO leads to increases the respiration rate (Karu, 2005). This has been shown both in isolated mitochondria and in whole cells (Borutaite, 2000). Therefore, LLLT also protects cells against NO-induced cell death (Hamblin, 2006).

- **Reactive oxygen species (ROS) and gene transcription**

Low-level laser thearpy was reported to produce a shift in overall cell redox potential in the direction of greater oxidation and increased ROS generation (Grossman *et al,* 1998). It is believed that the redox state of a cell can regulate the cellular signalling pathways that control gene expression. Therefore, alteration of the cellular redox state could either, activate or inhibit signalling pathways (Srinivasan, 2012).

Multiple regulatory pathways are mediated through the cellular redox state. Changes in redox state induce the activation of multiple intracellular signalling pathways, such as nucleic acid and protein synthesis, enzyme activation and also, cell cycle progression (Liu *et al.*, 2005).

- **Low-level laser therapy and gene expression**

The ability of LLLT to alter gene expression is partly explained by its ability to modulate cellular metabolism and alter transcription factors responsible for gene expression (Byrnes *et al*., 2005). Low-level laser (LLL) irradiation can affect the expression of many genes that belong to different function categories. Irradiation of LLL can stimulate cell growth either: directly through regulating the expression of genes related to cell proliferation or indirectly by

regulating the expression of genes related to the following aspects: cell migration and remodelling, DNA synthesis and repair, ion channel and membrane potential, and cell metabolism. Furthermore, irradiation by red light enhances cell proliferation through suppression of cell apoptosis (Song *et al.*, 2003).

Although different pathways of photobiomodulation have been identified, there remains a lack consensus as to the exact pathways through which LLLT achieves effects of pain relief and improved jaw mobility. To date, the most plausible and accepted of the theorem is that involving anti-inflammatory pathways activated as a net effect of increased secretion of B-endorphin, reduction of histamine and acetylcholine secretions. In addition, increased production of adenosine triphosphate causes muscle relaxation as well as creating increased blood microcirculation, clearance of catabolites from the tissues involved (de Godoy *et al.*, 2015).

1.8 Aim and objectives

The efficacy of LLLT in the management of painful TMDs is yet to be supported by evidence of sufficient strength. The reasons cited for the lack of evidence included: heterogeneity in study design, diagnoses and treatment methods. Also, poor diagnostic criteria, outcome measures and chosen controls were listed among the weaknesses of the primary studies (List and Axelsson, 2010).

Chen *et al*. (2015) recommended that future studies should focus on variables that would influence the effectiveness of LLLT such as the correct wavelength, exposure sites, duration of exposure, energy and dosage.

The aim of this study was to assess the efficacy of LLLT for pain relief and improvement of function related to TMDs. Strategies employed to negate some pitfalls of previous studies were the use of validated diagnostic criteria and data collection instruments, application of laser exposures that have been found to effect positive results amongst previous studies and finally, blinding of the observer, the treating clinician and patients.

The objectives of the study are as follows:

1. Establish level of pain and jaw functional limitation before and after treatment with LLLT.
2. Establish level of pain and jaw functional limitation before and after placebo treatment.
3. Compare level of pain and jaw functional limitation intra-groups (before/after).
4. Compare level of pain and jaw functional limitations inter-groups (at the same time intervals).

The null-hypotheses of the study are as follows:

1. There is no difference in pain and jaw functional limitation scores before and after treatment with LLLT.
2. There is no difference in pain and jaw functional limitation scores before and after placebo treatment.

There is no difference in pain and jaw functional limitation scores between active LLLT and placebo groups when comparing them at the same time intervals.

CHAPTER 2: METHODOLOGY

The purpose of this chapter is to describe the research design methodology used to test the null hypotheses mentioned in the previous chapter.

2.1 Study design and sampling

This was a prospective, randomized, placebo-controlled, triple-blinded (researcher, patient and laser therapist) clinical study **(Figure 1).**

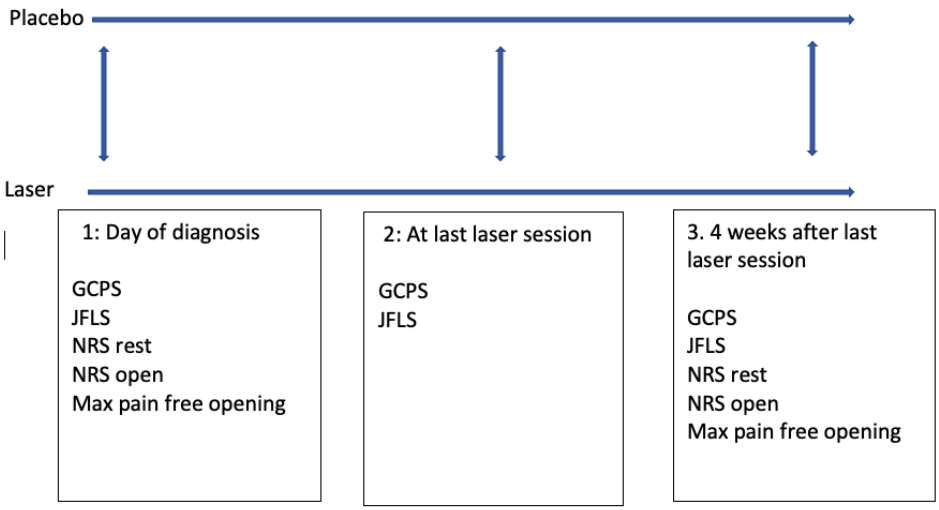


Figure 1: Study design. GCPS = graded chronic pain scale; JFLS = jaw functional limitation scale; NRS = numeric rating scale.

The participants for the study were recruited from the out-patients of the Oral Health Centre (OHC), Mitchell's Plain, who were referred for TMD treatment in the Department of Prosthodontics. The LLLT was done at the OHC, Mitchell's Plain and Tygerberg. Inclusion and exclusion criteria are shown in **Table 1**.

TABLE 1: INCLUSION/ EXCLUSION CRITERIA

Inclusion criteria	Exclusion criteria
Patients who have been diagnosed with myalgia and/or arthralgia according to the DC/TMD protocol, with or without limited mouth opening Symptoms present for longer than 30 days Patients older than 18 years	Patients who are pregnant Patients with pacemakers Medically confirmed musculo-articular pathologies Patients receiving prescription analgesic, changes in prescribed anti-depressive or sedative medication Patients who are receiving or have received any form of treatment for TMD in the last month (physical, chemical, surgical, occlusal, …) Patients with a recent history of trauma to the head - and neck region Patients with clinically and radiographically confirmed degenerative joint disease Malignant or benign head and neck pathology

2.2 Diagnosis, treatment and data collection

Routine and standardized medical and dental history, dental examination, completion of DC/TMD axis I and II instruments, radiographs (pantomograph and TMJ projections in open and closed positions) were performed for all participants.

Following a diagnosis of myalgia using the DC/TMD protocol, patients were informed about the study for possible inclusion. Informed consent was obtained from all patients who were willing to take part in the study (information sheet and consent form, **Addendum 1 and 2**).

Participants were randomly assigned to the active or placebo group. Randomization was done by means of a randomization table dividing them in 2 groups. Halfway the study, the groups were assessed for homogeneity in terms of gender and age, and adjustments made if necessary. Participants were referred to the laser-therapist who was blinded to the treatment (active or placebo). The laser safety officer (not the laser therapist) entered the energy values required for the treatment (zero or active). Study participants received standard homecare instructions and were instructed to avoid using any analgesic or anti-inflammatory medication during the treatment and evaluation period. For the LLLT, patients had to open an additional file at Mitchells Plain when they came from Tygerberg.

The laser therapist was not informed about presentation of the patient's symptoms. Bilateral treatment of the temporalis and masseter muscles was done as a standard for all patients. The laser operator was blinded to the regions of the muscle(s) affected by the pain. Treatment was performed using a Diode laser (Sirolase, SironaDentsply Bensheim Gremany). The biomodulation tip was be placed on the 3 regions of the masseter and temporalis muscles (**Figure 2**): posterior, middle and anterior region of the temporalis muscle; origin, middle and insertion region of the masseter muscle. The LLLT dose was 8J/cm^2 per region, for the active group and 0J/cm^2 for the placebo group. The laser safety officer entered the dosage values in order to maintain blinding of the laser therapist.

TABLE 2: OUTLINE OF LASER PARAMETERS

	Laser parameter
Type of laser	660 Diode
Emission mode	Laser device was set to Continuous Wave
Delivery system	Optical fibre
Power	0.05 Watt
Time on/Time off	86 sec
Spot diameter at tip	8000 μm
Spot area at tip	0.5027 cm^2
Power density at tip	0.09 W/cm^2
Total energy	4 Joules
Speed of movement	0 mm/sec
Energy density with movement	8 J/cm^2
Beam divergence	8 degrees

A memorandum of understanding (MOU) was signed by all persons involved in the trial. The MOU contains each co-operator's qualifications, experience roles and duties **(Addendum 3)**.

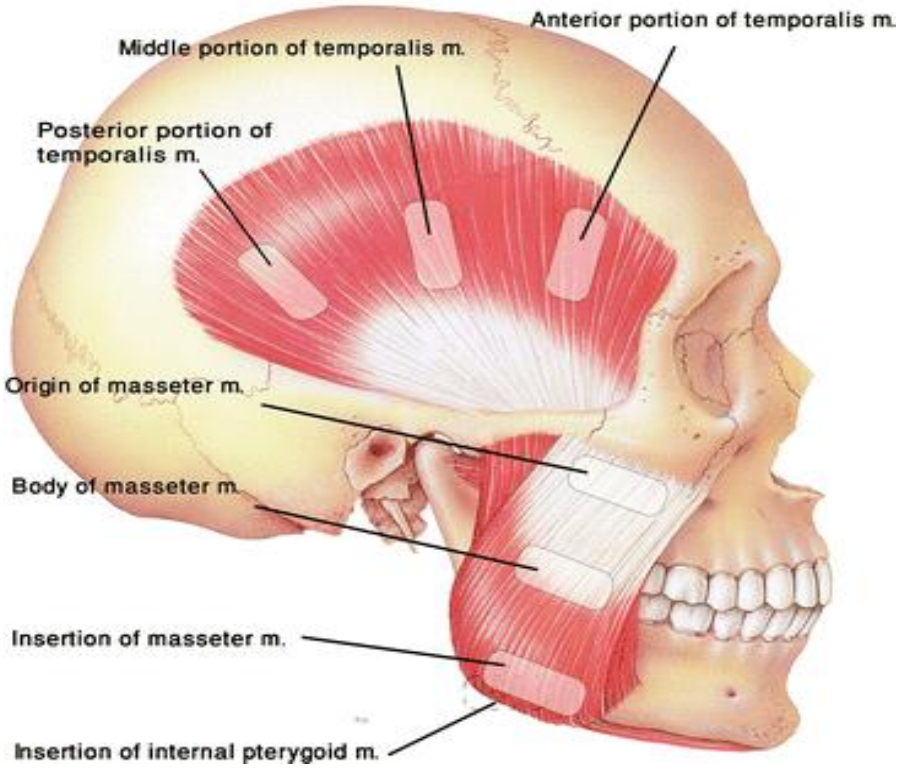


FIGURE 2: LASER EXPOSURE SITES

Figure 2: Laser exposure sites (temporalis muscle and masseter) (Ahrari *et al*., 2014).

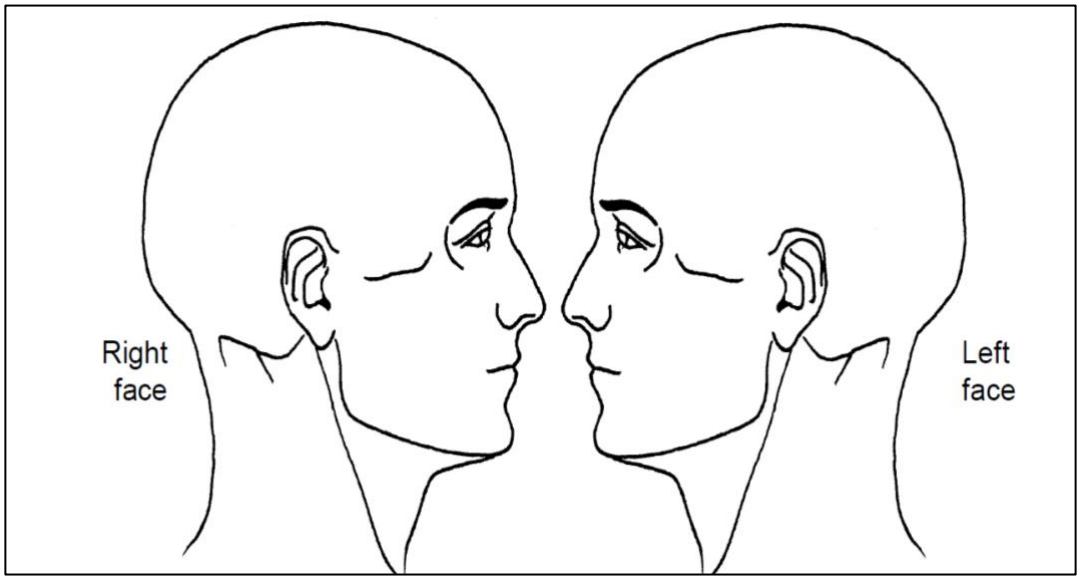


FIGURE 3: PAIN DRAWING

Figure 3: Pain drawing, International RDC/TMD Consortium Network. (Ohrbach and Knibbe, 2017).

Pain and function were assessed using Graded Chronic Pain Scale (GCPS) and Jaw Functional Limitation Scale (JFLS) (**Addendum 1 and 2**), numeric rating scales (NRS) (**Addendum 6**), and maximum-pain free opening is recorded on the DC/TMD examination form and on NRS forms. Scoring of the GCPS and JFLS were done according to the 'Scoring Manual for Self-Report Instruments' – version January 9, 2017 (Ohrbach and Knibbe, 2017).

All information was recorded on paper copies. The questionnaires and NRS scales, completed by the patients, was be entered in an unmarked envelope and stored in a box in the clinics. The investigator entered the maximum pain-free opening measurement in the patients' hospital file. Data collection was done using the data collection sheet (**Addendum 7**). The three investigators were responsible for retrieving the records from the patients' file. After completion of the study, when required, patients in the active as well as the placebo group received further treatment by means of a therapy modality deemed to be most appropriate.

2.3 Data analysis

Descriptive analysis:

Description of population sample in terms of gender, age, diagnosis, and pain and function scores.

***Analytical intragroup evaluation*:**

- Comparison of NRS scores (0-10) before and 4wks after treatment, for each group (2 time intervals).
- Comparison for mouth opening distances before and 4wks after treatment, for each group (2 time intervals).
- Comparison of GCPS scores before, immediately after treatment and at recall (3 time intervals).
- Comparison of JFLS scores before, immediately after treatment and at recall (3 time intervals).

***Analytical intergroup evaluation*:**

- Comparison of NRS scores (0-10) between the 2 groups for before and after treatment interval.
- Comparison of mouth opening distances between the 2 groups for before and after treatment interval.
- Comparison of GCPS scores between the active and placebo group for the 3 intervals.
- Comparison of JFLS scores before between the active and placebo group for the 3 intervals.

Statistical analysis was done by means of explorative categorical principal analysis and multivariate interdependent analysis. For the sake of proposal development, the number of participants was estimated based on previous studies. The final number of participants would be confirmed by a calculation of power based on NRS scores and/or maximum pain-free opening measurements. Level of significance was determined post-hoc. The trial was terminated due to the COVID-19 pandemic restrictions on clinical practice. Reporting important protocol deviations, missing data, patient recruitment, retention and attrition was reported according to the CONSORT statement (Schulz *et al.*, 2010).

CHAPTER 3: RESULTS

This chapter presents the findings of this study. The initial point will be a description of the sample and demographic. This includes information of the sample size calculation based on the outcomes of a pilot test. The chapter presents the data gathered in order to meet the predetermined objectives and to answer the research questions that were raised in the previous chapter. Validated instruments have been employed to investigate changes related to pain and functional limitation. This information allows for a comparison of the intervention in question.

3.1 Sample size calculation

A power calculation was performed using pain scores of a pilot group of 10 participants. The sample size estimation was based on a power of 0.60 and α at 0.05 two tailed since the direction of the change between pre and post treatment was not guaranteed. The sample size estimation was furthermore based on differences within and between groups. The difference between pre- and post- treatment measurement using pain scores in Group A equalled zero and did not allow the calculation of power. Before and after pain scores for Group B provided a basis of a power calculation: with P = 0.60 and P = 0.05, two tailed, a sample size of n = 25 was needed.

Figure 4 shows the Power curve of NRS between pre and post (pair) in Group B.

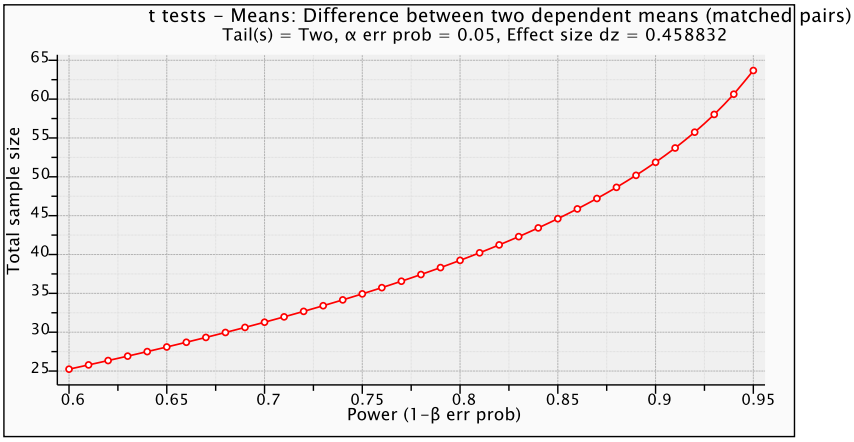


FIGURE 4: POWER CURVE BASED ON NRS VALUES

Over a period from 2017 until 2020, a total of 19 consecutive patients who conformed to the inclusion and exclusion criteria and who volunteered to participate in the study, were enrolled and randomly divided into one of 2 groups. All patients were diagnosed with myalgia according

to the diagnostic criteria of the DC/TMD protocol. Two patients (one female and one male) terminated participation after the first visit. As a result, data of 17 participants were collected. Unfortunately, due to the COVID-19 pandemic, all non-emergency dental service rendering and all non-COVID-19 clinical research on the Oral Health Platform was prohibited from end of March 2020 until recently. Time constraints prohibited the recruiting of more participants. Hence, not all data could be statistically analysed and presentation of some results are limited to a descriptive analysis.

Sixteen of the participants were female. Mean age was 52 with youngest patient 20 years of age and oldest patient 83 years of age. The variable gender was ignored due to low cell occurrences: there were only two male patients in group A and no male patients in group B.

All patients (n = 17) were diagnosed with myalgia, 14 of the patients had an additional diagnosis of arthralgia and or headaches attributed to TMD. This left 3 patients with a single diagnosis of myalgia. Further analysis according to diagnoses was not performed due to low cell occurrences and was not part of the initial study design.

3.2 Instruments

Four different instruments were used to evaluate the effect of two treatments: placebo and laser intervention, on a total of 17 patients: Pain-free opening; NRS; GCPS; and JFLS. Measurements were made over different time intervals.

3.2.1 Pain-free opening

Table 3 shows the measurements of maximum pain-free opening in mm before and 4 weeks after the last laser session, for both treatment groups. For group A, maximum pain-free opening remained the same or increased, except for 1 patient (mean increase in pain-free opening before-after = 6.22 mm). For group B, maximum pain-free opening increased for 6 patients and decreased for 2 (mean increase in pain-free opening = 3.13 mm). **Table 4** shows the mean values, standard error and confidence intervals for pain-free opening for both treatment groups.

TABLE 3: MAXIMUM PAIN-FREE OPENING

Treatment group	Max pain-free opening in mm		
	Before	**After**	**Difference**
A	45	44	-1
A	20	42	22
A	43	43	0
A	42	42	0
A	40	43	3
A	28	30	2
A	27	35	8
A	40	52	12
A	30	40	10
Mean	**35**	**41.22**	**6.22**
B	40	42	2
B	40	38	-2
B	42	44	2
B	18	32	14
B	46	47	1
B	32	30	-2
B	25	30	5
B	35	40	5
Mean	**34.75**	**37.88**	**3.13**

TABLE 4: MEAN PAIN-FREE OPENING

Group	Pain free	Mean	Std. Error	95% Confidence Interval	
				Lower Bound	Upper Bound
A	**Before**	**35.000**	**3.035**	**28.531**	**41.469**
	After	**41.222**	**2.105**	**36.735**	**45.710**
B	**Before**	**34.750**	**3.219**	**27.889**	**41.611**
	After	**37.875**	**2.233**	**33.115**	**42.635**

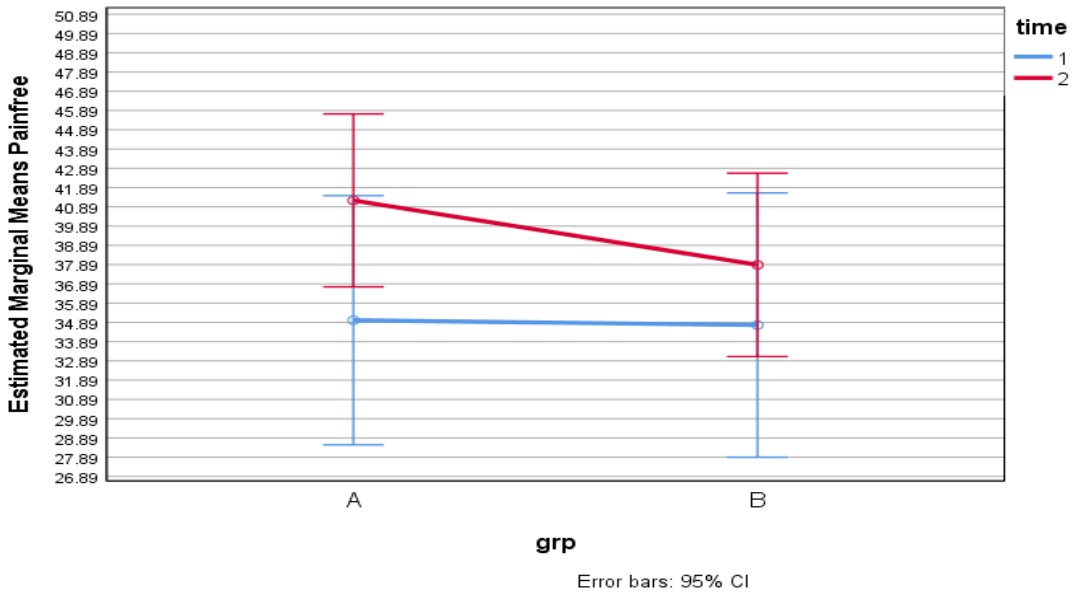


FIGURE 5: GRAPHICAL REPRESENTATION: MEAN PAIN-FREE OPENING FOR BOTH GROUPS AND TIME INTERVALS (1=BEFORE; 2= AFTER)

The difference between the group and treatment was tested in a between groups and repeated within design. The difference between groups was not significant. Although the assumptions of a between group repeated within design were not violated the sample size was too small to reach sufficient power to test between groups, $F_{1,15} = 0.270$, $p > 0.10$, power < 0.1 . The (overall) effect of treatment over time was significant $F_{1,15} = 8.640$, $p = 010$, power = 0.78.

3.2.2 Numeric Rating Scale for pain

The NRS tool was applied 4 times: At rest, before treatment and 4 weeks after the last laser treatment (recall); and during opening before treatment and 4 weeks after the last laser treatment (recall). **Table 5** shows the NRS values for rest and open mouth positions for the 2 time intervals**.**

TABLE 5: NRS DATA

Treatment group	NRS before		NRS recall	
	Rest	Open	Rest	Open
A	5	6	0	6
A	7	10	0	6
A	1	8	0	4
A	3	3	0	1
A	7	9	0	0
A	8	8	9	9
A	7	10	2	8
A	4	6	2	2
A	3	7	0	0
B	2	7	0	10
B	0	4	0	5
B	10	10	0	0
B	7	10	8	8
B	8	10	6	8
B	3	7	4	8
B	8	10	0	5
B	6	8	8	8

In the resting position, 12 patients (8 from group A and 4 from group B) had a higher score (more pain) before treatment as compared to the recall pain score that was lower (less pain). Four patients experienced increased pain after treatment (1 from group A and 3 from group B). One patient (group B) scored no difference in pain before and after (no pain in rest at all) (**Table 5 and 6**).

In the opening position, 11 patients (7 from group A and 4 from group B) had a higher score (more pain) before treatment than after treatment. Four patients reported an increase in pain level from before to at recall visit (1 from group A and 3 from group B). Two patients reported no difference, experiencing severe pain before and after (1 in group A and B each) (**Table 5 and 6**).

The NRS scores were categorized according to pain category (no pain; mild pain; moderate pain; severe pain – refer to methods chapter). The number of patients (nos /counts) per pain category, based on the NRS values, are shown in **Table 6**.

TABLE 6: NUMBER OF PATIENTS (NOS / COUNT) PER PAIN CATEGORY (BASED ON NRS)

NRS			Group		
			A	B	Total
			Count (nos)	Count (nos)	Count (nos)
Before	At rest	No pain	0	1	1
		Mild	1	1	2
		Moderate	4	2	6
		Severe	4	4	8
	Opening	No pain	0	0	0
		Mild	0	0	0
		Moderate	3	1	4
		Severe	6	7	13
Recall	At rest	No pain	6	4	10
		Mild	2	0	2
		Moderate	0	2	2
		Severe	1	2	3
	Opening	No pain	2	1	3
		Mild	2	0	2
		Moderate	3	2	5
		Severe	2	5	7

Table 6 reveals that, before treatment, all patients (n = 17; A = 9 and B = 8) had moderate to severe pain during opening. After treatment, 12 patients (A = 5 and B = 7) indicated to have moderate to severe pain during opening after treatment.

Table 7 shows the number of patients (count) with ordinal and categorical differences between pre- and post-treatment per group in rest and with opening.

TABLE 7: NUMBER OF PATIENTS (COUNT) ACCORDING TO ORDINAL AND CATEGORICAL DATA

NRS		Ordinal values		Categorized	
		A	B	A	B
		Count	Count	Count	Count
Rest	Pre > post	8	4	8	4
	Pre = post	0	1	1	3
	Pre < post	1	3	0	1
Open	Pre > post	7	4	6	2
	Pre = post	1	1	3	6
	Pre < post	1	3	0	0

Table 8 shows the number of cases with ordinal and categorical differences in pain between pre- and post-treatment per group in rest and with opening.

TABLE 8: PAIN CATEGORIES PER PATIENT, BEFORE AND AT RECALL IN REST AND WHILE OPENING

		At rest		Opening	
		Pre	**Post**	**Pre**	**Post**
Group	**Patient**				
A	**1**	Moderate	No pain	Moderate	Moderate
	3	Severe	No pain	Severe	Moderate
	4	Mild	No pain	Severe	Moderate
	5	Moderate	No pain	Moderate	Mild
	8	Severe	No pain	Severe	No pain
	10	Severe	Severe	Severe	Severe
	15	Severe	Mild	Severe	Severe
	16	Moderate	Mild	Moderate	Mild
	18	Moderate	No pain	Severe	No pain
	9	**9**	**9**	**9**	**9**
B	**2**	Mild	No pain	Severe	Severe
	7	No pain	No pain	Moderate	Moderate
	9	Severe	No pain	Severe	No pain
	12	Severe	Severe	Severe	Severe
	13	Severe	Moderate	Severe	Severe
	14	Moderate	Moderate	Severe	Severe
	17	Severe	No pain	Severe	Moderate
	19	Moderate	Severe	Severe	Severe
	8	8	8	8	8
Total	**17**	17	17	17	17

3.2.3 Graded Chronic Pain Scale

Table 9 shows the Characteristic Pain Intensity Scores and Characteristic Pain Intensity for the three intervals: at the day of the diagnosis, at the last intervention session and 4 weeks after the last intervention session. These scores are calculated from entries in the GCPS instrument. No statistical effects of time per and between groups were obtained for the CPI and IS results **(Table 10 and 11)**.

TABLE 9: CHARACTERISTIC PAIN INTENSITY SCORES AND INTERFERENCE SCORES FOR THE INTERVALS. CPI = CHARACTERISTIC PAIN INTENSITY SCORE; IS = INTERFERENCE SCORE

Treatment group	CPI	IS	CPI	IS	CPI	IS
	Before		At last treatment		4 weeks after last treatment	
A	26.67	33.33	13.33	23.33	0.00	0.00
A	50.00	0.00	43.33	0.00	0.00	0.00
A	100.00	100.00	33.33	0.00	0.00	0.00
A	86.67	66.67	76.67	50.00	76.67	50.00
A	26.67	3.33	10.00	0.00	6.67	0.00
A	93.33	100.00	93.33	90.00	93.33	100.00
A	56.67	6.67	46.67	13.33	23.33	0.00
A	93.33	93.33	76.67	86.67	60.00	60.00
A	93.33	80.00	33.33	26.67	46.67	20.00
B	13.33	0.00	3.33	0.00	50.00	0.00
B	90.00	100.00	63.33	76.67	60.00	66.67
B	80.00	53.33	70.00	43.33	70.00	0.00
B	100.00	0.00	86.67	23.33	80.00	33.33
B	53.33	50.00	83.33	70.00	83.33	70.00
B	63.33	53.33	0.00	0.00	16.67	0.00
B	76.67	70.00			0.00	0.00
B	86.67	73.33	83.33	70.00	63.33	13.33

TABLE 10: THE MEAN CHRONIC PAIN INTENSITY SCORES, STANDARD ERROR AND CONFIDENCE INTERVAL FOR GROUP A AND B OVER THE TIME INTERVALS

GCPS CPI					
Groups	**Time**	**Mean**	**Std. Error**	**95% Confidence Interval**	
				Lower Bound	**Upper Bound**
A	1	69.630	9.583	49.205	90.055
	2	47.407	11.581	22.723	72.090
	3	34.074	11.135	10.341	57.807
B	1	70.416	10.164	48.752	92.080
	2	55.714	14.040	25.770	85.630
	3	52.916	11.810	27.744	78.089

TABLE 11: THE MEAN INTERFERENCE SCORE, STANDARD ERROR AND CONFIDENCE INTERVAL FOR GROUP A AND B OVER THE TIME INTERVALS

GCPS IS					
Group	**Time**	**Mean**	**Std. Error**	**95% Confidence Interval**	
				Lower Bound	**Upper Bound**
A	1	53.667	13.112	25.718	81.615
	2	32.222	11.658	7.374	57.070
	3	25.556	11.249	1.579	49.532
B	1	49.875	13.908	20.231	79.519
	2	40.476	14.160	10.330	70.680
	3	22.875	11.931	-2.556	48.306

3.2.4 Jaw Functional Limitation

Table 10 shows the Mastication scores, Mobility scores, Verbal and Emotional Communication scores as well as the Global scores calculated from entries from the JFL instrument, for the 3 time periods. The JFL scores covered 1 month for the first time interval (beginning) and 2 weeks for the subsequent scorings (at the end of laser treatment and recall) The scale-key allows two summarising scores: Global-score 1 and Global-score 2.

The Global-score 1, measuring the actual Jaw Functional Limitation of a patient, is based on either the weighted means of the first 8 items or the weighted means of the items 1, 3, 6, 10, 11, 12, 13, and 19. The results below are based on the latter. The Global-score 2 of a patient is based on the weighted mean of its scores on the three subscales Mastication (items 1-6), Mobility (items 7-10) and Communication (items 13-20).

The weighted mean is a correction for the number of missing allowed per scale: 8 items 2 missing and the subscales respectively 2, 1, 2 missing. If a patient has more item missing than allowed, the patient must be removed from the analysis. The JFLS test was applied per patient three times: JFLS1 = before; JFLS2 = 4th visit; JFLS3 = recall.

Patients 9 and 16 were removed from the analysis of the Global score 1. No effect between group and no effect of time was statistically significant **(Table 13)**.

TABLE 12: MASTICATION SCORES, MOBILITY SCORES, VERBAL AND EMOTIONAL COMMUNICATION SCORES AND GLOBAL SCORE 2 FOR THE 3 TIME INTERVALS

Time 1					Time 2					Time 3				
Mastication (mean 1-6)	Mobility (mean 7-10)	Verbal and emotional communication (mean 13-20)	Global (mean Mastication, Mobility, Communication)		Mastication (mean 1-6)	Mobility (Mean 7-10)	Verbal and emotional communication (mean 13-20)	Global		Mastication	Mobility (me	Verbal and e	Global (mean M, M and C	
0	0	0	0	A	2.5	0	0	0.83333333	A	0	1	0	0.33333333	A
5.66666667	7.25	0.57142857	4.49603175	A	3.33333333	2.5	0	1.94444444	A	1.75	1.75	0	1.16666667	A
5.66666667	7.25	6.625	6.51388889	A	6.16666667	5.75	6.25	6.05555556	A	6.16666667	6	6	6.05555556	A
2	2.75	0.125	1.625	A	0.83333333	1.75	0	0.86111111	A	0.83333333	1.75	0	0.86111111	A
6.2	6.5	4.375	5.69166667	A	6.5	5.75	3.5	5.25	A	6.2	6.5	4.375	5.69166667	A
8.16666667	10	5.25	7.80555556	A	6	5.5	5.125	5.54166667	A	7.16666667	7.75	5.875	6.93055556	A
6.5	7.25	5.375	6.375	A	3.2	5.5	5.83333333	4.84444444	A	3.16666667	5	5.25	4.47222222	A
3	4	0.25	2.41666667	A	2.66666667	2.5	0	1.72222222	A	0	0	0	0	A
8.33333333	9	5	7.44444444	B	8	7.75	4.75	6.83333333	B	8.16666667	7	5.25	6.80555556	B
0.5	0.25	0	0.25	B	0.5	0.25	0	0.25	B	0	0.5	0	0.16666667	B
3.33333333	10	5	6.11111111	B	6.5	7	5.75	6.41666667	B	7	8.25	6.5	7.25	B
5.66666667	1	1	2.55555556	B	6.6	1	1	2.86666667	B	7	1.5	4.75	4.41666667	B
6.83333333	6.5	9	7.44444444	B	6.33333333	4.5	6	5.61111111	B	6.33333333	6	7.4	6.57777778	B
			4.368	Mean A				3.38	Mean A				3.189	Mean A
			4.76	Mean B				4.396	Mean B				5.046	Mean B

TABLE 13: JFLS GLOBAL SCORE, STANDARD ERROR AND CONFIDENCE INTERVAL

Global score 1					
Group	**Time**	**Mean**	**Std. Error**	**95% Confidence Interval**	
				Lower Bound	**Upper Bound**
A	1	3.849	.947	1.802	5.895
	2	3.169	.797	1.447	4.891
	3	2.971	1.022	.763	5.179
B	1	4.489	1.013	2.301	6.676
	2	3.437	.852	1.596	5.278
	3	3.761	1.093	1.401	6.122

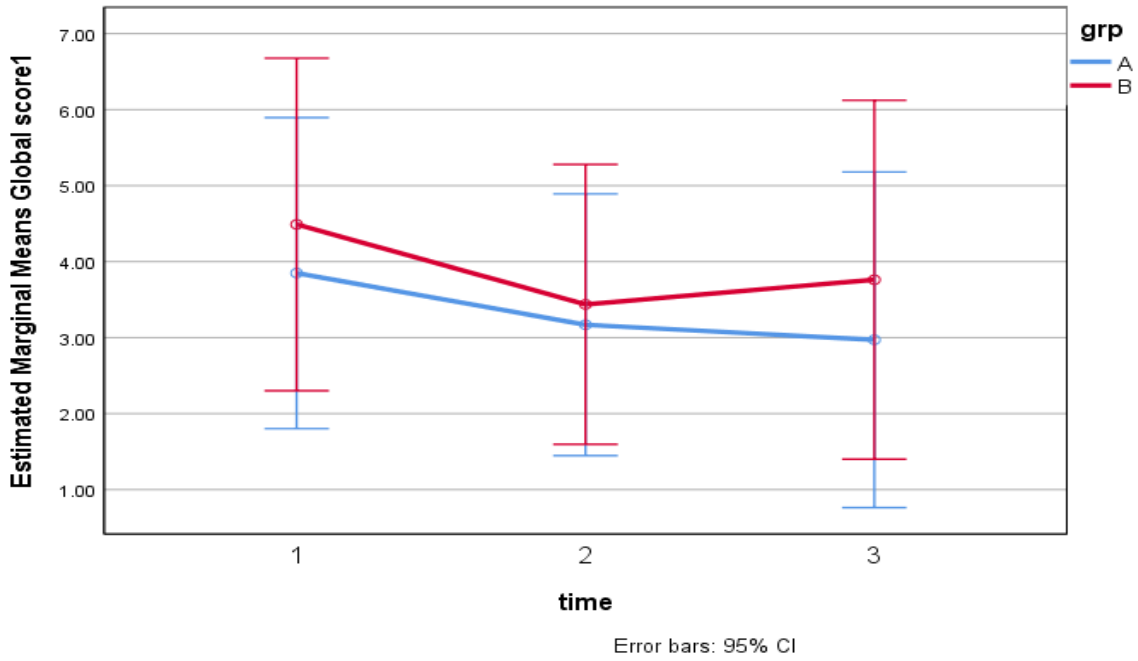


FIGURE 6: THE ESTIMATED MARGINAL MEANS FOR GLOBAL SCORE 1 OVER TIME FOR THE TWO GROUPS

Figure 6 shows the estimated marginal means for global score 1 over time for the two groups.

Patients 8, 9, 14 and 17 were removed from the analysis of the Global score 2. No effect between groups and no effect of time was statistically significant **(Table 14).**

TABLE 14: JFLS GLOBAL SCORE 2, STANDARD ERROR AND CONFIDENCE INTERVAL FOR THE TIME INTERVALS

Global score 2					
Group	**Time**	**Mean**	**Std. Error**	**95% Confidence Interval**	
				Lower Bound	**Upper Bound**
A	1	4.368	1.033	2.093	6.642
	2	3.380	.867	1.471	5.289
	3	3.189	1.025	.933	5.445
B	1	4.760	1.307	1.883	7.637
	2	4.396	1.097	1.982	6.810
	3	5.046	1.297	2.192	7.900

Figure 7 shows the estimated marginal means for global score 2 over time for the two groups.

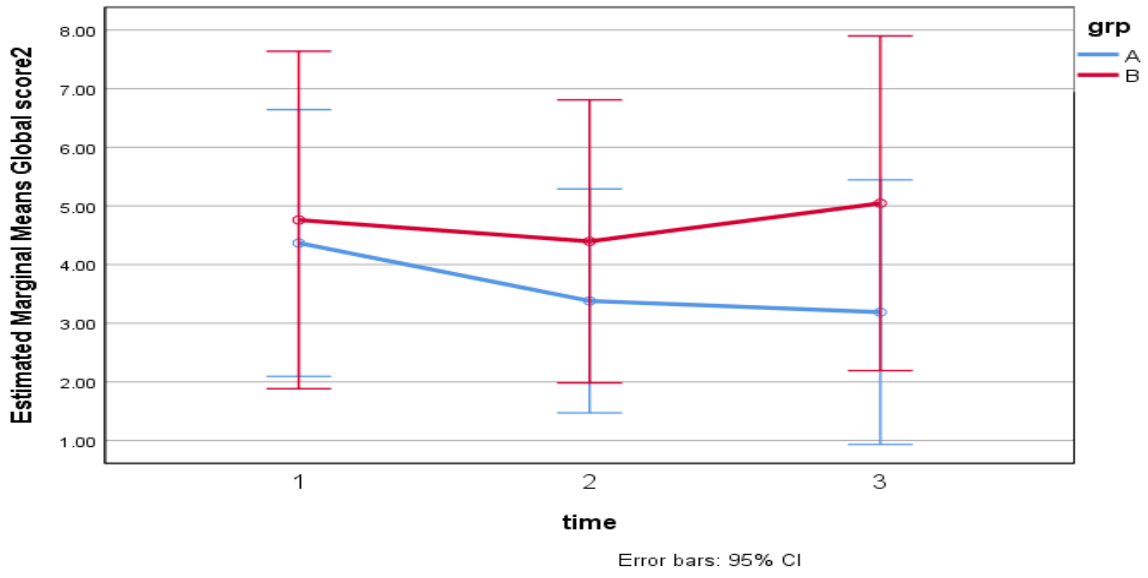


FIGURE 7: ESTIMATED MARGINAL MEANS FOR GLOBAL SCORE 2 OVER THE TIME INTERVALS FOR BOTH GROUPS

The results of the measurements of the construct Mobility (items 7-10 of the questionnaire) are presented in Table 15. No statistical effects of time per and between groups were obtained.

TABLE 15: MEAN JFLS MOBILITY SCORE, STANDARD ERROR AND CONFIDENCE INTERVAL FOR BOTH GROUPS OVER THE TIME INTERVALS

Group	Time	Mean	Std. Error	95% Confidence Interval	
				Lower Bound	Upper Bound
A	1	5.556	1.011	3.520	7.591
	2	3.861	1.011	1.825	5.897
	3	3.667	1.011	1.631	5.702
B	1	4.844	1.072	2.684	7.003
	2	3.469	1.072	1.309	5.628
	3	3.594	1.072	1.434	5.753

Table 16: Shows the Pearson correlation model which aims to detect linear correlation amongst the variables: Pnfr 1 (Pain free opening at interval 1), Pnfr 2 (Pain free opening at interval 1), CPI 1 (Chronic Pain Intensity at interval 1), CPI3 (Chronic Pain Intensity at interval 3), Mobi1(Mobility score at interval 1), Mobi3 (Mobility score at time interval 3)

TABLE 16: PEARSON CORRELATION

Correlations							
		Pnfr 1	**Pnfr2**	**CPI1**	**CPI3**	**Mobi1**	**Mobi3**
Pnfr1	**Pearson Correlation**	1	.660**	-.413	.221	-.582*	-.247
	Sig. (2-tailed)	.	.005	.112	.410	.018	.357
	N	16	16	16	16	16	16
Pnfr2	**Pearson Correlation**	.660**	1	-.079	.048	-.250	-.164
	Sig. (2-tailed)	.005	.	.770	.860	.351	.545
	N	16	16	16	16	16	16
CPI1	**Pearson Correlation**	-.413	-.079	1	.391	.671**	.691**
	Sig. (2-tailed)	.112	.770	.	.135	.004	.003
	N	16	16	16	16	16	16
CPI3	**Pearson Correlation**	.221	.048	.391	1	.125	.646**
	Sig. (2-tailed)	.410	.860	.135	.	.644	.007
	N	16	16	16	16	16	16
Mobi 1	**Pearson Correlation**	-.582*	-.250	.671**	.125	1	.784**
	Sig. (2-tailed)	.018	.351	.004	.644	.	.000
	N	16	16	16	16	16	16
Mobi 3	**Pearson Correlation**	-.247	-.164	.691**	.646**	.784**	1
	Sig. (2-tailed)	.357	.545	.003	.007	.000	
	N	16	16	16	16	16	16
****. Correlation is significant at the 0.01 level (2-tailed).**							
***. Correlation is significant at the 0.05 level (2-tailed).**							

Since the values of pain free were ordinal but CPI and Mobility generated at interval, scores were discretised. The CATPCA had an Eigenvalue of 2.853 for Dimension 1 and 2.106 for Dimension 2. The solution explained 70.84% of the variance.

The plot of components loadings in Figure 8 shows how the variables relate and their relative weight in determining a dimension (and contribution to the solution). Pnfr1 and Pnfr2 are clustering and strongly related but almost perpendicular (unrelated) to Mobi1, Mobi3 and CPI1 which also appear to cluster. CPI3 seems to measure something aspect not strongly shared with both other clusters.

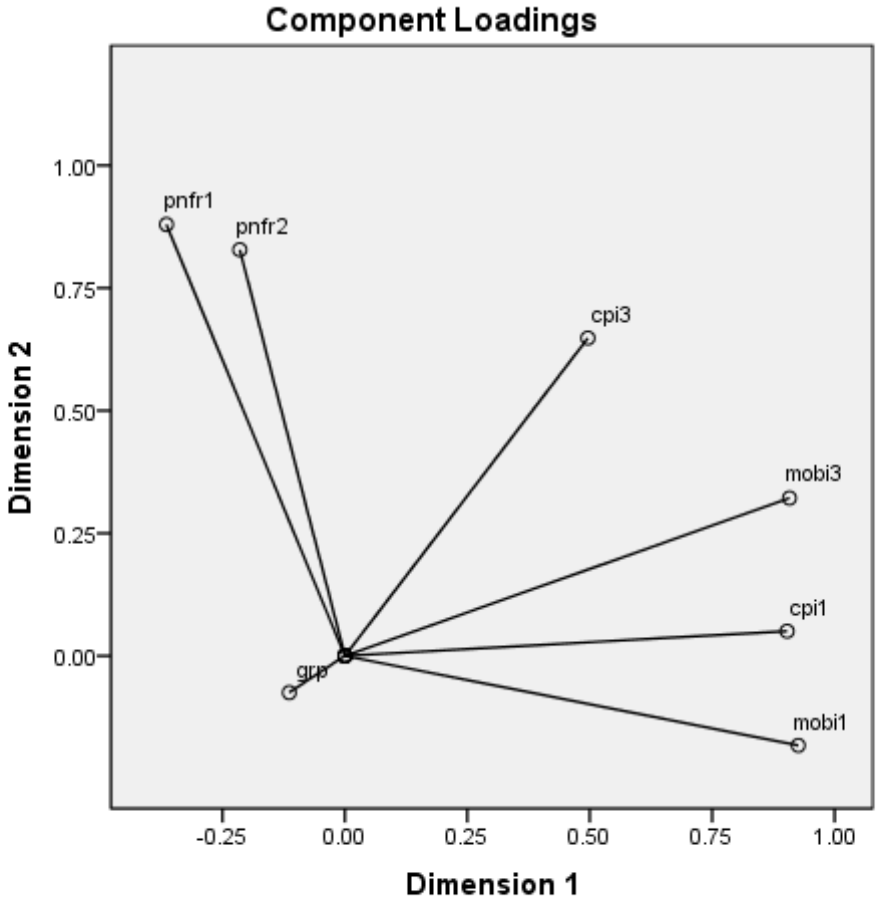
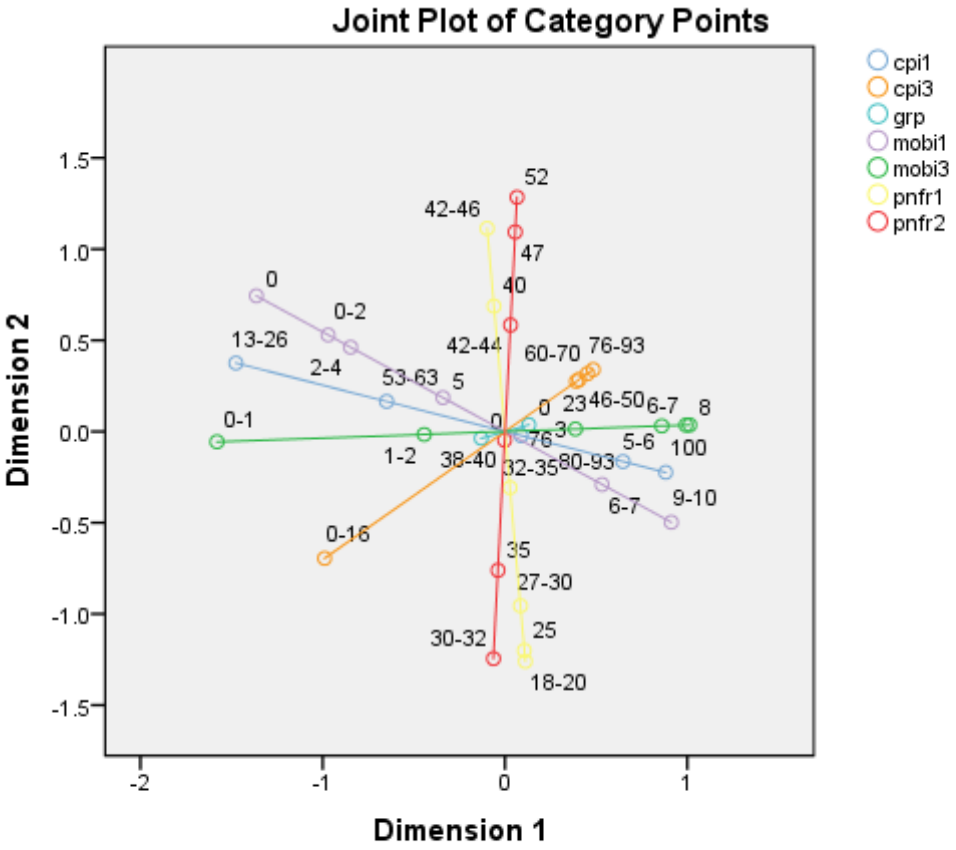


FIGURE 8: GRAPH OF COMPONENT LOADINGS

The plot in Figure 9 shows how the actual scores are distributed.



Variable Principal Normalization.

Rotation Method: Varimax with Kaiser Normalization.

FIGURE 9: JOINT PLOT OF CATEGORY POINTS

CHAPTER 4: DISCUSSION

4.1 Introduction

The aim of this study was to assess the efficacy of LLLT for pain relief and improvement of function related to TMDs. This was done through patient diagnoses, recruitment and randomisation into two treatment groups. The levels of pain and functional limitation were assessed before treatment, on the last day of treatment and one month after treatment. Comparisons of pain and functional limitation were then made intra-group (within the groups) and inter-group (amongst the groups) at the same time intervals.

Three null hypotheses were investigated through this study design. Firstly, that there was no difference in pain and functional limitation before and after treatment with LLLT. Secondly, that there was no difference in pain and functional limitation before and after the placebo treatment and thirdly, that there was no difference in pain and jaw functional limitation between the active and placebo groups when compared at the same time intervals. All three hypotheses were accepted.

The recruitment process took place from 2017 until March 2020. A total of 19 patients were recruited at the Tygerberg and Mitchells Plain OHC. A random sequence was generated through Microsoft Excel and patients were allocated into two treatment groups. Treatment was performed at the Mitchells Plain OHC, where the specified data was also collected during the treatment and recall visits. The data collection instruments that were used include: GCPS, NRS, JFLS and measures of Maximum pain free opening.

The previous chapter presented the results obtained in the present study. Comparisons were made amongst the various treatment groups at different time intervals and were possible. Therefore, in this chapter, the results of this study will be discussed in function of knowledge produced from previous studies.

The discussion will be led under the following headings: Population and sample, instruments used to collect data: NRS, GCPS, maximum pain free mouth opening and JFLS, as well as the choice of laser.

4.2 Population and sample

From 2017 until 2020, a total of 19 consecutive patients, (3 males and 16 females) who conformed to the inclusion and exclusion criteria and who volunteered to participate in the study, were enrolled and randomly allocated into one of 2 groups. All patients were diagnosed with myalgia according to the diagnostic criteria of the DC TMD protocol. Two patients (one female and one male) terminated participation after the first visit. As a result, data of 17 participants were collected (n = 15 female; n = 2 male). The collected sample may not have been desirable however previous studies have reported samples as low as n- 9 (de Godoy *et al*., 2015)

Epidemiological studies indicate that TMD affect both men and women around the world, with common symptoms in all age groups. Without discriminating between the types of TMD, literature states that incidence of TMDs peaks amongst the ages 20 – 45 years, with an overall prevalence rate of 2 – 4% (Fernandez-de-las-Penas and Svensson, 2015).

Amongst subjects with orofacial pain, it has been stated that the prevalence of Myofascial TMD pain can be up to 45% (Manfredini et al., 2011). Moreover, it has been reported that women are more than twice as likely to be affected than men in general population studies (Bagis *et al*., 2012; Liu and Steinkeler, 2013), whilst, number of women experiencing TMDs increases amongst treatment seeking cohorts. The gender occurrence data from the present study in 17 females vs 2 males were recruited, confirms the previous statement as TMD treatment seeking populations statistics do not resemble those of general population studies.

The sample of the current study is similar to that of Shirani *et al. (2009)*, who recorded a total sample of n = 16 patients (12 females and 4 males) in their randomized clinical trial.

The aspects of women's biology, psychology or social roles that predispose them to experiencing more TMD than men, have not yet been determined. However, several studies have reported that the differences between the genders is linked to various factors including: hormonal factors, cultural and social factors, higher levels of work stress for women, differences in pain sensitivity, and different health-seeking behaviours (Michelotti *et al*., 2010; Manfredini et al., *2011*).

4.3 Instruments used to collect data:

4.3.1 TMD Diagnoses: Diagnostic Criteria for Temporomandibular Disorders

Among the 17 participants in the present study, 14 patients presented with multiple TMD, whilst 3 patients presented with a single diagnosis of myalgia. TMD diagnosis has been mentioned as a possible factor relating to variation in the results amongst TMD laser efficacy studies. This could be due to invalidated diagnostic criteria being used or the inclusion of a heterogenous study sample. The latter was true for the current study, where, according to valid criteria, included patients were either diagnosed with Myalgia alone, or together with a diagnosis of headaches related to TMD and/or arthralgia.

Diagnosis data amongst similar studies remains difficult to compare as not all studies have employed standardised diagnostic tools such as the DC/TMD tool to separate TMD of articular origin and TMD of muscular origin (List and Axelsson, 2010). Kulekcioglu *et al. (*2003*),* in a similar study, palpated different TMJ muscles and subjected all patients to MRI scans to evaluate patients having atherogenic pain from pain of myogenic origin. While Dermikol *et al.* (2015), did not elaborate on their diagnostic process other than stating that it was standardised and that they used special tests such as MRI when needed. The different disease mechanisms behind each TMD phenotype are thought to be a possible reason behind inconsistent efficacy results in LLLT therapy studies. However, in this study, analysis based on gender and number of diagnoses could not be done due to the modest sample size of participants.

4.3.2 Numeric rating scale analysis

The NRS is a subjective measure in which participants rate their pain on an eleven-point numerical scale. The scale is composed of 0 (no pain at all) to 10 (severe pain or worst imaginable pain). The NRS is similar to the VAS in which the patient can select one number that best describes the pain. The NRS introductory question, recall periods and verbal descriptors may vary, but similar to the VAS, the most frequently used version is the 11-point (0-10) NRS. The NRS have well-documented validity; they correlate positively with other measures of pain and show sensitivity to treatments that are expected to affect pain (Chiarotto *et al.*, 2019).

For the above reasons, the NRS was deemed an appropriate tool for collection of pain data in this study. This tool was applied four times: twice (at rest and open position) before treatment and again at recall. The NRS raw data reveals that most patients had higher pain scores before than after treatment (n = 12 at rest and n = 11 in open position). At rest, more patients in the

experimental group (group A, n = 8) experienced pain reduction than in the control group (group B, n = 4). Similar observation was made in the open position, group A (n = 7) vs group B (n = 4).

Categorical data (**Table 4 – 6**) was generated that places patients in to different pain categories: no pain, mild, moderate or severe pain, according to the participant's pain scores. For example, looking at NRS during mouth opening as all patients (n = 17), 9 patients in group A and 8 patients in group B experienced moderate to severe symptoms before treatment, respectively. After treatment, there were less patients in group A (n = 5) with moderate to severe pain compared with group B (n = 7). They categorical data confirms the trends seen in the raw data, with slight variation for patients whose pain scores had changed but didn't necessarily place them into different categories. The observed trends indicate more patients with less pain after treatment in Group A (laser group); however, due to insufficient data, the results are inconclusive.

The NRS is a reliable tool of pain measurement at a specific moment in time (right now or past 24 hours); however, it may not be so effective when evaluating chronic pain which fluctuates and presents over a longer time duration (Chiarotto *et al*., 2019). Due to the above-mentioned reason, a second measure was included.

The GCPS assists in obtaining a qualitative description of the global severity of patients participating in the study and enhances the assessment of qualitative change at follow-up. The GCPS is a multidimensional measure that assesses 2 dimensions of overall chronic pain severity: pain intensity and pain-related disability. It is suitable for use in all chronic pain conditions, including chronic musculoskeletal and low back pain. This was the second tool used to evaluate changes in pain in the current study.

The GCPS CPI results indicated that according to the GCPS (scoring manual), the Mean CPI for groups A (CPI A - 69.63) (IS A- 53.66) and group B (CPI B -70.42) were reduced to (CPI A - 34.07) (IS A - 25.55) and (CPI B - 52.91) (IS B - 22.87). This shows an overall reduction in pain intensity and pain related disability, in both groups, as computed by the GCPS. However, no statistically significant effect was observed over time per and in between groups for the CPI and IS.

The results further show a trend towards greater pain reduction in group A. Although both groups experienced pain reduction, there were no statistical difference in pain intensity and

pain related disability per and in between the groups. The results are corroborated by a study conducted by Kulekcioglu *et al. (2003)*, in which they found no statistical difference between the active (laser) and placebo (exercise) group. However, both groups had experienced significant pain reduction at recall. In another study, Shirani *et al. (2009)*, used "sham laser" alone, for their placebo group, unlike what was done in the current study. Pain reduction was experienced in both groups leading the authors to believe that the pain relief felt amongst the placebo group was psychologically driven.

Pain relief has been achieved using different energy exposures targeted at painful muscles. Shirani *et al. (2009)*, applied a dose of 6J/cm^2 to achieve positive results while de Godoy *et al. (2005)* applied a significantly higher energy dosage, 33 J/cm^2 . Both studies achieved positive results; thus, further corroborating the heterogeneity amongst LLLT studies with regards to laser parameters.

4.3.3 Maximum pain-free opening

Restrictions of mouth opening, and pain are generally considered amongst the main clinical signs of TMD. An assessment of jaw mobility is included as part of the DC/TMD axis 1 clinical protocol. Vertical and horizontal movements are evaluated as well as the associated pain and sounds. In this study, maximum pain free mouth opening was used as one of the parameters to assess jaw function before and after treatment.

Initially, most of the patients had a slight restriction of the maximum voluntary opening when 40 mm was used as the normal reference to measure opening. However, after 6 sessions of therapy, there was a 6.222 mm increase in mouth opening for group A and a 3.125 mm increase in mouth opening for group B.

The results indicated that a significant improvement in mouth opening was achieved with LLLT; thus, suggesting its effectivity in increasing mouth opening in TMD patients. However, when compared to the placebo group over the same time intervals, no statistical differences were observed. The null hypothesis that LLLT is no different than placebo in reducing TMD pain was confirmed. Furthermore, the results are in support of the data obtained by Kogawa *et al.* (2005), in which an average mouth opening before therapy was 44.65 mm, and 48.5 mm after treatment with laser. The results of the current study indicate a significant improvement in mouth opening of group A, confirming those of the study by Çetiner *et al.* (2006*)*, in which LLLT improved mouth opening and reduced pain; thus, recommended as an appropriate treatment for TMD.

The JFLS, the second tool used to evaluate changes in function, consists of a valid 20 item scale that can be grouped to provide measures of: limitations in mastication, jaw mobility and expression (verbal and emotional). The JFLS tool also provides a single global construct score that can also be determined using a short (8 item) version of the JFLS. The JFLS-20 was found to be reliable and valid for measuring alterations in jaw functions deemed significant to individuals with orofacial disorders (Orbach *et al*., 2008).

The JFLS data constructs that were included for analysis in the present study were the Global score 1 and 2 (**Table 10-12**) as well as the mobility constructs (**Table 13**). In the current study, no statistically significant effect of time was noted upon inter and intra- group analysis.

Functional assessments in this study, reveal a significant change in mouth opening for the laser group over time but no statistical differences when compared with the placebo group over the same time intervals. While no statistical differences were noted (inter and intra-group) in the JFLS global scores as well as mobility constructs.

The increase in mouth opening and improvement in JFLS (although statistically insignificant) in both groups could be attributed to patients complying with jaw exercises. Lindorfs *et al.* (2020), found significant improvement in JFLS scores of the jaw exercise group when compared to the placebo group showing that jaw exercises, alone can have a positive effect on functional outcomes. Significant change in mouth opening for group A may imply the therapeutic effects of LLLT in combination with jaw exercises.

da Silva *et al.* (2021), achieved positive results in both pain reduction and increased range of mandibular movements. They compared different exposure values (52 J/cm^2 and 105 J/cm^2) with placebo treatment. It was concluded that higher exposure doses achieved a more rapid improvement in symptoms. For their study, patients with intra-articular disorders were included therefore the TMJ was also exposed to LLLT.

Considering findings of previous studies mentioned as well as results of the present study, perhaps, patients presenting with myalgia and arthralgia, be exposed at the muscles as well as at the TMJ at higher doses for more effective treatment.

4.4 The choice of laser

Chen *et al. (2015),* in a systematic review showed that various types of lasers (Hellium-Neon, Diode, ND:YAG) have been applied in clinical trials to treat TMD. Although not mentioned, this would've been likely due to their ability to all attain the required parameters for Photobiomodulation (Red and Infrared ranges). What stood out from their systematic review, was that 12 out of the 14 clinical trials included, had used the diode laser. The disproportion was not explained. They also mentioned that the most important factor affecting laser absorption into biological tissue the wavelength. According to Enwemeka, (2000), the 632.8 nm wavelength allows for deeper penetration of musculoskeletal tissue. Years later, a clinical study by Emshoff, (2008), confirmed positive results at the same wavelength.

Dentsply state that the Sirolaser is indicated for treatment of TMD in the Red wavelength (660nm). The Sirolaser was a practical tool to use for this study, not only because it fulfils the previously mentioned treatment parameters, but it was readily available in the department and added no extra cost to the study.

4.5 Associations

The following associations were observed within the data obtained:

- Negative correlation between Pain-free opening 1 and JFLS Mobility score 1
- Positive correlations made between CPI 1 and JFLS Mobi1. CPI 3 and JFLS Mobi3 also showed positive correlations.

The data shows an inverse relation between mouth opening and the JFLS mobility score, initially. While, also at initial visit, positive correlation was noted between CPI 1 and JFLS Mobi1.

CHAPTER 5: CONCLUSION AND LIMITATIONS

5.1 Conclusion

The aim of this study was to assess the efficacy of LLLT for pain relief and improvement of function related to TMDs. This was done through patient diagnoses, and randomisation into two treatment groups. Within the limitations of this study, it may be concluded that:

- There is no difference in pain and functional limitation before and after treatment with LLLT.
- There is no difference in pain and functional limitation before and after the placebo treatment.
- There is no difference in pain and jaw functional limitation between the active and placebo groups when compared at the same time intervals.

Although, the sample size was a limitation in this study, the present study demonstrated that, although statistically insignificant, higher levels of improvement in TMD pain and functional limitations could be achieved through LLLT. A larger study sample may have allowed for; analysis to be done based on gender and diagnoses. Also, the lager sample may contributed to an analysis with higher power and possibility of significant findings.

5.2 Limitations of study

5.2.1 Sample size

Sample size of 17 patients was a limitation in this study. The initial power calculation determined that 25 patients would be required, the recruitment had to be terminated prior to this number being reached. The main reason that qualifying patients declined to join the study was based around issues of scheduling and availability.

5.2.2 Follow-up periods

Another limitation of this study was that the follow periods were not as strictly adhered to, causing inconsistencies in the variable of follow up duration. This should be taken in to account when interpreting the data presented. This was again due to difficulty synchronizing schedules and also public holidays as well as school vacation.

5.2.3 Incomplete data

Instances where data collection forms were not completed fully also have been viewed as a limitation. In the current study, according to the JFLS scoring manual, when calculating the global constructs 1 and 2, it is stated that patients with more missing items than allowed by the formula be removed from the analysis. Therefore, the JFLS intervals were not calculated with a consistent number of patients. The JFLS values would've possibly changed had all the data been captured.

5.2.4 Bias

Co intervention bias

For ethical reasons, both the active laser and placebo laser groups of patients had received information and at home care instructions that included various jaw exercises. It is not clear whether all patients were compliant with the self-care strategies. It is also unclear that patients refrained from taking analgesics throughout the duration of the study.

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UNIVERSITY of the WESTERN CAPE

ADDENDUM 1

Patient information sheet (also in Afrikaans and Xhosa)

Title of the trial: **Efficacy of low level laser therapy in treatment of temporomandibular myalgia**

This study was approved by the Biomedical Research Ethics Committee at the University of the Western Cape, project number: …….

The main investigator is Dr N Netshilindi, a postgraduate student at the Faculty of Dentistry of the University of the Western Cape (UWC). My supervisors are Prof Geerts and Dr R Mulder, lecturers at the Faculty of Dentistry (UWC).

The trial will take place at the Mitchell's Plain and Tygerberg Oral Health Centres. The number of participants in the trial will be about 30.

The trial consists of treatment of your painful jaw condition by means of low level laser therapy (LLLT). The efficiency of LLLT in pain relief and improvement of function is still under investigation. Some studies report a positive outcome, others state that they have not been proven to be more effective than other treatments for painful jaw conditions.

Your treatment protocol consists of 6 laser sessions, 2 per week. The laser treatment therefore will last 3 weeks. For laser sessions you will have to come to the Tygerberg Oral Health Centre. Every session will last between 10 to 20 minutes. It is important to attend all sessions and to complete the full treatment. One month after the last laser treatment, there will be one recall session. *Participation in the trial consists of 7 visits.* Contact the main investigator Dr Netshilindi, if you anticipate transport challenges.

You will have to complete the same questionnaires before, just after LLLT and at the recall visit.

You will be assigned to one of two groups. One group will receive active laser treatment, the other group will receive mock laser treatment. You have a 50% chance to belong to one of the 2 groups, but you won't know to which one you belong. When the laser treatment is completed and you still need further treatment for your jaw pain, you will receive further alternative treatment by one of our dentists at the TMD clinic in Mitchell's Plain.

Low level laser therapy is viewed as a safe procedure with no recorded adverse reactions. All patients will be given standard protection during exposure. In advent of any "laser related"

unwanted reactions, the patient will receive appropriate treatment, provided for by the researchers.

Your participation in the study is voluntary. Refusal to participate or withdrawal from the trial will not prejudice ongoing care at the Oral Health Centre.

All information and data captured during the trial will be kept confidential and your identity will be protected at all times. Only your file number will be captured on the questionnaires and record sheets. Data will be captured on an access restricted, password protected computer.

None of the investigators have an interest in any product or equipment used in this trial.

The results of this trial will be published by means of a research report in the form of a mini-thesis and publication in a peer-reviewed scientific journal.

……

Dr N Netshilindi,

Main investigator (Tygerberg and Mitchell's Plain)

Contact details: Tel: (021) 937 3170; Mobile: 082 4388349

……

Prof G Geerts,

Supervisor (Mitchell's Plain)

Contact details: Tel: (021) 937 3095

……

Dr R Mulder

Supervisor (Tygerberg)

Contact details: Tel: (021) 9373107

ADDENDUM 2

(also in Afrikaans & Xhosa)

Informed consent to take part in the clinical study with the title:

Efficacy of low level laser therapy in treatment of temporomandibular myalgia

---

I (name of participant)

……...

have read and have been explained the content of the information sheet. I understand the content and I have been given enough opportunity to ask questions.

I agree to participate in the trial.

……..	……..
Signature participant	Date
…….	……..
Signature Dr Netshilindi	Date
…….	……..
Signature Prof Geerts	Date
…….	……..
Signature Dr Mulder	Date

ADDENDUM 3

Memorandum of understanding:
"Efficacy of low level laser therapy in treatment of temporo-mandibular myalgia: A randomized controlled trial"

This memorandum of understanding exists among the investigators and co-workers Dr Netshilindi, Prof Geerts, Dr Mulder and Dr Booley. Their qualifications, experience, roles and duties are listed in this document. With signing of this MOU, the investigators and co-worker declare that the information in this MOU is correct and that they will comply with the protocol, duties and roles assigned to them related to this trial. They also commit to report any event that may influence any aspect or operations of the trial in time and timeously to all other co-worker/investigators.

Dr Netshilindi
BChD(UWC)
Dentist
Postgraduate student specializing in Prosthodontics
Experience in DC/TMD examination and diagnosis protocol since 2016
Role and function:

- Literature review and assistance with proposal development
- Communicating and informing colleagues and staff at the TMD clinic in Mitchell's Plain about the study.
- Identification of study participants
- Coordination of laser appointments for patients
- Tracking patients
- Responsibility for the availability of paper questionnaires, VAS scales and boxes for participants
- To perform the recall visit for all participants
- Cooperation with co-investigators and co-workers according to co-workers' MOU
- Writing of minithesis
- Assistance with the writing of a scientific publication. Authorship to be determined later.

GAVM Geerts

BChD, PDD (Implantology), MChD (Prosthodontics), PhD (Prosthetic Dentistry)

Prosthodontist

Experience in DC/TMD protocol since 2014

GCP accredited (2017-2019)

Role and function:

Conceptualization and proposal development

Supervision of the clinical examination, diagnosis and record keeping at the TMD Clinic, Oral Health Centre, Mitchell's Plain

Identification and enrolling study participants within the TMD clinic from pool of patients seen by all postgraduate students.

Monitoring progress of trial

Cooperation with co-investigators and co-workers according to co-workers' MOU

Supporting and mentoring Dr Netshilindi according to supervisors' MOU

Supervision of mini-thesis writing and preparation for examination

Writing of scientific publication Authorship to be determined later.

Dr Mulder

BChD(UWC), MSc(UWC)

Dentist

Laser safety officer

Experience in laser treatments

Role and function:

Development of the proposal with respect to the laser component

Supervision of the laser treatment and data recording at the Oral Health Centre at Tygerberg

Communicating the requirements of the trial to the laser therapist

Entering of laser treatment specifications in his capacity as laser safety officer before treatment of each patient

Monitoring progress of trial

Cooperation with co-investigators and co-workers according to co-workers' MOU

Supporting and mentoring Dr Netshilindi according to supervisors' MOU

Supervision of mini-thesis writing and preparation for examination

Writing of scientific publication. Authorship to be determined later.

Dr Booley

BChD (UWC), PDD Orth(UWC), MSc (U Warwick UK), MSc Dental laser (UniGe Italy), PDD Implant(UWC)

Laser therapist

Laser safety officer

Role and function

- Commitment to the trial and follow instructions
- Perform the laser treatment
- Confirm next visit with the patient
- Give questionnaires and VAS scales to patients after the last laser treatment
- Cooperation with co-investigators and co-workers according to co-workers' MOU
- Will be acknowledged in any publication based on the trial

……. ……..

Signature Dr N Netshilindi Date

……. ……..

Signature Prof G Geerts Date

……. ……..

Signature Dr Mulder Date

……. ……..

Signature Dr Booley Date

ADDENDUM 4

Graded chronic pain scale (visit 1)

1. On how many days in the **last 6 months** have you had facial pain? _____ Days

2. How would you rate your facial pain **RIGHT NOW?** Use a scale from 0 to 10, where 0 is "no pain" and 10 is "pain as bad as could be".

No pain										Pain as bad as could be
0	1	2	3	4	5	6	7	8	9	10

3. In the LAST 30 DAYS, how would you rate your **WORST** facial pain? Use the same scale, where 0 is "no pain" and 10 is "pain as bad as could be".

No pain										Pain as bad as could be
0	1	2	3	4	5	6	7	8	9	10

4. In the LAST 30 DAYS, **ON AVERAGE**, how would you rate your facial pain? Use the same scale, where 0 is "no pain" and 10 is "pain as bad as could be". [That is, *your usual pain* at times you were in pain.]

No pain										Pain as bad as could be
0	1	2	3	4	5	6	7	8	9	10

5. In the LAST 30 DAYS, how many days did your facial pain keep you from doing your **USUAL ACTIVITIES** like work, school, or housework? (every day = 30 days)

_____ Days

6. In the LAST 30 DAYS, how much has facial pain interfered with your **DAILY ACTIVITIES**? Use a 0-10 scale, where 0 is "no interference: and 10 is "unable to carry on any activities".

No interference										Unable to carry on any activities
0	1	2	3	4	5	6	7	8	9	10

7. In the LAST 30 DAYS, how much has facial pain interfered with your **RECREATIONAL, SOCIAL AND FAMILY ACTIVITIES**? Use the same scale, where 0 is "no interference: and 10 is "unable to carry on any activities".

No interference										Unable to carry on any activities
0	1	2	3	4	5	6	7	8	9	10

8. In the LAST 30 DAYS, how much has facial pain interfered with your **ABILITY TO WORK**, including housework? Use the same scale, where 0 is "no interference: and 10 is "unable to carry on any activities".

No interference										Unable to carry on any activities
0	1	2	3	4	5	6	7	8	9	10

Graded Chronic Pain scale 2.0

File number	date	Open/ rest

1. **How many days in the last 15 days have you had facial pain? _____ Days**
3. **How would you rate your pain right now from 0-10< where 0 is no pain and 10 is "pain as bad as could be".**

1	2	3	4	5	6	7	8	9	10

4. **In the LAST 15 DAYS, how would you rate your worst facial pain? Use the same scale where 0 is no pain and 10 is "pain as bad as could be".**

1	2	3	4	5	6	7	8	9	10

5. **In the last 15 DAYS, how many days did your facial pain keep you from doing your usual activity like work school or housework? (everyday = 15days) _____Days**
6. **In the LAST 15 DAYS, how much has facial pain interfered with your daily activities? Use a scale, where 0 is "no interference and 10 is unable to carry on any activities.**

1	2	3	4	5	6	7	8	9	10

7. **In the last 15 days how much has facial pain interfered with your RECREATIONAL, FAMILY AND SOCIAL ACTIVITIES? Use a scale, where 0 is "no interference and 10 is unable to carry on any activities.**

1	2	3	4	5	6	7	8	9	10

8. **In the last 15 days, how much has facial pain interfered with your ability to work including house work? Use a scale, where 0 is "no interference and 10 is unable to carry on any activities.**

1	2	3	4	5	6	7	8	9	10

ADDENDUM 5

Jaw functional limitation scale (visit 1) **Folder no. ……**

For each of the items below, please indicate the level of limitation during the last month.

If the activity has been completely avoided because it is too difficult, then circle '10'.

If you avoid an activity for reasons other than pain or difficulty, leave the item blank.

No limitation **Severe limitation**

1. Chew tough food

0 1 2 3 4 5 6 7 8 9 10

2. Chew hard bread

0 1 2 3 4 5 6 7 8 9 10

3. Chew chicken (e.g., prepared in oven)

0 1 2 3 4 5 6 7 8 9 10

4. Chew crackers

0 1 2 3 4 5 6 7 8 9 10

5. Chew soft food (e.g., macaroni, canned or soft fruits, cooked vegetables, fish)

0 1 2 3 4 5 6 7 8 9 10

6. Eat soft food requiring no chewing (e.g. mashed potatoes, apple sauce, pudding, pureed food)

0 1 2 3 4 5 6 7 8 9 10

7. Open wide enough to bite from a whole apple

0 1 2 3 4 5 6 7 8 9 10

8. Open wide enough to bite into a sandwich

0 1 2 3 4 5 6 7 8 9 10

9. Open wide enough to talk

0 1 2 3 4 5 6 7 8 9 10

10. Open wide enough to drink from a cup

0 1 2 3 4 5 6 7 8 9 10

11. Swallow

0 1 2 3 4 5 6 7 8 9 10

12. Yawn

0 1 2 3 4 5 6 7 8 9 10

13. Talk

0 1 2 3 4 5 6 7 8 9 10

14. Sing

0 1 2 3 4 5 6 7 8 9 10

15. Putting on a happy face

0 1 2 3 4 5 6 7 8 9 10

16. Putting on an angry face

0 1 2 3 4 5 6 7 8 9 10

17. Frown

0 1 2 3 4 5 6 7 8 9 10

18. Kiss

0 1 2 3 4 5 6 7 8 9 10

19. Smile

0 1 2 3 4 5 6 7 8 9 10

20. Laugh

0 1 2 3 4 5 6 7 8 9 10

Jaw functional limitation scale (at last LLLT visit and recall)

Folder no. ……

For each of the items below, please indicate the level of limitation during the last 2 weeks.

If the activity has been completely avoided because it is too difficult, then circle '10'.

If you avoid an activity for reasons other than pain or difficulty, leave the item blank.

No limitation **Severe limitation**

1. Chew tough food

0 1 2 3 4 5 6 7 8 9 10

2. Chew hard bread

0 1 2 3 4 5 6 7 8 9 10

3. Chew chicken (e.g., prepared in oven)

0 1 2 3 4 5 6 7 8 9 10

4. Chew crackers

0 1 2 3 4 5 6 7 8 9 10

5. Chew soft food (e.g., macaroni, canned or soft fruits, cooked vegetables, fish)

0 1 2 3 4 5 6 7 8 9 10

6. Eat soft food requiring no chewing (e.g. mashed potatoes, apple sauce, pudding, pureed food)

0 1 2 3 4 5 6 7 8 9 10

7. Open wide enough to bite from a whole apple

0 1 2 3 4 5 6 7 8 9 10

8. Open wide enough to bite into a sandwich

0 1 2 3 4 5 6 7 8 9 10

9. Open wide enough to talk

0 1 2 3 4 5 6 7 8 9 10

10. Open wide enough to drink from a cup

0 1 2 3 4 5 6 7 8 9 10

11. Swallow

0 1 2 3 4 5 6 7 8 9 10

12. Yawn

0 1 2 3 4 5 6 7 8 9 10

13. Talk

0 1 2 3 4 5 6 7 8 9 10

14. Sing

0 1 2 3 4 5 6 7 8 9 10

15. Putting on a happy face

0 1 2 3 4 5 6 7 8 9 10

16. Putting on an angry face

0 1 2 3 4 5 6 7 8 9 10

17. Frown

0 1 2 3 4 5 6 7 8 9 10

18. Kiss

0 1 2 3 4 5 6 7 8 9 10

19. Smile

0 1 2 3 4 5 6 7 8 9 10

20. Laugh

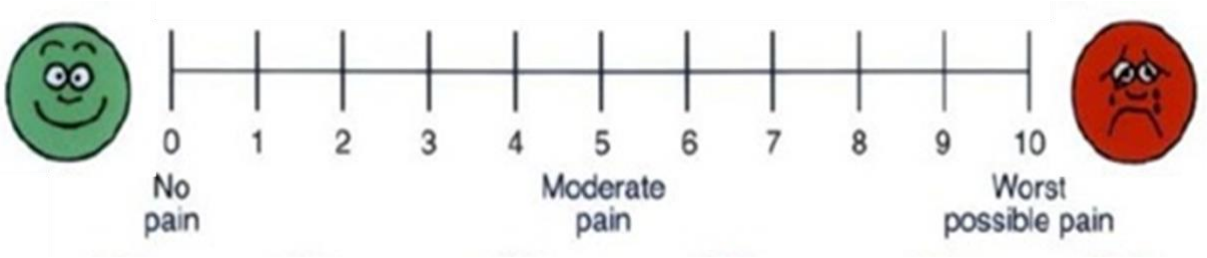
0 1 2 3 4 5 6 7 8 9 10

ADDENDUM 6

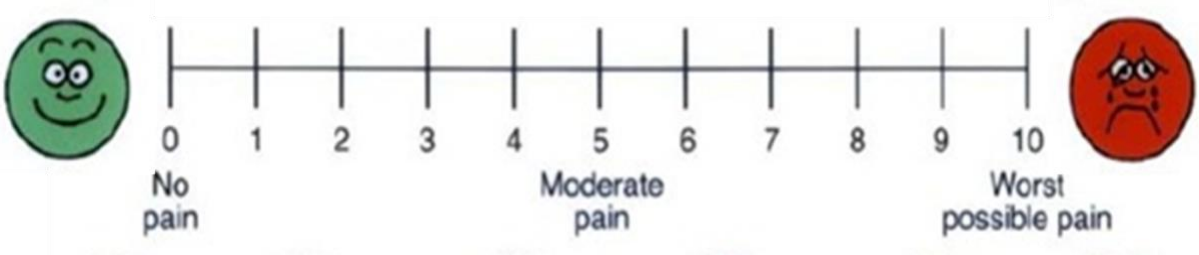
NRS

Patient folder number	Date	Max pain-free open (mm)

1. **At rest**



2. **Open**



ADDENDUM 7

Data collection sheet

Patient	Date	Gender	Age	Group Active / placebo	VAS rest Before	VAS open Before	Max painfree open before	GCPS before	GCPS 6 sessions	GCPS recall	JFLS before	JFLS 6 sessions	JFLS recall	VAS rest recall	VAS open recall	Max painfree open recall
1																
2																
3																
4																
5																
6																
7																
9																
10																
11																
12																
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29																
30																

Patient code	Age	Gender	Pain screene	TMD Diagnosis				Treatment	Max painfree opening		NRS before		NRS recall	
				myalgia	arthralgia	headache	referred pain	Group	Before	After	Rest	Open	Rest	Open
1		F	1	myalgia	arthralgia - Right and left			A	**45**	**44**	5	6	0	6
8	47	F		myalgia		headache		A	**40**	**43**	7	9	0	0
18	32	M		myalgia				A	**30**	**40**	3	7	0	0
3	72	F		myalgia	arthralgia-right and left			A	**20**	**42**	7	10	0	6
10	57	M		myalgia	arthralgia-left & right			A	**28**	**30**	8	8	9	9
4	34	F	8	myalgia				A	**43**	**43**	1	8	0	4
15	25	F		myalgia	arthralgia-right			A	**27**	**35**	7	10	2	8
16	57	F		myalgia	arthralgia-left			A	**40**	**52**	4	6	2	2
5	79	F	1	myalgia				A	**42**	**42**	3	3	0	1
2		F	6	myalgia	arthralgia-right	headache		B	**40**	**42**	2	7	0	10
6		F		myalgia	Arthralgia-left			B	**45**					
7	66	F		myalgia	arthralgia-right			B	**40**	**38**	0	4	0	5
9	49	F		myalgia	Arthralgia-left			B	**42**	**44**	10	10	0	0
12	22	F		myalgia	arthralgia-right			B	**18**	**32**	7	10	8	8
13	83	F		myalgia	arthralgia-left			B	**46**	**47**	8	10	6	8
14	42	F		myalgia	arthralgia-left & right		myofascial pain with refferal	B	**32**	**30**	3	7	4	8
17	76	F		myalgia	arthralgia-left & right			B	**25**	**30**	8	10	0	5
19		F		myalgia	arthralgia-right and left	Headache		B	**35**	**40**	6	8	8	8

Patient code	GCPS scores: Before treatment											
	#1 (no. of days)	#2	#3	#4	#5 (no. of days)	#6	#7	#8	Disability points for number of days with interference (based on item #5)	disabilty points for interference score (column AC)	**Characteristic Pain intensity (CPI)**	**Interference score (IS)**
1	5	5	5	5	0	0	0	0	0	0	**50.00**	**0.00**
8		6	5	6	0	1	1	0	0	0	**56.67**	**6.67**
18	80	2	4	2	0	0	0	10	0	1	**26.67**	**33.33**
3	30	10	10	10	30	10	10	10	3	3	**100.00**	**100.00**
10	180	10	9	9	30	10	10	10	3	3	**93.33**	**100.00**
4		8	10	8	20	7	7	6	3	2	**86.67**	**66.67**
15	150	9	10	9	27	9	10	9	3	3	**93.33**	**93.33**
16	7	10	10	8	1	8	7	9	0	3	**93.33**	**80.00**
5	24	0	4	4	0	0	0	1	0	0	**26.67**	**3.33**
2		8	8	8	0	0	8	8	0	2	**80.00**	**53.33**
6												
7	10	2	1	1		0	0	0		0	**13.33**	**0.00**
9	180	9	9	9	30	10	10	10	3	3	**90.00**	**100.00**
12	10	10	10	10	0	0	0	0	0	0	**100.00**	**0.00**
13	90	0	10	6	15	5	5	5	3	2	**53.33**	**50.00**
14		5	9	5		6	5	5		2	**63.33**	**53.33**
17	180	8	9	6	2	7	7	7	3	3	**76.67**	**70.00**
19		7	10	9	30	7	8	7	3	3	**86.67**	**73.33**

Patient code		GCPS scores: After 4th visit										
		#1 (number of days)	#2	#3	#4	#5 (number of days)	#6	#7	#8	points for dia	points for int	**Characteristic Pain intensity (CPI)**	**Interference score (IS)**
1			5	3	5		0	0	0	0	2	**43.33**	**0.00**
8		5	5	4	5	0	0	2	2			**46.67**	**13.33**
18		7	0	2	2	0	0	0	7			**13.33**	**23.33**
3		3	2	5	3	0	0	0	0			**33.33**	**0.00**
10		14	9	10	9	30	9	9	9			**93.33**	**90.00**
4		14	8	8	7		5	5	5			**76.67**	**50.00**
15		4	7	8	8	26	9	8	9			**76.67**	**86.67**
16		1	0	2	8	8	3	3	2			**33.33**	**26.67**
5		6	0	1	2	0	0	0	0			**10.00**	**0.00**
2		7	7	8	6	0	0	6	7			**70.00**	**43.33**
6													
7		4	1	0	0		0	0	0			**3.33**	**0.00**
9		14	0	10	9	30	6	8	9			**63.33**	**76.67**
12		10	8	9	9	0	7	0	0			**86.67**	**23.33**
13		10	10	10	5	21	7	7	7	70	2	**83.33**	**70.00**
14		2	0	0	0		0	0	0			**0.00**	**0.00**
17													
19		7	8	9	8	5	7	7	7			**83.33**	**70.00**

Patient code	GCPS scores: At recall											
	#1 (number of days)	#2	#3	#4	#5 (number of days)	#6	#7	#8	points for dia	points for int	**Characteristic Pain intensity (CPI)**	**Interference score (IS)**
1	0	0		0	0	0	0	0	0	0	**0.00**	**0.00**
8	1	4	2	1	0	0	0	0			**23.33**	**0.00**
18	0	0	0	0	0	0	0	0			**0.00**	**0.00**
3	0	0	0	0	0	0	0	0	2	0	**0.00**	**0.00**
10	14	10	9	9	30	10	10	10			**93.33**	**100.00**
4	14	7	8	8		5	5	5			**76.67**	**50.00**
15		7	5	6	20	6	6	6			**60.00**	**60.00**
16		2	4	8	2	2	2	2			**46.67**	**20.00**
5	0	0	1	1	0	0	0	0			**6.67**	**0.00**
2		5	8	8	0	0	0	0			**70.00**	**0.00**
6												
7	5	5	5	5	0	0	0	0			**50.00**	**0.00**
9	10	0	10	8	30	5	7	8			**60.00**	**66.67**
12	6	7	9	8	0	5	5	0			**80.00**	**33.33**
13	10	10	10	5		7	7	7			**83.33**	**70.00**
14	5	1	3	1		0	0	0			**16.67**	**0.00**
17	0	0	0	0	0	0	0	0			**0.00**	**0.00**
19		7	7	5	0	0	4	0			**63.33**	**13.33**

Patient code	JFLS scores: Before Treatment																				sum	missing	8-missing	JFLS-8	Mastication (mean 1-6)	Mobility (mean 7-10)	Verbal and emotional communication (mean 13-20)	Global (mean Mastication, Mobility, Communication)
	#1	#2	#3	#4	#5	#6	#7	#8	#9	#10	#11	#12	#13	#14	#15	#16	#17	#18	#19	#20								
1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	8	0	**0.00**	**0.00**	**0.00**	**0.00**
8		2	2	3	3	6			5	5	2	7	6	5	9	8	7	5	8	8	91	3	5	18.2	**3.20**	**5.00**	**7.00**	**5.07**
18	5	5	2	2	2	2	9	2	3	2	0	0	0	0	0	0	2	0	0	0	36	0	8	4.5	**3.00**	**4.00**	**0.25**	**2.42**
3	8	9	9	8	0	0	10	9	10	0	0	10	0	0	0	2	2		0	0	77	1	7	11	**5.67**	**7.25**	**0.57**	**4.50**
10	9	7	9		2	4	9	7	7	3	10	6	4	1	5	6	4	6	4	5	108	1	7	15.4285714	**6.20**	**6.50**	**4.38**	**5.69**
4	6	5	7	6	6	4	8	7	7	7	6	5	6	7	7	7	6	7	7	6	127	0	8	15.875	**5.67**	**7.25**	**6.63**	**6.51**
15	10	9	10	10	5	5	10	10	10	10	2	10	10	10	8	0	0	2	2	10	143	0	8	17.875	**8.17**	**10.00**	**5.25**	**7.81**
16	10	8	7	4	4	6	10	6	5	8	7	10	7	6	5	3	8	6	4	4	128	0	8	16	**6.50**	**7.25**	**5.38**	**6.38**
5	3	3	3	3	0	0	5	3	1	2	0	3	0	0	0	0	0	0	0	1	27	0	8	3.375	**2.00**	**2.75**	**0.13**	**1.63**
2	10	8	8	8	8	8	10	10	8	8	0	10	0	10	8	8	8	2	2	2	136	0	8	17	**8.33**	**9.00**	**5.00**	**7.44**
6																					0		8	0				
7	2			0	0	0	1	0	0	0	0	5	0	0	0	0	0	0	0	0	8	2	6	1.33333333	**0.50**	**0.25**	**0.00**	**0.25**
9	6	6	3	7	1	0	1	1	1	0	0	5	0	0	0	0	0	0	0	0	31	0	8	3.875	**3.83**	**0.75**	**0.00**	**1.53**
12	10	10	0	0	0	0	10	10	10	10	0	10	0	10	10	0	0	10	10	0	110	0	8	13.75	**3.33**	**10.00**	**5.00**	**6.11**
13	10	10	5	5	3	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	48	0	8	6	**5.67**	**1.00**	**1.00**	**2.56**
14				0	0	0	4	1	2	2	4	4	2	2	0	0	0	0	0	0	21	3	5	4.2	**0.00**	**2.25**	**0.50**	**0.92**
17	10				8	6	10	10	9	7	6	10	5		4	5	4			6	100	6	2	50	**8.00**	**9.00**	**4.80**	**7.27**
19	9	8	9	7	5	3	7	7	6	6		9	8	8	9	9			10	10	130	3	5	26	**6.83**	**6.50**	**9.00**	7.44

Patient code	JFLS scores: after 4th visit																											
	#1	#2	#3	#4	#5	#6	#7	#8	#9	#10	#11	#12	#13	#14	#15	#16	#17	#18	#19	#20	sum	missing	8-missing	JFLS-8	**Mastication (mean 1-6)**	**Mobility (Mean 7-10)**	**Verbal and emotional communication (mean 13-20)**	**Global**
1	5	5	5	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	15	0	8	1.875	**2.50**	**0.00**	**0.00**	**0.83**
8		2	2		3	3	6	6	5	5	2	7	6	5	9	8	7	5	8	8	97	2	6	16.1666667	**2.50**	**5.50**	**7.00**	**5.00**
18	4	4	2	2	2	2	7	2	1	0	0	0	0	0	0	0	0	0	0		26	0	8	3.25	**2.67**	**2.50**	**0.00**	**1.72**
3	10	10	0	0	0	0	10	0	0	0	0	0	0	0	0	0	0	0	0	0	30	0	8	3.75	**3.33**	**2.50**	**0.00**	**1.94**
10	8	9	5	8	5	4	9	6	4	4	7	9	6	0	4	5	3	3	3	4	106	0	8	13.25	**6.50**	**5.75**	**3.50**	**5.25**
4	7	8	6	7	5	4	7	6	6	4	4	6	5	8	8	4	4	7	7	7	120	0	8	15	**6.17**	**5.75**	**6.25**	**6.06**
15	6	7	6	7	5	5	6	6	5	5	4	5	5	5	4	4	4	5	7	7	108	0	8	13.5	**6.00**	**5.50**	**5.13**	**5.54**
16	0	0		5	6	5	5	6	6	5			6	8		3	0	9	9		73	3	5	14.6	**3.20**	**5.50**	**5.83**	**4.84**
5	2	2	0	1	0	0	2	2	2	1	0	2	0	0	0	0	0	0	0	0	14	0	8	1.75	**0.83**	**1.75**	**0.00**	**0.86**
2	8	8	8	8	8	8	9	10	6	6	0	10	0	8	8	8	8	2	2	2	127	0	8	15.875	**8.00**	**7.75**	**4.75**	**6.83**
6																					0			#DIV/0!				
7	2			0	0	0	1	0	0	0	0	2	0	0	0	0	0	0	0	0	5	2	6	0.83333333	**0.50**	**0.25**	**0.00**	**0.25**
9	9	9	7	7	1		3	2	1	1		1	1	1	10						53	7	1	53	**6.60**	**1.75**	**4.00**	**4.12**
12	7	8	6	7	6	5	9	7	6	6	5	9	6	5	6	4	4	8	6	7	127	0	8	15.875	**6.50**	**7.00**	**5.75**	**6.42**
13	10	10	5	5	3		1	1	1	1	1	1	1	1	1	1	1	1	1	1	47	1	7	6.71428571	**6.60**	**1.00**	**1.00**	**2.87**
14	4	4	0	0	0	0	4	0	0	0	0	4	0	4	0	0	0	0	0	0	20	0	8	2.5	**1.33**	**1.00**	**0.50**	**0.94**
17	3	3	5	4	3		6	6	3	3	2	4	3	2	2	0	0	0	1	1	51	1	7	7.28571429	**3.60**	**4.50**	**1.13**	**3.08**
19	7	7	8	8	5	3	7	6	4	1	1	9	4	4	6	6	6		8	8	108	1	7	15.4285714	**6.33**	**4.50**	**6.00**	**5.61**

Patient code	JFLS scores: At recall																											
	#1	#2	#3	#4	#5	#6	#7	#8	#9	#10	#11	#12	#13	#14	#15	#16	#17	#18	#19	#20	sum	missing	8-missing	JFLS-8	**Mastication (mean 1 - 6)**	**Mobility (mean 7-10)**	**Verbal and emotional Communication (mean 13-20)**	**Global (mean M, M and C)**
1	0	0	0	0	0	0	4	0	0	0	0	0	0	0	0	0	0	0	0	0	4	0	8	0.5	**0.00**	**1.00**	**0.00**	**0.33**
8	3	3	4	4	5	1	3	3	3	4	3	4	3	4	4	4	4	4	4	5	72	0	8	9	**3.33**	**3.25**	**4.00**	**3.53**
18	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	8	0	**0.00**	**0.00**	**0.00**	**0.00**
3	0		3		3	1	6	1	0	0	0	5	0	0	0	0	0	0	0	0	19	2	6	3.16666667	**1.75**	**1.75**	**0.00**	**1.17**
10	9	7	9		2	4	9	7	7	3	10	6	4	1	5	6	4	6	4	5	108	1	7	15.4285714	**6.20**	**6.50**	**4.38**	**5.69**
4	7	8	7	7	4	4	7	6	6	5	5	7	6	7	7	4	4	7	7	6	121	0	8	15.125	**6.17**	**6.00**	**6.00**	**6.06**
15	7	8	7	8	7	6	8	8	8	7	5	9	6	6	5	5	3	8	6	8	135	0	8	16.875	**7.17**	**7.75**	**5.88**	**6.93**
16	5	0	5	0	9	0	5		5	5	5	5	5	8	8	5	0	0	8	8	86	1	7	12.2857143	**3.17**	**5.00**	**5.25**	**4.47**
5	2	2	0	1	0	0	2	2	2	1	0	2	0	0	0	0	0	0	0	0	14	0	8	1.75	**0.83**	**1.75**	**0.00**	**0.86**
2	9	9	9	7	7	8	10	10	8	0	9	9	9	10	8	8	7	0	0	0	137	0	8	17.125	**8.17**	**7.00**	**5.25**	**6.81**
6																					0			#DIV/0!				
7	0	0	0	0	0	0	2	0	0	0	0	3	0	0	0	0	0	0	0	0	5	0	8	0.625	**0.00**	**0.50**	**0.00**	**0.17**
9	7	7	7	7	1	3	3	2	1	1		1	1	1	10						52	5	3	17.3333333	**5.33**	**1.75**	**4.00**	**3.69**
12	10	8	7	7	6	4	10	9	8	6	5	10	5	5	7	5	5	10	7	8	142	0	8	17.75	**7.00**	**8.25**	**6.50**	**7.25**
13	10	10	7	7	5	3	3	3	0	0	7		0	7	5	2	7	7	5	5	93	1	7	13.2857143	**7.00**	**1.50**	**4.75**	**4.42**
14	4	4	0	0	0	0	5	0	0	0	0	4	0	0	0	0	0	0	0	0	17	0	8	2.125	**1.33**	**1.25**	**0.00**	**0.86**
17	2	2	3	2	1		4	4	1	1	0	1	0	0	0	0	0	0	0	0	21	1	7	3	**2.00**	**2.50**	**0.00**	**1.50**
19	8	7	8	6	5	4	8	6	7	3	3	9	7	7	8	7				8	111	3	5	22.2	**6.33**	**6.00**	**7.40**	**6.58**