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ORIGINAL ARTICLE

Multi-wave locked system laser therapy in chronic non-specific neck pain: a double-blind placebo randomized-controlled trial

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ABSTRACT

BACKGROUND: Multi-wave locked system (MLS) laser therapy has shown efficacy in reducing pain in various musculoskeletal conditions. However, its standalone effects on pain and function in patients with chronic non-specific neck pain (CNNP) remain unclear.
AIM: The aim of this study was to evaluate the effects of MLS laser therapy on pain, function, and disability in patients with CNNP compared to a placebo treatment.
DESIGN: Randomized controlled study.
SETTING: Outpatient.
POPULATION: Patients aged 20-65 years with CNNP and a neck pain score between 4 and 7 on a Visual Analogue Scale.
METHODS: Forty-seven patients were randomized into two groups: MLS Laser and Sham Laser, receiving 8 sessions of their respective treatments. Assessments were conducted at baseline (T0), end of therapy (T1), and one month post-therapy (T2) for neck pain (VAS), function (kinematics and electromyography of head movements), and disability (Neck Disability Index, NDI). Within- and between-group differences were analyzed across these time points.
RESULTS: The MLS Laser group showed significant improvements ($P<0.05$) in the range of motion for head lateral bending and rotation compared to the Sham Laser group, which exhibited no changes. Both groups demonstrated increased movement velocity ($P<0.05$) and reduced pain and disability scores ($P<0.05$). However, either VAS and NDI did not reach the thresholds for minimal clinically important differences (MCID). At T2, a trend towards greater pain reduction was observed in the MLS Laser group ($P=0.05$).
CONCLUSIONS: Both MLS Laser and Sham Laser therapies resulted in statistically significant improvements in pain, disability, and movement velocity. However, these changes were not clinically meaningful. MLS Laser therapy provided more pronounced and sustained pain relief and improved range of motion in head movements.
CLINICAL REHABILITATION IMPACT: MLS Laser therapy improves neck range of motion as a standalone treatment for chronic non-specific neck pain, despite similar effects on pain and disability reduction with placebo.

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KEY WORDS: Neck; Biomechanical phenomena; Electromyography.

Chronic non-specific neck pain (CNNP) is one of the most common musculoskeletal issues[1] affecting both adults and young individuals and causing disability and consistent medical care.[2, 3] CNNP is defined as neck pain

lasting for over 3 months,[4] mainly resulting from mechanical issues, often linked to poor posture that alters neck biomechanics. This definition excludes other potential causes of neck pain, such as vertebral fractures, spinal surgeries, and systemic conditions like metabolic, rheumatic, tumoral, or infectious diseases.[5-8]

Common treatments for CNNP are pain drugs, or conservative therapies such as exercise and physical therapy,[9, 10] but to date there is no clear evidence on the short as well as the long-term efficacy of all these treatments.[11] It has been shown that laser therapies can provide an analgesic and anti-inflammatory effect,[12, 13] and for this reason they have been widely used for the treatment of several musculoskeletal issues to decrease pain and pain-related disability. However, a heterogeneity of protocols has been used for laser therapy treatments thus making difficult to clearly identify direct beneficial effects of laser therapy. In fact, it has been frequently used as an additional therapy to physical,[14-18] or other therapeutic interventions.[19, 20] Furthermore, there is a high heterogeneity of settings used for laser therapy (*i.e.*, waveforms, wavelengths, and pulses timing)[21] and thus it is difficult to draw conclusions on the effectiveness of the sole laser therapy since the effects of the concomitant therapies may have masked its effects.

Multiwave locked system (MLS) laser therapy is a high-power laser featured by a dual waveform which is delivered with a continuous and synchronized emission. Previous literature has reported a deeper capacity of passing through the tissues, thus providing higher improvements in chronic pain when compared to other kind of laser therapies,[22, 23] and there is evidence that it can provide positive effects when combined with physical exercise in patients with CNNP.[24] However, to the best of the authors knowledge, it is not known which are the effects MLS therapy when applied without additional therapies in patients with CNNP.

This study hypothesized that MLS Laser therapy would significantly reduce pain intensity and related disability in patients with chronic non-specific neck pain, as these are the most immediate and impactful issues reported by this patient population. Pain and disability were thus chosen as primary outcomes, given their direct influence on quality of life and their common use as core measures in clinical trials for chronic pain interventions. A secondary hypothesis was that MLS Laser therapy would improve neck function, measured by range of motion and muscle activation. This functional improvement was designated as a secondary aim, as it may be influenced indirectly by reductions in pain and disability and may require longer observation to be fully assessed. Consequently, the study's design prioritizes pain and disability reduction to reflect the primary concerns of patients, while functional gains are explored as a potential additional improvements.

Materials and methods

Patients

The study has been conducted in accordance with the declaration of Helsinki and the study protocol was recorded on ClinicalTrials.gov (NCT05753540). Patients seeking care for CNP at the participating center as outpatients, were consecutively recruited. After being screened for inclusion and exclusion criteria, those meeting the inclusion criteria were invited to participate. All the participants signed an informed consent. The study started following the approval by the local Ethical Committee "Comitato Etico Area Vasta Emilia Centro" (CE AVEC: 587/2021/Disp/IOR). No changes to methods occurred after the starting date (2022-03-21).

From March 21st, 2022 to March 31st, 2023, among patients eligible for the study, forty-seven subjects with CNNP were recruited and divided into two groups, the MLS Laser group (N.=24) and Sham Laser group (N.=23). A medical doctor specialized in Physical and Medicine Rehabilitation conducted the clinical evaluation by gathering the patient's medical history, reviewing radiological examinations, and personally assessing each patient. Patients' characteristics in each of the two groups are reported in Table I. A CONSORT flow-chart of patients' recruitment is shown in Figure 1. Inclusion criteria were: 1) CNNP since at least 3 months; 2) age between 20 and 65 years; 3) neck pain score between 4 and 7 on a 0-10 Visual Analogue Scale (VAS); 4) BMI<30. Exclusion criteria were: 1) spine surgery; 2) vertebral fractures or other pathologies; 4) back deformities; 5) tendinopathy or other conditions affecting the shoulder; 6) skin abrasions or tattoos

TABLE I.—*Patients' characteristics.*

	Gender	Age (yrs)	Mass (kg)	Height (cm)	BMI	NP months
MLS laser group	20 F/4 M	51±12	70±12	165±6	25±4	68±76
Sham laser group	17 F/6 M	48±14	68±14	166±9	25±4	69±59

Number of males and females in each group, age, body mass, body height, Body Mass Index (BMI), and duration of neck pain (NP) in months.

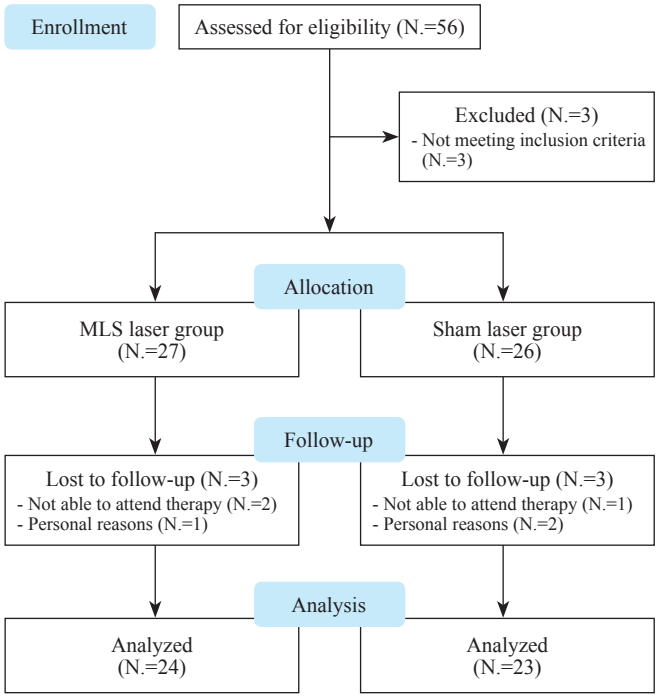

Figure 1.—Flow chart of patient's recruitment.

in the site of application of the laser therapy; 7) steroids injections during the 3 weeks before preceding the start of the study; 8) metabolic, psychiatric, rheumatic, cardiovascular, tumoral and infective diseases; 9) epilepsy; 10) all conditions in which heat is contraindicated. Patients were asked to refrain from taking pain drugs among the whole duration of the study.

Sample size

Sample size has been calculated based on data of a previous study studying the effects of laser therapy on neck pain measured with a VAS scale.[25] The VAS minimal clinically important difference (MCID) for chronic neck pain ranged from 4.6 to 21.4 mm on a 0-10 cm scale.[26] For this study, we adopted an MCID of 15 mm. Assuming a standard deviation of 20 mm (2.0 cm) in VAS scores, a two-tailed test with a significance level (α) of 0.05, and a power (1-β) of 0.80, the required sample size per group was calculated to be 23 participants. Based on a *t*-test for independent samples, a power of 80% and an α error of 0.05, a minimum of 23 patients for each group were needed for the study. This sample size ensures robust power to detect a significant between-group difference in pain reduction, consistent with findings from previous studies on VAS in populations affected by chronic neck pain.[26] We used the G*Power software (version 3.1.9.7) to calculate the required sample size for this study. The calculation was based on an expected effect size (Cohen's d) of 0.80, which is considered a large effect size, drawn from previous studies evaluating laser therapy's impact on chronic pain conditions. We chose this effect size as it aligns with clinically meaningful changes observed in similar trials. A two-tailed test with an alpha level of 0.05 and a power (1-β) of 0.80 indicated that a minimum of 23 participants per group would be necessary to detect significant differences between the groups.

Treatment

MLS laser and sham laser therapies consisted in 8 sessions delivered at alternate days (from Monday to Friday) at the Physical Medicine and Rehabilitation Unit of the Rizzoli Orthopaedic Institute in Bologna, Italy. During laser therapy sessions, patients were positioned face down on a bed. Each session lasted 7 minutes and 40 seconds. The MLS laser treatment was performed with a laser machine (ASA, Arcugnano, Vicenza, Italy) providing synchronized dual wavelengths (*i.e.* 808nm continuous laser and 905nm pulsed laser) with continuous and pulsed emissions, and a 5 J/cm^2 energy which was applied over a (20x5 cm) 100 cm^2 surface of the cervical portion of the spine and a (20x7.5 cm) 150 cm^2 surface corresponding to each side of the trapezius muscle (Figure 2). The laser scanner was adjusted

Figure 2.—Laser treatment.

to 20 cm above the patient's skin, as recommended by the manufacturer. The exact location of the treatment area was highlighted by a red light. The movement of the column and arm of the laser machine and the robotized rotation of its head, enabled the proper positioning and laser delivery on the target areas. The beginning of the automatic treatment, was accompanied by an audible signal. For the sham laser, the robotic head was positioned, the skin area was illuminated with red light, and pressing "Start" activated the device, accompanied by an audible signal.

The sham laser therapy consisted in the same number of sessions of the same duration, performed with an identical laser machine emitting the same color light and the same starting signal of the of the real MLS laser machine used for the MLS laser group. Laser therapy was applied by a trained physical therapist, with a minimum of three years of clinical experience in musculoskeletal rehabilitation.

Potential risks associated with laser treatment were communicated to patients and detailed in the informed consent, signed before treatment. According to manufacturer's indications, the application is also contraindicated in certain conditions: during pregnancy, in the presence of active bleeding, in patients who have taken photosensitizing medications, and in the presence of neoplasms. To avoid the irradiation of eyes and periocular areas, both the patient and the operator wore laser safety goggles during the laser treatment. The Laser device is CE0123 marked, certified under EU MDR.

No additional treatments, such as drugs, manual therapy, or injections, were permitted during the intervention period to prevent any influence on the outcomes.

Blinding and allocation concealment

Patients were allocated to either the MLS Laser group or the Sham Laser group in accordance with a randomization formulated a priori using a system of computer-generated random numbers. The physical therapists and the patients were blinded on their allocation, as well as those who conducted data analysis. Only the manufacturing company of the two laser machines was aware of which was the MLS or the Sham Laser machine. This information was revealed to all the experimenters once the statistical analysis was finished.

Compliance rates

Adherence to the treatment protocol was meticulously tracked, with all participants completing the full course of their assigned intervention (either MLS Laser or Sham Laser therapy) across the eight sessions. Consequently, both groups achieved a 100% compliance rate, with no missed sessions or deviations from the planned protocol. There were no missing data.

Outcomes

The primary outcomes of this study were pain intensity, measured using the VAS,[25] and disability, assessed with the Neck Disability Index (NDI). Secondary outcomes included neck function improvements, such as range of motion and velocity during head movements, assessed via kinematic and electromyographic analyses.

The VAS is a reliable tool with a minimal clinically important difference (MCID) for chronic neck pain ranged from 4.6 to 21.4 mm on a 0-10 cm scale.[26]

The validated Italian version of the Neck Disability Index was used.[27] This version has been shown to have strong psychometric properties, including high internal consistency (Cronbach's alpha >0.80) and test-retest reliability (Intraclass Correlation Coefficient >0.90). The MCID for the NDI in chronic neck pain is generally reported as 5 points on the 0-50 scale, indicating the smallest clinically meaningful change for patients.

Pain

Patients were asked to quantify their neck pain on a 0-10 VAA, where 0 represented absence of pain and 10 represented the worst imaginable pain. Scores recorded at each assessment were used for statistical analysis.

Function

Function was assessed by means of a kinematic and electromyographic analysis of the neck mobility and muscle activation during a right/left head inclination, a head flexion/extension, and a right/left head rotation movement. Each movement was performed at a self-selected speed and was repeated three times. A two minutes rest was allowed after each movement. Muscle activations were recorded by means of wireless bipolar surface electromyography (FreeEMG, BTS Bioengineering, Milano, Italy). Pre-gelled self-adhesive EMG electrodes were applied over the sternocleiomastoideus (SC) and the *semispinalis capitis* (SS) muscles in both the right and the left sides in accordance with SENIAM recommendations.[28] A triaxial accelerometer (G-Walk, BTS Bioengineering, Milano, Italy) was applied in the middle of the back of the head of the patients and secured by means of an ad hoc adherent belt. The EMG and accelerometer were part of the same synchronized system and data were recorded at

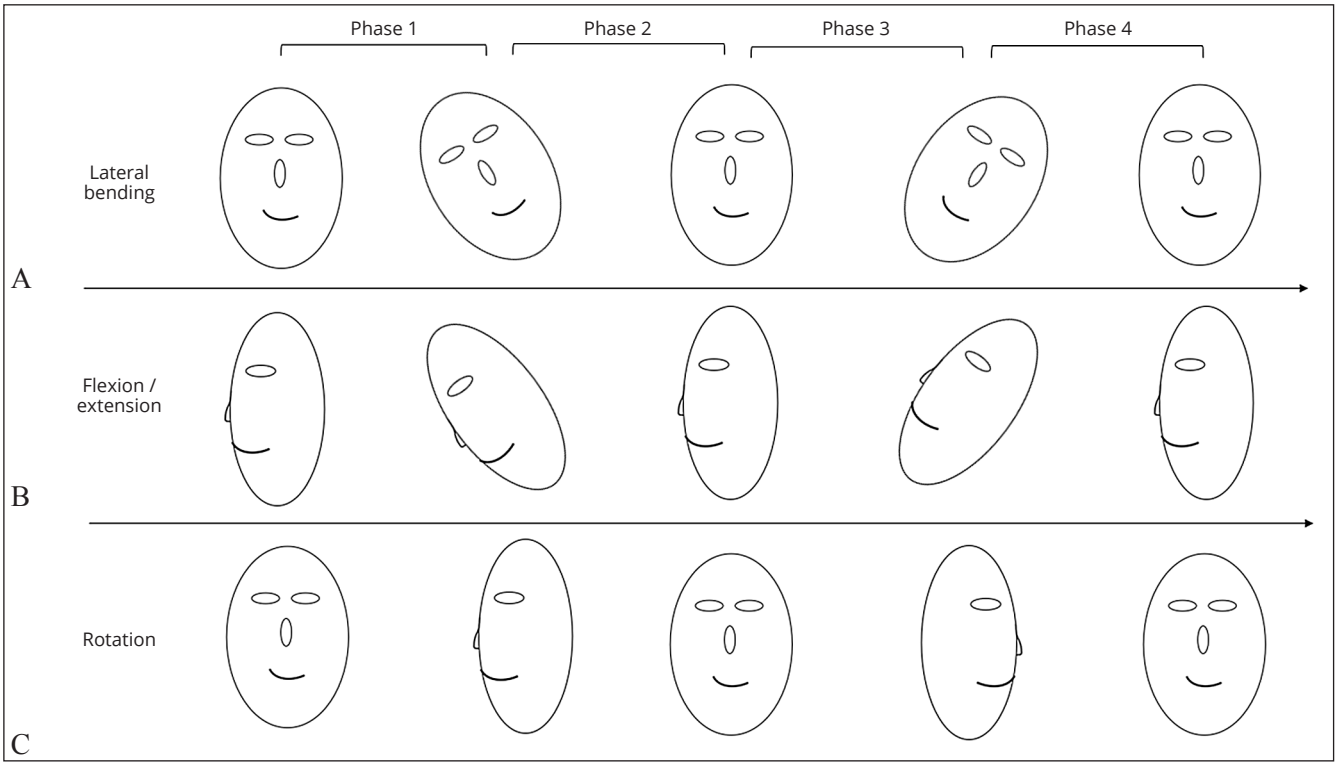

Figure 3.—Phases of the head lateral bending (A), head flexion/extension (B) and rotation (C).

a 1000 Hz frequency. Data were analysed by means of an automatized routine of analysis (Cervical Spine Mobility Protocol, BTS Bioengineering, Milan, Italy) as follows. For right/left head inclination, four movement phases were identified (Figure 3A). Phase 1 was identified from the start of the movement (neutral position of the head) to the maximum of right inclination. Phase 2 was identified from the maximum of right inclination to the return to a neutral position of the head. Phase 3 was identified from the reached neutral position of the head to the maximum of left inclination. Phase 4 was identified from the maximum of left inclination to the return to the neutral position of the head. For the head flexion/extension, four movement phases were identified (Figure 3B). Phase 1 was identified from the start of the movement (neutral position of the head) to the maximum of head flexion. Phase 2 was identified from the maximum of head flexion to the return to a neutral position of the head. Phase 3 was identified from the reached neutral position of the head to the maximum of head extension. Phase 4 was identified from the maximum of head extension to the return to the neutral position of the head. For the right/left head rotation, four movement phases were identified (Figure 3C). Phase 1 was identified from the start of the movement (neutral position of the head) to the maximum of right rotation. Phase 2 was identified from the maximum of right rotation to the return to a neutral position of the head. Phase 3 was identified from the reached neutral position of the head to the maximum of left rotation. Phase 4 was identified from the maximum of left rotation to the return to the neutral position of the head. Regarding kinematic analysis, for each phase of each of the three movements were calculated: 1) the duration of each phase; 2) the velocity of each phase; 3) the maximum range of motion. Regarding EMG analysis, the root-mean-square (RMS) of the rectified EMG signal during each phase was calculated. The RMS of each muscle during each phase, and the symmetry between the right and left of each pair of muscles were used for further analysis. Finally, the mean of the three trials for each parameter was used for statistical analysis.

Disability

To quantify the disability related to neck pain, patients were asked to fill the Neck Disability Index questionnaire.[27] It is composed by 10 sections, *i.e.*, pain intensity, personal care, lifting, reading, headaches, concentration,

work, driving, sleeping, and recreation. As higher is the final score of the questionnaire as high is the disability. The final score at each assessment was used for statistical analysis.

Assessments and data acquisitions

Pain, function, and disability were assessed before starting the treatments (T0), at the end of treatments (T1), and 1 month after the end of the treatments (T2).

The enrolment process, along with the application of the VAS scale and NDI questionnaire, was conducted by a medical doctor, while the measurements of cervical range of motion and muscle activation were carried out by an experienced PhD researcher and a licensed physical therapist trained in administering and evaluating kinematic and electromyographic assessments.

Statistical analysis

The VAS and Neck Disability Index (NDI) scores were treated as continuous variables in the statistical analyses. A Mixed Model ANOVA was employed to evaluate the primary and secondary outcomes. This approach enabled the assessment of:

- group effect: differences between the MLS Laser and Sham Laser groups;
- time effect: changes over the three assessment points (T0, T1, T2);
- group-by-time interaction effect: variations in the differences between groups across time points, which measure whether the evolution over time differs between groups.

Descriptive statistics were calculated for all variables, and assumptions for the parametric analyses were verified. The results include P values for the group, time, and interaction effects. A significance level of $P<0.05$ was adopted for all analyses. Data analysis was performed using SPSS software (version 23, SPSS Inc., Chicago, IL, USA).

Results are presented in a summary table that includes pre-treatment, post-treatment, and follow-up means (SD) for each group, along with P values for the group, time, and interaction effects.

Results

Pain

A trend to significance was found for the T2 assessment, with patients in the MLS Laser group having a lower pain score in comparison to patients in the Sham Laser group (2.4±1.9 *vs.* 3.7±2.4; P=0.05). No significant differences between the MLS Laser group and the Sham Laser group for VAS scores at T0 (5.2±1.1 *vs.* 5.6±1.2) and T1 (2.8±2.4 *vs.* 3.2±1.9). The Kruskal-Wallis ANOVA showed a significant effect of time for pain VAS scores in both the MLS Laser group (x^2=22.065; $P<0.001$) and the Sham Laser group (x^2=13.875; $P<0.001$). *Post-hoc* analysis showed that VAS pain scores were significantly lower at T1 ($P<0.001$) and T2 ($P<0.001$) in comparison with T0 in both groups (Table II).

No side effects were reported, except for one patient who experienced transient redness in the treated area of the skin the day after the session.

Disability

The Mann-Whitney showed no differences between the two groups for the Disability index scores, while the Kruskal-Wallis ANOVA showed a significant effect of time for both the MLS Laser group (x^2 =15.025; $P<0.01$) and for the Sham Laser group (x^2=8.739; $P<0.05$). The post-hoc analysis showed a significant decrease in the Disability scores between T0 and T1, and between T0 and T2 in both MLS Laser group (T0=26.2±13.3 *vs.* T1=15.2±14.4; $P<0.001$ and T0=26.2±13.3 *vs.* T2=12.8±12.1; $P<0.001$) and Sham Laser group (T0=27.4±14.8 *vs.* T1=15.9±15.0; $P<0.001$ and T0=27.4±14.8 *vs.* T2=17.0±16.6; $P<0.001$). Mean and standard deviations of the Disability Index in the two groups are reported in Table II.

Kinematics and EMG data

Right-left lateral bending of the head

Mean values and standard deviations of lateral bending kinematics are reported in Supplementary Digital Material

TABLE II.—*Summary of outcome measures (VAS and NDI) for MLS laser and sham laser groups.*

Outcome measure	Group	Pre-treatment (T0) mean (SD)	Post-treatment (T1) mean (SD)	Follow-up (T2) mean (SD)	Group effect (P value)	Time effect (P value)	Interaction effect (P value)
VAS	MLS Laser	5.2 (1.1)	2.8 (2.4)	2.4 (1.9)	0.049	<0.001	0.043
	Sham Laser	5.6 (1.2)	3.2 (1.9)	3.7 (2.4)			
NDI	MLS Laser	26.2 (13.3)	15.2 (14.4)	12.8 (12.1)	0.052	<0.001	0.046
	Sham Laser	27.4 (14.8)	15.9 (15.0)	17.0 (16.6)			

P values for group, time, and interaction effects are based on the Mixed Model ANOVA.

1, Supplementary Table I. The ANOVA showed an effect of time for the total duration of the movement (F=6.699; P<0.01), and for the duration of phase 1 (F=6.423; P<0.01), phase 2 (F=3.955; P<0.05), phase 3 (F=5.450; P<0.05), and phase 4 (F=3.841; P<0.05) of the movement. A significant effect of time was found also for the velocity of phase 1 (F=5.385; P<0.01), phase 2 (F=5.890; P<0.01), phase 3 (F=4.968; P<0.05) and phase 4 (F=3.250; P<0.05) of the movement, with patients in both groups showing a general increase in the velocity and decrease in the duration of the movement across the three assessments.

A significant effect of time (F=3.321; P<0.05) was also found for the ROM of the movement during right lateral head bending, with patients in the MLS Laser group showing a significant increase in the ROM in the right side from T0 to T1 (32.1±7.6 *vs.* 34.2±7.5; P<0.05). No significant changes in ROM were observed in the Sham Laser group.

Forward flexion-backward extension of the head

Mean values and standard deviations of flexion-extension kinematics are reported in Supplementary Digital Material 2: Supplementary Table II. The ANOVA showed an effect of time for the total duration of the movement (F=17.673; P<0.001), and for the duration of phase 1 (F=14.521; P<0.001), phase 2 (F=6.127; P<0.01), phase 3 (F=7.846; P<0.01), and phase 4 (F=8.218; P<0.01) of the movement. A significant effect of time was found also for the velocity of phase 1 (F=16.623; P<0.001), phase 3 (F=17.753; P<0.001) and phase 4 (F=10.006; P<0.001) of the movement, with patients in both groups showing a general increase in the velocity and decrease in the duration of the movement across the three assessments.

No significant changes in ROM were observed in the two groups.

Right-left rotation of the head

Mean values and standard deviations of rotations kinematics are reported in Supplementary Digital Material 3, Supplementary Table III. The ANOVA showed an effect of time for the total duration of the movement (F=6.828; P<0.01), and for the duration of phase 1 (F=6.625; P<0.01), phase 2 (F=3.913; P<0.05), and phase 3 (F=3.113; P<0.05) of the movement. A significant effect of time was found also for the velocity of phase 1 (F=6.971; P<0.01), phase 2 (F=8.156; P<0.01), phase 3 (F=5.337; P<0.05) and phase 4 (F=6.625; P<0.01) of the movement, with patients in both groups showing a general increase in the velocity and decease in the duration of the movement across the three assessments.

A significant time to treatment interaction (F=4.728; P<0.05) was found for the ROM of the movement, with patients in the MLS Laser group showing a significant increase in the ROM in the right side from T0 to T1 (51.9±7.9 *vs.* 56.9±8.3; P<0.05) and from T0 to T2 (51.9±7.9 *vs.* 58.4±6.2; P<0.01), and in the left side from T0 to T2 (60.6±13.3 *vs.* 69.7±9.6; P<0.05). No significant changes in ROM were observed in the Sham Laser group.

EMG data

No between-groups or across time differences were found for EMG data.

Discussion

The main result of this study was that an 8-session MLS Laser therapy on CNNP led to a significant increase in the range of motion of head lateral bending and rotation in comparison to the Sham Laser group which reported no changes in the range of motion. Furthermore, a significant increase in the velocity of all the three movements was observed in both groups. Finally, a significant decrease in pain and disability was reported in both groups, with a tendency towards a lower pain in the MLS Laser group compared to the Sham Laser group.

This last result is in accordance with previous literature on laser therapy for musculoskeletal condition featured by chronic pain. In fact, several studies have reported a reduction in pain and disability following laser therapy mainly when combined to other therapies.[15, 19, 20, 24, 29, 30] It has been shown that laser therapy can lead to a reduction of pain as it contributes in regulating the levels of certain neurotransmitters, as prostaglandin,[31] involved in neural pathways related to pain. In addition, it has been shown that patients' expectations in response to a therapy may positively or negatively influence treatment outcomes by means of an endogenous release of pain modulators,[32, 33] thus it can be stated that placebo effect has affected our results. The present and several previous studies have found a reduction in pain in the placebo control.[34-36] In the present study, however, a trend towards a lower pain the MLS Laser group was found in the longer term assessment, thus suggesting that a certain level of pain pathways modulation might be ascribed to laser therapy beyond the placebo effect. It should be also noted that the level of self-reported disability decreased, and movement velocity increased, in both groups, consistently with the reduction of pain. These results further confirm the idea that patients' expectations regarding a treatment play a determinant role in the treat-

ment's outcomes, and are in accordance with previous authors which reported a decrease in self-reported disability in the placebo control groups of their studies.[34-38]

However, despite an increase in movement velocity in both groups, an increase in the neck range of motion following treatment was only observed in the MLS Laser group. It is plausible to think that the capacity of the MLS Laser to deeply pass throughout tissues may have contributed to tissue mobility.[39, 40] It is not clear why this result was observed only in head rotations and lateral bending, and not in forward/backward head flexion. Regarding this point, it should be mentioned that laser therapy was applied only on posterior neck muscles. In addition, the lack of a control group of healthy age-matched individuals may have limited of understanding of normal values of head flexion/extension and neck movement abnormalities in patients with CNNP compared to controls. In line with this, systematic literature reviews have reported inconsistencies and lack of clear results regarding range of motion limitations in patients with neck pain claiming additional research.[41]

It remains also unclear why we observed a change in neck kinematic without a concomitant change in muscles activations. This result might be explained by three points. The first is that the duration of the laser therapy proposed (8 sessions of therapy over two weeks and a half) was probably a too short time frame to generate adaptations in muscles activation. The second can be related to an ineffectiveness of laser therapy on muscle activation. The third is related to the fact that there's no control group of healthy individuals for reference values of normal neck muscle activation, nor it is known if muscle activations abnormalities exist in patients with CNNP. To the best of the authors knowledge there are no studies investigating the effects of laser therapy on neck kinematics and muscles activations, thus it is not possible to compare our results with previous research.

In clinical practice, to evaluate treatment effects, it is essential to consider both the statistical significance of the results and their clinical relevance, emphasizing the importance of understanding what constitutes a clinically meaningful difference or change. According to the literature,[42, 43] our data indicate that the proposed protocol of MLS laser treatment does not attain clinically relevant levels in reducing pain and is not superior to placebo laser treatment in increasing neck function as evaluated with NDI. Nevertheless, the significant results we have reported on the increase in the velocity of neck movements, and better ROM of lateral bending and rotation in the MLS laser group support a beneficial effect of the treatment on neck tissues.

The findings of this study are primarily generalizable to adults aged 20 to 65 with chronic non-specific neck pain, who meet the study specified inclusion criteria. The study was conducted in a controlled outpatient rehabilitation setting where the effects of MLS Laser and Sham Laser therapy were isolated without concurrent treatments. Therefore, while the results support MLS Laser therapy in this controlled context, caution should be taken when generalizing to broader populations, particularly those with additional comorbidities, different baseline pain characteristics, or in diverse clinical settings, such as inpatient facilities or primary care practices.

Limitations of the study

This study has several limitations that should be considered when interpreting the findings. First, the absence of a healthy control group limits the possibility to compare the observed improvements against normative data for neck mobility and pain perception. Second, the limited number of laser sessions (only 8), and the relatively short follow-up, restricted the ability to assess the long-term efficacy of MLS Laser therapy in chronic neck pain management. Third, the study design excluded additional treatment modalities, such as physical therapy exercises or manual therapy, which restricts the generalizability of the findings to clinical settings that typically employ multi-modal approaches. Finally, the controlled outpatient setting of this study may differ from real clinical environments, where patient characteristics and treatment adherence could vary. This study demonstrated that MLS Laser therapy provided statistically significant improvements in the primary outcomes of pain intensity and disability. For the secondary outcomes, significant improvements were observed in neck range of motion and movement velocity.

Future studies are needed to assess whether combined protocols including MLS laser and physiotherapy/manual therapy can reach clinical relevance.

Conclusions

Our findings indicate that MLS Laser therapy provides statistically significant improvements in pain intensity, function, and range of motion in patients with chronic non-specific neck pain. However, these improvements did not meet the criteria for minimal clinically important differences (MCID) for the primary outcomes (VAS, NDI). The group-by-time interaction effects suggest that the MLS

Laser group achieved more sustained improvements over time compared to the Sham Laser group. Future studies should investigate whether combining MLS Laser therapy with other interventions could achieve clinically meaningful outcomes.

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Conflicts of interest
The authors certify that there is no conflict of interest with any financial organization regarding the material discussed in the manuscript.

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Authors' contributions
Luciana Labanca: data collection, data analysis, writing – original draft; writing – review and editing; Daniela Platano: supervision, writing – review and editing, final approval; Roberto Tedeschi and Elena Cappelli: data collection, data analysis, final approval; Maria G. Benedetti: study conceptualization, supervision, writing – review and editing, final approval; Lisa Berti: study conceptualization, supervision, writing – review and editing, final approval. All authors read and approved the final version of the manuscript.

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Supplementary data
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