What is the ideal dose and power output of low-level laser therapy (810 nm) on muscle performance and post-exercise recovery? Study protocol for a double-blind, randomized, placebo-controlled trial

Adriano Rodrigues de Oliveira¹, Adriane Aver Vanin², Thiago De Marchi³, Fernanda Colella Antonialli², Vanessa dos Santos Grandinetti¹, Paulo Roberto Vicente de Paiva¹, Gianna Môes Albuquerque Pontes¹, Larissa Aline Santos², Ivo de Oliveira Aleixo Junior², Paulo de Tarso Camillo de Carvalho¹,², Jan Magnus Bjordal⁴ and Ernesto Cesar Pinto Leal-Junior¹,²*

Abstract

Background: Recent studies involving phototherapy applied prior to exercise have demonstrated positive results regarding the attenuation of muscle fatigue and the expression of biochemical markers associated with recovery. However, a number of factors remain unknown, such as the ideal dose and application parameters, mechanisms of action and long-term effects on muscle recovery. The aims of the proposed project are to evaluate the long-term effects of low-level laser therapy on post-exercise musculoskeletal recovery and identify the best dose and application power/irradiation time.

Design and methods: A double-blind, randomized, placebo-controlled clinical trial with will be conducted. After fulfilling the eligibility criteria, 28 high-performance athletes will be allocated to four groups of seven volunteers each. In phase 1, the laser power will be 200 mW and different doses will be tested: Group A (2 J), Group B (6 J), Group C (10 J) and Group D (0 J). In phase 2, the best dose obtained in phase 1 will be used with the same distribution of the volunteers, but with different powers: Group A (100 mW), Group B (200 mW), Group C (400 mW) and Group D (0 mW). The isokinetic test will be performed based on maximum voluntary contraction prior to the application of the laser and after the eccentric contraction protocol, which will also be performed using the isokinetic dynamometer. The following variables related to physical performance will be analyzed: peak torque/maximum voluntary contraction, delayed onset muscle soreness (algometer), biochemical markers of muscle damage, inflammation and oxidative stress.

Discussion: Our intention is to determine optimal laser therapy application parameters capable of slowing down the physiologic muscle fatigue process, reducing injuries or micro-injuries in skeletal muscle stemming from physical exertion and accelerating post-exercise muscle recovery. We believe that, unlike drug therapy, LLLT has a biphasic dose–response pattern.

Trial registration: The protocol for this study is registered with the Protocol Registry System, ClinicalTrials.gov identifier NCT01844271.

Keywords: Low-level laser therapy, Skeletal muscle fatigue, Skeletal muscle recovery, Phototherapy parameters, Exercise

* Correspondence: ernesto.lealjunior@gmail.com
¹Postgraduate Program in Biophotonics Applied to Health Sciences, Universidade Nove de Julho (UNINOVE), Rua Vergueiro 235, São Paulo, SP 01504-001, Brazil
²Postgraduate Program in Rehabilitation Sciences, Universidade Nove de Julho (UNINOVE), Rua Vergueiro 235, São Paulo, SP 01504-001, Brazil
Full list of author information is available at the end of the article

© 2014 de Oliveira et al; licensee BioMed Central Ltd. This is an Open Access article distributed under the terms of the Creative Commons Attribution License (http://creativecommons.org/licenses/by/2.0), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly credited. The Creative Commons Public Domain Dedication waiver (http://creativecommons.org/publicdomain/zero/1.0/) applies to the data made available in this article, unless otherwise stated.
Background
Muscle fatigue is a dynamic, time-dependent failure to maintain a desired level of yield or work during a repetitive or sustained activity [1]. Fatigue has a central and peripheral component, both of which affect the production of force during muscle performance. The decline in muscle activity varies in accordance with the type of muscle fiber and intensity of the exercise [2,3]. Fatigue can also contribute to the development of muscle damage, which is characterized by an inflammatory response [4,5], an increase in muscle proteins in the blood [6] and late-onset muscle pain [7-9]. These events occur in a more accentuated fashion when eccentric contractions are employed [6,10,11].

High-performance athletes are prone to muscle damage stemming from training and competition, compromising their performance for a given period of time, which can range from minutes or hours to several days or even months [12]. A large number of therapies are currently employed after sport activities to enhance muscle recovery, such as active recovery [13-15], cryotherapy [9,16], stretching [12] and electrical stimulation [17]. The aim of post-exercise therapy is to reverse muscle damage, with no attempt made to prevent or attenuate the occurrence of muscle damage.

Recent studies by our research group involving low-level laser therapy (LLLT) and LED therapy have demonstrated positive results when applied prior to exercise, with the attenuation of muscle fatigue [18-24] and favoring the recovery of biochemical markers related to muscle damage [25-27]. The findings suggest that LLLT can minimize the occurrence of injury and optimize an athlete’s return to his/her activities in a shorter period of time.

Despite the positive results obtained in the studies cited above, a number of variables remain unknown, such as the ideal dose and application parameters, mechanisms of action and long-term effects on muscle recovery. Based on our line of research, LLLT is a valuable tool for the attenuation of muscle fatigue and the acceleration of post-exercise muscle recovery. As the same biphasic dose–response pattern has been seen in other musculoskeletal disorders and both power and irradiation time exert an influence on the efficacy of therapy, these outcomes justify the development of the proposed study.

Methods and study design
Characterization and purpose of study
A double-blind, placebo-controlled, randomized, clinical trial will be carried out in two phases. The study will be conducted at the Laboratory of Phototherapy in Sport and Exercise at Nove de Julho University (UNINOVE) in the city of São Paulo, Brazil. The project has received approval from the Human Research Ethics Committee of the university under protocol number 397774/2011 and the study is supported by a Young Researcher award grant from the Brazilian fostering agency, Sao Paulo Research Foundation (FAPESP), under process number 2010/52404-0.

Characterization of sample
Twenty-eight male high-level soccer athletes from the same team will participate in each phase of the study. The decision to recruit volunteers from the same team was made to enhance the homogeneity of the sample. For recruitment of volunteers an initial contact will be made with head coaches of several Brazilian soccer teams. If the head coach accepts that the team can be part of the study, then a personal invitation will be made for athletes individually. Afterwards, the research team will ask athletes about their personal data in order to identify if they meet the inclusion criteria or if they need to be excluded from the clinical trial.

Calculation of sample size
The sample size was calculated based on a previous study [28], in which a similar experimental model and exercise protocol was employed as that to be used in the proposed study. The sample size calculation considered a β of 20% and α of 5%. In the study used as reference for this calculation of Baroni et al. [28], LLLT led to the post-exercise recovery of creatine kinase (CK) (muscle injury marker) to 435.95 U/l (standard deviation: 238.04), whereas placebo treatment led to an increase in CK to 1,327.58 ± 949.82 U/l. Using these parameters, a total of seven volunteers would be needed for each of the four groups in each phase of the study (total of 28 volunteers per phase).

Inclusion criteria
The following inclusion criteria will be employed:

- Professional soccer athletes;
- Age between 18 and 35 years;
- Male gender;
- Minimum of 80% participation in team practice sessions;
- Light or intermediate skin color [29];
- Agreement to participate through signed statement of informed consent.

Exclusion criteria
Participants with the following will be excluded from the study:

- History of musculoskeletal injury to hips or knees in the previous 2 months;
- Use of pharmacological agents or nutritional supplements;
• Occurrence of musculoskeletal injury during the study;
• Any change in practice routine in relation to the rest of the team during the study.

Composition of groups and randomization process
The volunteers will be randomly allocated to four experimental groups (n = 7 per group) based on the LLLT dose (phase 1) and power (phase 2) (Figure 1). Randomization will be carried out by a simple drawing of lots (A, B, C or D). The laser unit will emit the same sound regardless of the programmed power output. Randomization labels will be created using a randomization table at a central office, where a series of sealed, opaque, numbered envelopes will be used to ensure confidentiality. Randomization will be conducted by a participating researcher, who will have the function of programming the laser device based on the randomization results. This researcher will be instructed not to inform the participants or other researchers regarding the LLLT dose (phase 1) or power (phase 2) until the study has been completed. Thus, the researcher in charge of the administration of the LLLT will be blinded to the dose and power applied to the volunteers.

Experimental protocol

Evaluations and informative procedures
Evaluations will be carried out before and at the end of the isokinetic protocol by a researcher blinded to the LLLT dose (phase 1) and power (phase 2). The volunteers will then be informed about the procedures and will sign a statement of informed consent in compliance with Resolution 196/96 of the Brazilian National Board of Health prior to the execution of the study. All individuals in both phases will be submitted to the same evaluation protocol, which will involve the aspects described below.

Personal data
A questionnaire will be administered addressing age (years), body mass (kilograms), height (centimeters), dominant lower leg, schooling (no schooling, elementary school education, high school education, university education or postgraduate degree) and marital status (single, married or widowed).

Blood samples and biochemical analyses
Following the informative process and randomization, blood samples (10 ml) will be collected from the antecubital vein before and 1 minute after the eccentric contraction protocol. Blood samples will also be collected 1, 24, 48, 72 and 96 hours after the protocol. The samples will be taken by a nurse blinded to the allocation of the volunteers to the four experimental groups. One hour after collection, each sample will be centrifuged at 3,000 rpm for 20 minutes. Pipettes will be used to transfer the serum to Eppendorf® tubes (Eppendorf, Hamburg, Germany), which will be stored at −80°C until analysis.

Blood analysis will involve the determination of CK and lactate dehydrogenase (LDH) activity as indirect markers of muscle damage, using spectrophotometry and specific reagent kits (Labtest Diagnóstica, Lagoa Santa, MG, Brazil); IL-1β, IL-6 and TNF-α levels as inflammatory markers, using ELISA and specific reagents (R&D Systems, Minneapolis, MN, USA); and thiobarbituric acid reactive substances (TBARS), carboxylated proteins, catalase (CAT) and superoxide dismutase (SOD) as markers of oxidative stress, using spectrophotometry and specific reactions.

Evaluation of delayed onset muscle soreness (DOMS)
Delayed onset muscle soreness (DOMS) will be evaluated based on the pressure pain threshold, using an analog algometer (Baseline®, Rome, Italy). This device consists of a rod with a rounded rubber tip coupled to a pressure (force) meter. The display presents values in kilograms. As the surface of the rubber tip measures 1 cm², the reading is expressed in kilograms per square centimeter (kg/cm²). Values range from 0 to 10 kg, with a precision of 0.1 kg. The most sensitive areas of the knee extensors (medial, lateral and central) of the non-dominant lower limb will be located through palpation by an examiner blinded to the allocation of the volunteers to the different groups and will be marked with a dermographic marker. The cylindrical end of the equipment will be positioned perpendicularly to the demarcated area. Pressure will be applied to the surface of the skin with a gradual increase in increments of 0.1 kg. The volunteers will be instructed to say ‘yes’ when the pressure exerted becomes painful. Three measures will be taken with the algometer on the same demarcated point of the aforementioned muscle sites. The mean pressure pain threshold will be determined from the three readings of each of the three sites and the mean values will be used in the statistical analysis. Readings will be taken prior to stretching and warm-up, 1 minute after the eccentric contraction protocol as well as 1, 24, 48, 72 and 96 hours after the execution of the protocol.

Stretching and warm-up
Prior to the isokinetic protocol, the volunteers will perform three 60-second sets of active stretching of the knee extensors of the non-dominant lower limb. The volunteers will then perform a warm-up exercise consisting of pedaling a stationary bike (Inbramed, Porto Alegre, RS, Brazil) at 100 rpm for 5 minutes without load.

Isokinetic protocol: maximum voluntary contraction (MVC)
An isometric dynamometer will be used for the evaluation of muscle function and the execution of the exercise protocol. This instrument is considered the method...
with the greatest reliability for the measure of the musculoskeletal performance. Immediately after the stretching and warm-up exercises, the maximum voluntary contraction (MVC) test will be performed. For such, the volunteers will sit on the seat of the isokinetic dynamometer (System 4, Biodex Medical Systems, Inc., Shirley, NY, USA) with an angle of 100° between the trunk and hip and the non-dominant leg positioned with the knee at 60° of flexion (0° corresponds to complete knee extension) and attached to the seat of the dynamometer.
by a strap. The dominant leg will be positioned at 100° of hip flexion and will also be attached to the seat by a strap. The volunteers will also be attached to the seat of the dynamometer through the use of two straps crossing the trunk. The volunteers will be instructed to cross their arms over the trunk and the axis of the dynamometer will be positioned parallel to the center of the knee. The MVC test will consist of three 5-second isometric contractions of the knee extensors of the non-dominant leg. The highest torque value of the three contractions (peak torque) will be used for the statistical analysis. The choice of this parameter is due to the fact that this variable reflects the maximum generation of force by the muscle. Instructions on how to execute the test will be given first and the volunteers will receive verbal encouragement during the execution of the test. This test has demonstrated reliability and reproducibility in a previous study carried out [28]. The MVC will be performed immediately (1 minute) after the eccentric contraction protocol as well as 1, 24, 48, 72 and 96 hours after the eccentric contraction protocol to evaluate post-exercise muscle recovery.

**Low-level laser therapy (LLLT)**

**Specifications**

A five-diode cluster laser device (each cluster with 0.0364 cm²; wavelength: 810 nm; power: 0, 100, 200 or 400 mW in each diode; continuous light emission) (Thor Photomedicine, Chesham, UK) will be used for LLLT. The functioning of the laser will be verified prior to the treatment of each volunteer, with an inspection of the energy source, application points and energy measurement. To ensure blinding, the device will emit the same sounds regardless of the programmed mode (active or placebo).

**Variation of dose (phase 1)**

In phase 1, the output power will be fixed at 200 mW and LLLT will be applied 2 minutes prior to the pre-exercise MVC test with the cluster in direct contact with the skin at six distinct sites of the knee extensor musculature of the non-dominant limb (two medial, two lateral and two central sites). As the cluster has five diodes and six different sites will be irradiated, a total of 30 points will be irradiated in the musculature. Based on the results of the randomization, the volunteers of the four experimental groups will receive the following doses: Group A, 2 J per diode, 10 J on each application of the cluster with 200 mW (10 seconds of irradiation at each site), 60 J of total irradiated energy on the muscle (60 seconds of total irradiation time); Group B, 6 J per diode, 30 J on each application of the cluster with 200 mW (30 seconds of irradiation at each site), 180 J of total irradiated energy on the muscle (180 seconds of total irradiation time); Group C, 10 J per diode, 50 J on each application of the cluster with 200 mW (50 seconds of irradiation at each site), 300 J of total irradiated energy on the muscle (300 seconds of total irradiation time); and Group D, 0 J per diode (placebo) (20 seconds of irradiation at each site, 120 seconds of total time, but without effective irradiation).

**Variation of power (phase 2)**

The aim of phase 2 is to determine the best power/irradiation time (Watts/s) for use on humans to enhance muscle recovery following physical exercise. For such, the dose with the best results in phase 1 will be used and the same methodological and evaluative measures will be employed. Thus, only the power of the equipment (and consequently irradiation time) will be varied (100, 200, 400 or 0 mW). As energy (E) expressed in Joules is equal to power (P) expressed in Watts multiplied by time (t) measured in seconds, different power variations will lead to the same total energy delivered to the tissue. A priori, if the best dose were determined to be 10 J, the following would be the parameters:

- 10 J = 0.1 W (100 mW) × 100 s
- 10 J = 0.2 W (200 mW) × 50 s
- 10 J = 0.4 W (400 mW) × 25 s
- 10 J = 0.0 W (placebo, 60 s)

**Isokinetic protocol: eccentric contractions**

Precisely 3 minutes after the end of LLLT, the volunteers will perform the eccentric contraction protocol, which will consist of 75 eccentric isokinetic contractions of the knee extensor musculature in the non-dominant leg (five sets of 15 repetitions, 30-second rest interval between sets) at a velocity of 60°.seg⁻¹ in both the eccentric and concentric movements with a 60° range of motion (between 90° and 30° of knee flexion). At each contraction, the dynamometer will automatically (passively) position the knee at 30°; the dynamometer will then flex the knee until reaching 90°. The volunteers will be instructed to resist the knee flexion movement imposed by the dynamometer with maximum force. Instructions on how to execute the maneuver will be given first and the volunteers will receive verbal encouragement throughout the protocol. Despite the diversity of protocols proposed for the execution of eccentric exercises on isokinetic dynamometers, the protocol described here was chosen based on a previous study carried out [28] in which this method proved effective and reproducible for the exercise-induced muscle damage.

**Data analysis**

The intention-to-treat analysis will be followed. The primary outcome will be peak torque obtained from MVC at different time-points. Secondary outcomes will be biochemical markers CK, LDH, IL-1β, IL-6, TNF-α, TBARS, carbonylated proteins, CAT and SOD.
Data will be expressed as mean and standard deviation and will be firstly tested regarding normal distribution using Shapiro–Wilk test. ANOVA test with repeated measurements for the time factor will be performed to test between-groups differences (followed by the Bonferroni post hoc test). The level of significance for the statistical analysis will be set at 5% ($P \leq 0.05$).

**Discussion**

In the proposed study, the ideal LLLT application dose and power will be identified and the long-term effects of LLLT on post-exercise muscle fatigue and musculoskeletal recovery will be evaluated. For such, evaluations will be carried out of peak torque during MVC, late-onset muscle pain will be determined and biochemical analyses will be performed to determine changes in markers of inflammation, oxidative stress and muscle damage. The inflammatory process is known to be a definitive reaction against injury. This process has been extensively studied in its different aspects. Briefly, the main inflammation events are: 1) tissue injury; 2) the release of vasoactive substances by the injured tissue; 3) vasodilatation; 4) leukocyte adherence; 5) the migration of leukocytes from the blood stream to the injury site; and 6) tissue repair. Thus, muscle inflammation is a natural consequence of exercise-induced muscle damage [30].

Over time, LLLT exhibits a biphasic, dose–response pattern. This means that intermediate doses within a ‘therapeutic window’ trigger stimulation effects in biological tissue, whereas doses outside this range do not trigger any effects [31-34]. However, the therapeutic window varies depending on the condition to be treated [31]. Likewise, the power and irradiation time employed are extremely important to obtaining the best results. Thus, a short irradiation time and an output power that trigger any effects [31-34]. However, the therapeutic logical tissue, whereas doses outside this range do not.

**Trial status**

At the time of manuscript submission, the volunteers were being recruited.

**Acknowledgements**

This study receives support from the Nove de Julho University (UNINOVE) and grant number 2010/52404-0 from Sào Paulo Research Foundation (FAPESP).

**References**

1. Chadler T, Berelowitz G, Pawlikowska T, Watts L, Wessely S, Wright D, Wallace EP: Development of a fatigue scale. J Psychosom Res 1993, 37:147–153.
2. Kawakami Y, Amemiya K, Kaneshita H, Iwagawa S, Fujikawa T: Fatigue responses of human triceps surae muscles during repetitive maximal contractions. J Appl Physiol 1969–1975, 2000:88.
3. Pasquet B, Carpentier A, Duchateau J, Hainaut K: Muscle fatigue during concentric and eccentric contractions. Muscle Nerve 2000, 23:1727–1735.
4. Toru T, Wang K, Svensson P, De Laat A, Fuji H, Arendt-Nielsen L: Effects of muscle fatigue induced by low-level clenching on experimental muscle pain and resting jaw muscle activity: gender differences. Exp Brain Res 2006, 174:566–574.
5. Totsuka M, Nakaji S, Suzuki K, Sugawara K, Sato K: Break point of serum creatine kinase release after endurance exercise. J Appl Physiol 2002, 93:1280–1286.
6. Proskie U, Morgan DL: Muscle damage from eccentric exercise: mechanism, mechanical signs, adaptation and clinical applications. J Physiol 2001, 537(2):333–345.
7. Morgan DL, Allen DG: Early events in stretch-induced muscle damage. J Appl Physiol 2007–2015, 1999:87.
8. Byrne C, Twist C, Eston R: Neuromuscular function after exercise-induced muscle damage—methodological and applied implications. Sports Med 2004, 34:99–109.
9. Clarkston PM, Hubal MJ: Exercise-induced muscle damage. Am J Phys Med Rehabil 2002, 81:552–569.
10. Cheung K, Hume P, Maxwell L: Delayed onset muscle soreness: treatment strategies and performance factors. Sports Med 2003, 33:145–164.
11. Hovisand G, van Someren KA: The prevention and treatment of exercise-induced muscle damage. Sports Med 2008, 38:483–490.
12. Barnett A: Using recovery modalities between training sessions in elite athletes: does it help? Sports Med 2006, 36:781–796.
13. Ahmadi S, Granier P, Taoutaou Z, Mercier J, Dubouchaud H, Prefaut C: Effects of active recovery on plasma lactate and anaerobic power following repeated intensive exercise. Med Sci Sports Exerc 1996, 28:450–456.

**Competing interests**

ECPIL received research support from Multi Radiance Medical (Solon, OH, USA), a laser device manufacturer. Multi Radiance Medical had no role in the planning of this experiment, and the laser device used was not theirs. They had no influence on study design, decision to publish or preparation of the manuscript. The remaining authors declare that they have no conflicts of interest.

**Authors’ contributions**

AAV, TDM, FCA and ECPIL contributed to the conception and study design. ARO, VSG, PRVP, GMAP, LAS, IOAJ, PTCC, JMB and ECPLJ established the hypothesis and drafted the original proposal. ARO, AAV, TDM, FCA, VSG, PRVP, GMAP, LAS, IOAJ, PTCC, JMB and ECPIL drafted the final version of the manuscript. All authors read and approved the final version of the manuscript.

**Received**: 13 October 2013 **Accepted**: 11 February 2014 **Published**: 27 February 2014

---

**Abbreviations**

ANCOVA: Analysis of variance; CAT: Catalase; CK: Creatine kinase; DOMS: Delayed onset muscle soreness; ELISA: Enzyme-linked immunosorbent assay; FAPESP: Sao Paulo Research Foundation; IL: Interleukin; LDH: Lactate dehydrogenase; LED: Light-emitting diode; LLLT: Low-level laser therapy; MVC: Maximum voluntary contraction; SOD: Superoxide dismutase; TBARS: Thiobarbituric acid reactive substances; TNF: Tumor necrosis factor; UNINOVE: Nove de Julho University.
14. Baldari C, Videira M, Madeira F, Sergio J, Guidetti L: Lactate removal during active recovery related to the individual anaerobic and ventilatory thresholds in soccer players. *Eur J Appl Physiol* 2004, 93:224–230.

15. Martin NA, Zoller RF, Robertson RJ, Lephart SM: The comparative effects of sports massage, active recovery, and rest in promoting blood lactate clearance after supramaximal leg exercise. *J Athl Train* 1998, 33:30–35.

16. Howatzon G, Goodall S, van Someren KA: The influence of cold water immersions on adaptation following a single bout of damaging exercise. *Eur J Appl Physiol* 2009, 105:615–621.

17. Lattier G, Millet GY, Martin A, Martin V: Fatigue and recovery after high-intensity exercise. Part II: recovery interventions. *Int J Sports Med* 2004, 25:509–515.

18. Leal Junior EC, Lopes-Martins RA, Dalan F, Ferrari M, Skabo FM, Generosi RA, Baroni BM, Penna SC, Iversen W, Bjordal JM: Effect of 655-nm low-level laser therapy on exercise-induced skeletal muscle fatigue in humans. *Photomed Laser Surg* 2008, 26:419–424.

19. Leal Junior EC, Lopes-Martins RA, Vanin AA, Baroni BM, Grosselli D, De Marchi T, Iversen VV, Bjordal JM: Effect of 830 nm low-level laser therapy in exercise-induced skeletal muscle fatigue in humans. *Lasers Med Sci* 2009, 24:425–431.

20. Leal Junior EC, Lopes-Martins RA, Rossi RP, De Marchi T, Baroni BM, de Godoi V, Marcos RL, Ramos L, Bjordal JM: Effect of cluster multi-diode light emitting diode therapy (LEDT) on exercise-induced skeletal muscle fatigue and skeletal muscle recovery in humans. *Lasers Surg Med* 2009, 41:572–577.

21. Leal Junior EC, Lopes-Martins RA, de Almeida P, Ramos L, Iversen VV, Bjordal JM: Effect of low-level laser therapy (660 nm) in skeletal muscle fatigue and biochemical markers of muscle damage in rats. *Eur J Appl Physiol* 2010, 108:1083–1088.

22. Leal Junior EC, Lopes-Martins RA, Frigo L, De Marchi T, Rossi RP, de Godoi V, Tomazoni SS, da Silva DP, Basso M, Lotti Filho P, Corsetti FV, Iversen VV, Bjordal JM: Effects of low-level laser therapy (LLLT) in the development of exercise-induced skeletal muscle fatigue and changes in biochemical markers related to post-exercise recovery. *J Orthop Sports Phys Ther* 2010, 40:524–532.

23. De Marchi T, Leal Junior EC, Bortoli C, Tomazoni SS, Lopes-Martins RA, Salvador M: Low-level laser therapy (LLLT) in human progressive-intensity running: effects on exercise performance, skeletal muscle status, and oxidative stress. *Lasers Med Sci* 2012, 27:231–236.

24. Almeida P, Lopes-Martins RA, De Marchi T, Tomazoni SS, Albertini R, Conta JC, Rossi RP, Machado GP, da Silva DP, Bjordal JM, Leal Junior EC: Red (660 nm) and infrared (830 nm) low-level laser therapy in skeletal muscle fatigue in humans: what is better? *Lasers Med Sci* 2012, 27:453–458.

25. Leal Junior EC, Lopes-Martins RA, Baroni BM, De Marchi T, Rossi RP, Grosselli D, Generosi RA, de Godoi V, Basso M, Mancalossi JL, Bjordal JM: Comparison between single-diode low-level laser therapy (LLLT) and LED multi-diode (cluster) therapy (LEDT) applications before high-intensity exercise. *Photomed Laser Surg* 2009, 27:617–623.

26. Leal Junior EC, Lopes-Martins RA, Baroni BM, De Marchi T, Tauer D, Manfrin DS, Rech M, Danina V, Grosselli D, Generosi RA, Marcos RL, Ramos L, Bjordal JM: Effect of 830 nm low-level laser therapy applied before high-intensity exercises on skeletal muscle recovery in athletes. *Lasers Med Sci* 2009, 24:857–863.

27. Leal Junior EC, de Godoi V, Mancalossi JL, Rossi RP, De Marchi T, Parente M, Grosselli D, Generosi RA, Basso M, Frigo L, Tomazoni SS, Bjordal JM, Lopes-Martins RA: Comparison between cold water immersion therapy (CWIT) and light emitting diode therapy (LEDT) in short-term skeletal muscle recovery after high-intensity exercise in athletes: preliminary results. *Lasers Med Sci* 2011, 26:493–501.

28. Baroni BM, Leal Junior EC, De Marchi T, Lopes AL, Salvador M, Vaz MA: Low level laser therapy before eccentric exercise reduces muscle damage markers in humans. *Eur J Appl Physiol* 2010, 110:789–796.

29. Joensen J, Demmink JH, Johnson ML, Iversen VV, Lopes-Martins RAB, Bjordal JM: The thermal effects of therapeutic with 810 and 904 nm wave-lengths on human skin. *Photomed and Laser Surg* 2011, 29:145–153.

30. Malm C: Exercise-induced muscle damage and inflammation: fact or fiction? *Acta Physiol Scand* 2001, 171:233–239.

31. Huang YY, Chen AC, Carrol JD, Hamblin MR: Biphasic dose response in low level light therapy. *Dose Response* 2009, 7:358–383.

32. Chow RT, Johnson MJ, Lopes-Martins RA, Bjordal JM: Efficacy of low-level laser therapy in the management of neck pain: a systematic review and meta-analysis of randomised placebo or active-treatment controlled trials. *Lancet* 1897–1908, 2009:574.