

Effect of phototherapy (low-level laser therapy and light-emitting diode therapy) on exercise performance and markers of exercise recovery: a systematic review with meta-analysis

Ernesto Cesar Pinto Leal-Junior · Adriane Aver Vanin ·
Eduardo Foschini Miranda · Paulo de Tarso Camillo de Carvalho ·
Simone Dal Corso · Jan Magnus Bjordal

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Abstract Recent studies have explored if phototherapy with low-level laser therapy (LLLT) or narrow-band light-emitting diode therapy (LEDT) can modulate activity-induced skeletal muscle fatigue or subsequently protect against muscle injury. We performed a systematic review with meta-analysis to investigate the effects of phototherapy applied before, during and after exercises. A literature search was performed in Pubmed/Medline database for randomized controlled trials (RCTs) published from 2000 through 2012. Trial quality was assessed with the ten-item PEDro scale. Main outcome measures were selected as: number of repetitions and time until exhaustion for muscle performance, and creatine kinase (CK) activity to evaluate risk for exercise-induced muscle damage. The literature search resulted in 16 RCTs, and three articles were excluded due to poor quality assessment scores. From 13 RCTs with acceptable methodological quality (≥ 6 of 10 items), 12 RCTs irradiated phototherapy before exercise, and 10 RCTs reported significant improvement for the main outcome measures related to performance. The time until exhaustion increased significantly compared to placebo by 4.12 s (95 % CI 1.21–7.02, $p < 0.005$) and the number of repetitions increased by 5.47 (95 % CI 2.35–8.59,

$p < 0.0006$) after phototherapy. Heterogeneity in trial design and results precluded meta-analyses for biochemical markers, but a quantitative analysis showed positive results in 13 out of 16 comparisons. The most significant and consistent results were found with red or infrared wavelengths and phototherapy application before exercises, power outputs between 50 and 200 mW and doses of 5 and 6 J per point (spot). We conclude that phototherapy (with lasers and LEDs) improves muscular performance and accelerate recovery mainly when applied before exercise.

Keywords Low-level laser therapy · Light-emitting diode therapy · Exercise performance · Exercise recovery · Sports

Introduction

Muscle fatigue is often described as the gradual activity-induced decrease in contractile function, and thereby reduction in the capacity to generate force. Skeletal muscle fatigue occurs during heavy and/or prolonged muscle activity, and it is a complex and multifaceted process involving physiological, biochemical and psychological elements [1]. Due to large variability of muscle characteristics between subjects, it is difficult to determinate an accurate fatigue threshold [2].

Electrophysical agents, such as low-level laser therapy (LLLT) and light-emitting diode therapy (LEDT), have been investigated in the treatment of muscle injuries [3]. But more recently, the research focus has been expanded to include delayed development of muscle fatigue and prevention of muscle injury. In brief words, LLLT and LEDT seem to induce photochemical effects in cells through the absorption of light by photoreceptors [4, 5]. This phenomenon is often described as “photobiostimulation” or “photobiomodulation” [6].

E. C. P. Leal-Junior · A. A. Vanin · E. F. Miranda ·
P. d. T. C. de Carvalho · S. Dal Corso
Postgraduate Program in Rehabilitation Sciences, Universidade
Nove de Julho, Rua Vergueiro, 235, 01504-001 São Paulo, SP, Brazil

E. C. P. Leal-Junior (✉) · P. d. T. C. de Carvalho
Postgraduate Program in Biophotonics Applied to Health Sciences,
Universidade Nove de Julho, Rua Vergueiro, 235, 01504-001 São
Paulo, SP, Brazil
e-mail: ernesto.leal.junior@gmail.com

J. M. Bjordal
Physiotherapy Research Group, Faculty of Medicine and Dentistry,
University of Bergen, Bergen, Norway

Photobiomodulation occurs through the application of monochromatic or narrow-band light in tissues and may influence cellular activity by either stimulation or inhibition of chemical and physiological functions. The magnitude of the photobiomodulation effect is influenced by wavelength, energy density (or fluence), power density, type of injury, and the absorption spectrum of photoreceptor [4, 7]. In the pioneering animal study on muscle fatigue and phototherapy, Lopes-Martins et al. [8] observed a possible protective effect of phototherapy against muscle damage and fatigue development in rats submitted to electrically induced muscle contractions. Recent studies have used LLLT and LEDT phototherapy to evaluate if pre-treatment with phototherapy can affect exercise performance and decrease creatine kinase (CK) activity and blood lactate production [9].

It is important to mention that muscle injuries are common in sports and often lead to loss of muscle function and consequently decreases the quality of life in injured athletes [10]. In addition, better performance in training and competitions has always been sought by athletes, and a hundredth of a second can make the difference between successful results or not for high-level athletes.

In this perspective, phototherapy seems to emerge as a promising non-invasive if it enables a delay in development of fatigue and preservation against muscle injuries. The aim of this study was to perform a systematic review of phototherapy effects (LLLT and LEDT) on exercise performance and preservation against muscle damage (i.e., muscle recovery).

Methods

Search strategy

A literature search was performed in PubMed and MEDLINE databases for randomized controlled trials (RCTs) published from 2000 through 2012. Study identification commenced by electronic searching, from October 1st to December 20th 2012. Search terms used were as follows: LLLT, LEDT, skeletal muscle, muscle performance, and phototherapy. An overview of the systematic review process is seen in Fig. 1.

Quality assessment

Two independent reviewers assessed the quality of included trials by the ten-item validity criteria on the PEDro (physiotherapy evidence database) scale [11]. Standardized forms were developed in order to extract data information from each trial included in the review.

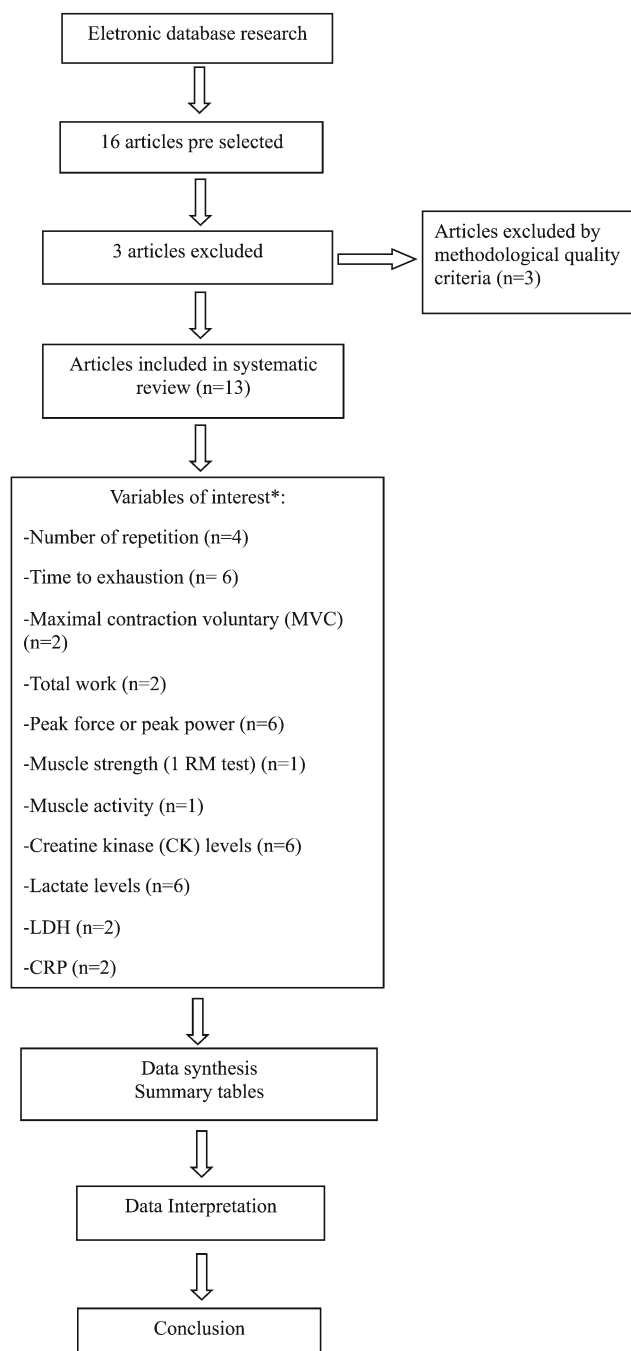


Fig. 1 Flowchart showing studies included in the review. * The sum of articles for each category add more than the total number of the articles included in the review because some studies reported more than one outcome assessed

Inclusion criteria

Articles were included if they used phototherapy (LLLT or LEDT) to modulate skeletal muscle performance in healthy subjects or early biochemical markers of muscle injury. Studies were selected by the following inclusion criteria: RCTs, outcomes of fatigue development (time to exhaustion,

Table 1 Phototherapy parameters employed in RCTs

Authors	Source of light	Wavelength (nm)	Energy density per diode (J/cm^2)	Energy per site (J)	Power density per diode (w/cm^2)	Spot size (cm^2)	Treatment time per point or site (s)	Power output per diode (mw)	Total energy delivered (J)	Number of treated points or sites	Muscle treated	Total sessions/ sessions per week
Leal Junior et al. [16]	Laser	655	500	5	5	0.01	100	50	20	4	Biceps brachii	2/1
Gorgey et al. [17]	Laser	808	na	3 or 7 ^a	0.0083	na	300 or 600	500	3 or 7 ^a	Whole quadriceps (Scanning mode)	Quadriceps	3/3
Leal Junior et al. [18]	Laser	830	1,785	5	35.7	0.0028	50	100	20	4	Biceps brachii	2/1 crossed placebo × laser
Leal Junior et al. [19]	Laser/LED	810/660 and 850	164.84/1.5 and 4.5	6/41.7	5.50/0.05 and 0.15	0.0364/0.2	30/30	200/10 and 30	24/166.8	2 sites per limb with a single diode laser or a multidiode LED cluster (69 LEDs, 34 red and 35 infrared)	Rectus femoris	3/1 crossed placebo × laser × LED
Leal Junior et al. [20]	LED	660 and 850	1.5 and 4.5	41.7	0.05 and 0.15	0.2	30	10 and 30	41.7	1 site with a LED cluster (69 LEDs, 34 red and 35 infrared)	Biceps brachii	2/1 crossed placebo × LED
Leal Junior et al. [21]	Laser	830	1,428.57 or 1,071.43	4 or 3	35.7	0.0028	40 or 30	100	40 or 30	5 each leg = 10 in total	Rectus femoris	2/1 crossed placebo × laser
Leal Junior et al. [22]	Laser	810	164.85	30	5.5	0.0364	30	200	60	2 sites with a multidiode cluster with 5 spots (6 J each spot)	Biceps brachii	2/1 crossed placebo × laser
Kelencz et al. [23]	LED	640	2, 4, or 6	1.044, 2.088, or 3.132	0.222	0.522	9, 18, or 27	116	8.352, 16.70, or 25.06	8	Right masseter	1/1
Baroni et al. [24]	LED	660 and 850	1.5 and 4.5	41.7	0.05 and 0.15	0.2	30	10 and 30	125.1	Three points with a LED multidiode cluster (69 LEDs, 34 red and 35 infrared)	Quadriceps	2/1 crossed placebo × LED
Baroni et al. [25]	Laser	810	164.85	30	5.5	0.0364	30	200	180	6	Quadriceps	3/3
Ferraresi et al. [26]	Laser	808	214.28	0.6	21.42	0.0028	10	60	50.4 (25.2 per lower limb)	42 per limb (total of 84 points)	Quadriceps	24/2
De Marchi et al. [27]	Laser	810	164.85	30	5.5	0.0364	30	200	720 (360 per lower limb)	12 sites each lower limb with a multidiode cluster with 5 spots (6 J each spot)	Quadriceps (6 sites), hamstrings (4 sites), gastrocnemius (2 sites)	2/1 crossed placebo × laser
Almeida et al. [28]	Laser	660 or 830	1,785	5	17.85	0.0028	100	50	20	4	Biceps brachii	3/1 crossed infra × red × placebo

LLLT low-level laser therapy, LEDT light-emitting diode therapy, PL placebo, TLG training with LLLT TG training only, CG control group

^a We considered energy per site as the same as total energy delivered since authors have used scanning mode covering whole quadriceps muscle

Table 2 Methods, main outcomes, and PEDro scores of RCTs

Authors	Exercise protocol	Duration of trial	Number of active phototherapy treatment	Outcomes analyzed	When phototherapy was applied?	Summary of results	Positive effects in performance	Percentage of improvement in performance	Score Pedro scale
Leal Junior et al. [16]	Isotonic contraction of elbow flexors	8 days	One	Number of repetitions, time until exhaustion, and lactate	Before exercise	LLLT increased number of repetitions, and time until exhaustion	YES	Repetitions 57 %, Time until exhaustion 39.01 %	8/10
Gorgey et al. [17]	Neuromuscular electrical stimulation of quadriceps	7 days	Two	Maximal voluntary contraction	Before protocol	No significant differences in the outcomes analyzed	NO	–	6/10
Leal Junior et al. [18]	Isotonic contraction of elbow flexors	8 days	One	Number of repetitions; blood lactate levels; time until exhaustion	Before exercise	LLLT increased number of repetitions without significant differences in other outcomes	YES	17.57 %	8/10
Leal Junior et al. [19]	Wingate test	15 days	Two	Peak and average power output, CK and lactate	Before exercise	No differences in muscular performance nor lactate levels, LEDT significantly decreased CK activity	NO	–	7/10
Leal Junior et al. [20]	Isotonic contraction of elbow flexors	8 days	One	Number of repetitions, time until exhaustion, CK, CRP, and lactate	Before exercise	LEDT improved all outcomes tested	YES	Repetitions 12.9 %; Time until exhaustion 11.6 %	7/10
Leal Junior et al. [21]	Wingate test	8 days	One	Work performed, lactate levels and CK	Before exercise	LLLT decreased CK activity and lactate levels after exercise compared to placebo group	NO	–	8/10
Leal Junior et al. [22]	Isotonic contraction of elbow flexors	8 days	One	Number of repetitions, time until exhaustion, CK, CRP, and lactate	Before exercise	LLLT improved all outcomes tested	YES	Increase in time until exhaustion 8 %; Increase in number of repetitions 14.5 %	8/10
Kelencz et al. [23]	Maximal voluntary isometric contraction	1 day	One	Electrical activity of the masseter muscle, and time until fatigue	Before protocol	LEDT increased muscle activity; with 1.044 J per point, and increased time until fatigue with 2.088 J	YES	26.34 %	6/10
Baroni et al. [24]	Isokinetic knee extension/flexion	8 days	One	Peak torque during exercise protocol and maximal voluntary contraction	Before exercise	LLLT increased MVC post-exercise	YES	5.31 %	8/10
Baroni et al. [25]	Isokinetic eccentric knee flexion-extension exercise	3 days	One	Maximal voluntary contraction, LDH and CK	Before exercise	LLLT improved all outcomes tested	YES	23 %	6/10
Ferraresi et al. [26]	Leg-press training protocol	12 weeks	24	Peak force (torque), 1 Repetition maximum (IRM)	After training sessions	LLLT associated with training increased peak torque compared to baseline, LLLT only increased outcomes compared to non-irradiated trained group (TLG × TG) in percentage of increase in IRM test	YES	28.76 %	7/10

Table 2 (continued)

Authors	Exercise protocol	Duration of trial	Number of active phototherapy treatment	Outcomes analyzed	When phototherapy was applied?	Summary of results	Positive effects in performance	Percentage of improvement in performance	Score PEDro scale
De Marchi et al. [27]	Progressive running protocol in treadmill	8 days	One	Exercise performance (VO ₂ max), time until exhaustion, CK, LDH, oxidative stress, and antioxidant activity	Before exercise	LLLT increased VO ₂ max and time until exhaustion, decreased CK and LDH activity, decreased oxidative stress and increased antioxidant activity	YES	2.02 %	6/10
Almeida et al. [28]	Isometric contraction of elbow flexors	15 days	Two	Peak and average force	Before exercise	LLLT increased average strength and peak strength	YES	Peak force: red laser 12.14 %, infrared laser 14.49 %; Average force: red laser 13.09 %, infrared laser 13.24 %	8/10

LLLT Low-level laser therapy, LEDT Light-emitting diode therapy, PL Placebo, TLG training with LLLT, TG Training only, CG control group

number of repetitions, muscle force), and/or biochemical markers related to risk of developing muscle injury.

Studies that investigated drugs or other electrophysical modalities than phototherapy (LLLT and LEDT), and studies that did not include control groups were excluded. Additionally, studies scoring less than 6 in the methodological assessment by the PEDro scale were also excluded from the analysis.

All articles were analyzed in their entirety through a structured protocol for the following items: method scoring by the PEDro scale based on the Delphi list [12], outcome measures, and result presentation. For the meta-analysis, means and variance data were extracted from the included trials. If values were only presented in graphs, absolute values were visually extracted and imputed in the meta-analyses. For the meta-analyses, the software package REVMAN ver. 5.1.4 was used. We used analyses of weighted mean differences between LLLT/LEDT and control groups in fixed effects models, unless significant heterogeneity was detected. In the latter case, a random effects model was picked for analysis.

Results

Sixteen abstracts met the inclusion criteria and were then assessed for methodological quality with the PEDro scale. The average methodological quality of the 13 selected studies was 7 on the PEDro scale, whereas three studies were excluded with method scores of four [13–15]. Ten studies reported positive effects in favor of phototherapy regarding improvement of performance and three reported neutral effects. The parameters of the laser or LED in RCTs are shown in Table 1.

The different exercise protocols, trial designs and PEDro scores are shown in Table 2.

An overview of blood lactate levels, CK activity, C-reactive protein (CRP) levels, number of repetitions, time to exhaustion, lactate dehydrogenase (LDH) activity, peak force, and peak power performed during exercise protocol, maximum voluntary contraction (MVC), work performed, one-repetition maximum (1RM) test, and electrical muscle activity in RCTs are shown in Tables 3, 4, 5, 6, 7.

Similarly, Table 8 summarizes outcome measures used and group results across the included trials.

The outcome measures selected to analyze the combined effects of phototherapy in performance and fatigue were extracted as: number of repetitions [16, 18, 20, 22] and time until exhaustion [16, 18, 20, 22, 23, 27]. Other outcome measures like serum CK activity to assess risk of muscle damage [19–22, 25, 27], maximal voluntary contraction [24, 25, 28], muscle power [19, 21], torque [17, 26], electrical muscle activity [23], and oxygen uptake [27] were not combined due heterogeneity in trial designs, muscles involved, and results (Table 2).

Table 3 Blood lactate levels

Authors	Lactate	Before PL	Before LLLT	After LLLT	After PL
Leal Junior et al. [16]	Before LLLT 2.38±0.27 <i>p</i> >0.05	2.4±0.31	3.92±0.50	3.65±0.51	
Gorgey et al. [17]	Not applicable				
Leal Junior et al. [18]	Before LLLT 2.31±0.36 <i>p</i> =0.200	Before PL 2.16±0.37	Change after LLLT 1.35±0.90	Change after PL 1.78±1.10	
Leal Junior et al. [19]	Before LEDT 1.55±0.54 <i>p</i> >0.05	Before PL 1.66±0.42	LEDT 10' 9.29±2.94 <i>p</i> >0.05	LEDT 15' 8.60±2.05 <i>p</i> >0.05	PL 15' 9.38±0.85
Leal Junior et al. [20]	Before LEDT 3.40±1.07 <i>p</i> >0.05	Before PL 3.70±1.25	Change after LEDT 8.20±3.99 <i>p</i> =0.042*	Change after PL 11.50±3.21	
Leal Junior et al. [21]	Before LLLT 2.52±0.52 <i>p</i> >0.05	Before PL 2.24±0.33	LLL 10' 10.63±2.17 <i>p</i> >0.05	LLL 15' 8.55±2.14 <i>p</i> =0.01*	PL 15' 10.52±1.82
Leal Junior et al. [22]	Before LLLT 1.30±0.10 <i>p</i> >0.05	Before PL 1.43±0.25 <i>p</i> <0.01*	PL 5' 5.32±3.19 <i>p</i> >0.05	PL 10' 4.84±2.26 <i>p</i> >0.05	PL 20' 3.57±0.54 <i>p</i> >0.05
Kelencz et al. [23]	Not applicable				
Baroni et al. [24]	Not applicable				
Baroni et al. [25]	Not applicable				
Ferraresi et al. [26]	Not applicable				
De Marchi et al. [27]	Not applicable				
Almeida et al. [28]	Not applicable				

LLLTL low-level laser therapy, LEDTL light-emitting diode therapy, PL placebo, TLG training with LLLT, TG training only, CG control group

Table 4 Creatine kinase (CK) activity and C-reactive protein (CRP) levels

Authors	CK	CRP
Leal Junior et al. [16]	Not applicable	Not applicable
Gorgey et al. [17]	Not applicable	Not applicable
Leal Junior et al. [18]	Not applicable	Not applicable
Leal Junior et al. [19]	Before LEDT 190.75±93.19 p<0.05* Change after LEDT × Change after LLLT	Change after LEDT 43.38±32.90 Change after LLLT 26.88±15.18 Change after PL 26.88±15.18
Leal Junior et al. [20]	Before LEDT 53.62±23.37 p>0.05	Before LEDT 1,536.00±742.09 p>0.05
Leal Junior et al. [21]	Before LLLT 108.64±33.68 p=0.7737	Before PL 1,077.60±643.24 Change after LEDT 364.80±616.86 p=0.030*
Leal Junior et al. [22]	Before LLLT 281±196.3 p>0.05	Before LLLT 38.7±44 p>0.05
Kelencz et al. [23]	Not applicable	Not applicable
Baroni et al. [24]	Not applicable	Not applicable
Baroni et al. [25]	Baseline LLLT 144.69±59.01 p<0.05* Change after LEDT × Change after LLLT	Change after LLLT 2.52±7.04 p=0.0133* Change after PL 28.49±22.62
Ferraresi et al. [26]	Not applicable	Not applicable
De Marchi et al. [27]	Before LLLT 151.74±45.15	Before PL 26.7±29.3 After LLLT 525.7±386.5 p=0.047*
Almeida et al. [28]	Not applicable	Not applicable

LLLT low-level laser therapy, LEDT light-emitting diode therapy, PL placebo, TLG training with LLLT TG training only, CG control group

Table 5 Number of repetitions, time to reach exhaustion and Lactate Dehydrogenase (LDH) activity

Authors	Number of repetitions		Time to exhaustion (seconds)		LDH	
	LLLT	PL	LLLT	PL	Not applicable	Not applicable
Leal Junior et al. [16]	29.33±7.9	19.17±7.1	53.8 (CI: 46.2–61.4)	41.1 (CI: 33.6–48.7)	Not applicable	Not applicable
Gorgey et al. [17]	Not applicable	Not applicable	$p=0.0022^*$	Not applicable	Not applicable	Not applicable
Leal Junior et al. [18]	30.10±8.08	25.60±6.15	37.15±6.45	34.34±6.77	Not applicable	Not applicable
Leal Junior et al. [19]	Not applicable	Not applicable	$p=0.042^*$	$p=0.096$	Not applicable	Not applicable
Leal Junior et al. [20]	LEDT	PL	LEDT	PL	Not applicable	Not applicable
Leal Junior et al. [21]	38.6±9.03	34.2±8.6	47.37±11.50	42.46±13.81	Not applicable	Not applicable
Leal Junior et al. [22]	$p=0.021^*$	Not applicable	$p=0.036^*$	Not applicable	Not applicable	Not applicable
Kelencz et al. [23]	Not applicable	Not applicable	Treated 2.088 J (LED)	Control 2.088 J (LED)	Not applicable	Not applicable
Baroni et al. [24]	Not applicable	Not applicable	42.2±14.7*	33.4±12.4	Not applicable	Not applicable
Baroni et al. [25]	Not applicable	Not applicable	$p<0.01^*$	Not applicable	Not applicable	Not applicable
Ferraresi et al. [26]	Not applicable	Not applicable	Not applicable	Not applicable	Baseline LLLT	Baseline PL
De Marchi et al. [27]	Not applicable	Not applicable	Not applicable	Not applicable	186.02±44.92	182.59±43.84
Almeida et al. [28]	Not applicable	Not applicable	Not applicable	Not applicable	24 h LLLT	24 h PL
					296.93±99.98	290.10±87.54
					274.93±37.62	276.80±32.86
					Before PL	After LLLT
					281.89±44.36	332.72±63.07
					$p=0.0001^*$	Not applicable
					Not applicable	Not applicable

LLLT: Low-level laser therapy, LEDT: Light emitting diode therapy, PL: Placebo, TLG: Training with LLLT, TG: Training only, CG: Control group.

Table 6 Peak force and peak power during exercise protocol and maximum voluntary contraction (MVC)

Authors	Peak force, peak torque or peak power during exercise protocol	MVC (N m)
Leal Junior et al. [16]	Not applicable	Not applicable
Gogey et al. [17]	Not applicable	Control 3 J LLLT 7 J LLLT 47±16 N m 45±17 N m 47±17 N m $p=0.99$
Leal Junior et al. [18]	Not applicable	Not applicable
Leal Junior et al. [19]	LEDT 12.31±0.83 W/kg $p>0.05$	Not applicable
Leal Junior et al. [20]	Not applicable	Not applicable
Leal Junior et al. [21]	Not applicable	Not applicable
Leal Junior et al. [22]	Not applicable	Not applicable
Kelencz et al. [23]	Control (1.044 J) 33.6±9.8 kgf Treated (1.044 J) 37.4±13.9 kgf (2.088 J) 31.7±9.7 kgf (2.088 J) 32.8±8.0 kgf Treated (3.132 J) 20.3±7.8 kgf	Not applicable
Baroni et al. [24]	LEDT 153.62±27.11 N m $p=0.231$	Before LEDT 284.81±54.52 After LEDT 237.68±48.82 $p=0.034^*$ - After LEDT × After PL
Baroni et al. [25]	Not applicable	Before PL 282.65±53.64 After PL 225.68±44.14 Immediately after PL 24 h 24 h PL 48 h 48 h PL LLLT LLLT LLLT LLLT Baseline PL 188.93±154.03±249.43±205.09±216.14± 42.93 47.07 43.04 34.57 42.61 43.52 37.40 50.17 MVC immediately after $p<0.05^*$; MVC 24 h $p<0.05^*$; MVC 48 h $p<0.05^*$ (compared to placebo)
Ferraresi et al. [26]	Baseline TLG 12 weeks TLG 12 weeks TG 12 weeks CG 309±47 (N m/BM)× 323.5±49.5 (N m/BM)× 322.5±24.5 (N m/BM)× 326±54 (N m/BM)× 100 m/BM)× 100 m/BM)× 100 m/BM)× 100 m/BM)× 100 100 100 100	Not applicable
De Marchi et al. [27]	Not applicable	Not applicable
Almeida et al. [28]	Red LLLT 23.83±4.51 kgf Red LLLT×PL $p<0.05^*$ Infrared LLLT×PL $p<0.01^*$ Red LLLT×Infrared LLLT $p>0.05$	Not applicable

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Table 7 Total work, one-repetition maximum (1RM) test, and electrical muscle activity

Authors	Total work(J)	1 RM test [(Load/BM)×100]	Muscle activity (μV)
Leal Junior et al. [16]	Not applicable	Not applicable	Not applicable
Gorgey et al. [17]	Not applicable	Not applicable	Not applicable
Leal Junior et al. [18]	Not applicable	Not applicable	Not applicable
Leal Junior et al. [19]	Not applicable	Not applicable	Not applicable
Leal Junior et al. [20]	Not applicable	Not applicable	Not applicable
Leal Junior et al. [21]	LLLT (volleyball) 21,888.31± 2,062.98 $p=0.3583$	PL (volleyball) 22,429.79± 2,842.71	Not applicable
	LLLT (soccer) 16,214.97± 1,639.88 $p=0.8681$	PL (soccer) 16,289.21± 1,700.34	
Leal Junior et al. [22]	Not applicable	Not applicable	Not applicable
Kelencz et al. [23]	Not applicable	Not applicable	Right side Control 1.044 J Treated 1.044 J 33.6±12.5 37.6±16.3* 1.044 J, $p<0.05^*$ Left side Control 1.044 J Treated 1.044 J 33.6±15.0 38.2±16.9* 1.044 J, $p<0.05^*$ Not applicable
Baroni et al. [24]	LEDT 4,113.25± 677.31 $p=0.182$	PL 4,205.19± 746.15	Control 2.088 J Treated 2.088 J 3.132 J 3.132 J 26.3±8.8 27.9±9.3 28.7±15.6 26.2±8.2 25.9±8.4
Baroni et al. [25]	Not applicable	Not applicable	Not applicable
Ferraresi et al. [26]	Not applicable	Baseline 12 weeks TLG 468.75±43.75 TLG 725±87.5 Baseline 12 weeks TLG 512.5±86.5 TLG 651±111.5 Baseline 12 weeks CG 459.37±78.13 CG 459.37±78.13 TLG (baseline×12th week), $p<0.001^*$ / TLG×CG (12th week), $p<0.001^*$ / TG (baseline×12th week), $p<0.001^*$ / TG×CG (12th week), $p<0.008^*$ / TLG×TG (12th week), $p>0.05$. P.S.: Data were not reported in manuscript text and were extracted from graphs.	Not applicable
De Marchi et al. [27]	Not applicable	Not applicable	Not applicable
Almeida et al. [28]	Not applicable	Not applicable	Not applicable

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Table 8 Outcomes summary of RCTs

Authors	Lactate	CK	CRP	Number of repetitions	Time to exhaustion	LDH	Peak force, peak torque or peak power	MVC (Nm)	Total work (J)	1 RM test	Muscle activity
Leal Junior et al. [16]	Ineffective $p > 0.05$	-	-	Effective $p = 0.0001^*$	Effective $p = 0.0022^*$	-	-	-	-	-	-
Gorgey et al. [17]	-	-	-	-	-	-	-	Ineffective $p = 0.99$	-	-	-
Leal Junior et al. [18]	Ineffective $p = 0.200$	-	-	Effective $p = 0.042$	Ineffective $p = 0.096$	-	-	-	-	-	-
Leal Junior et al. [19]	Ineffective $p > 0.05$	Effective LED cluster× Laser probe $p < 0.05$	-	-	-	-	Ineffective	-	-	-	-
	$3'$	LED cluster× placebo $p < 0.01^*$	-	-	-	-	$p > 0.05$	-	-	-	-
	> 0.05		-	-	-	-		-	-	-	-
	$10'$		-	-	-	-		-	-	-	-
	$15'$		-	-	-	-		-	-	-	-
Leal Junior et al. [20]	Effective $p = 0.042^*$	Effective $p = 0.035^*$	Effective $p = 0.03^*$	Effective $p = 0.021^*$	Effective $p = 0.036^*$	-	-	-	-	-	-
Leal Junior et al. [21]	Effective $15'$ $p > 0.05$	Effective $p = 0.0133^*$	-	-	-	-	-	-	Ineffective $p = 0.3583$, volleyball $p = 0.8681$, soccer	-	-
	$3'$		-	-	-	-		-		-	-
	$10'$		-	-	-	-		-		-	-
	$15'$		-	-	-	-		-		-	-
Leal Junior et al. [22]	Effective $p < 0.01^*$	Effective $p = 0.017^*$	Effective $p = 0.047^*$	Effective $p = 0.037^*$	Effective $p = 0.034^*$	-	-	-	-	-	-
Kelencz et al. [23]	-	-	-	-	Effective only with 2.088 J, $p < 0.01^*$	-	Ineffective, $p > 0.05$	-	-	-	Effective only with 1.044 J in both of sides (control and treated), $p < 0.05^*$
Baroni et al. [24]	-	-	-	-	-	-	Ineffective $p = 0.231$	Effective $p = 0.034^*$	Ineffective $p = 0.182$	-	-
Baroni et al. [25]	-	Effective 24 h and 48 h $p = 0.020^*$, 24 h $p < 0.001^*$, 48 h	-	-	Effective 48 h $p < 0.05^*$	-	-	Effective immediately after 24 and 48 h $p < 0.05^*$ immediately $p < 0.05^*$, 24 h $p < 0.05^*$, 48 h	-	-	-
Ferraresi et al. [26]	-	-	-	-	-	-	Effective TLG: baseline× 12th week, $p = 0.036^*$	-	-	Effective TLG: baseline× 12th week, $p < 0.001^*$	-

Table 8 (continued)

Authors	Lactate	CK	CRP	Number of repetitions	Time to exhaustion	LDH	Peak force, peak torque or peak power	MVC (Nm)	Total work (J)	1 RM test	Muscle activity
De Marchi et al. [27]	—	Effective $p=0.0001^*$	—	—	Effective $p=0.0467^*$	Effective $p=0.0001^*$	Ineffective TLG×TG, $p>0.05$ TLG×CG $p>0.05$	—	—	Ineffective TLG×TG (12th week), $p>0.05$ P.S.: TLG×TG were effective ($p=0.033$) when percentage of increase was analyzed between groups	—
Almeida et al. [28]	—	—	—	—	—	—	Peak force effective red and infrared LLLT compared to placebo	—	—	—	—

LLLT low-level laser therapy, LEDT light-emitting diode therapy, PL Placebo, TLG training with LLLT, TG training only, CG control group

The meta-analysis showed consistent and significant results in favor of phototherapy for the main outcome measures. The time until exhaustion (Fig. 2) increased significantly by 4.12 s (95 % CI 1.21–7.02, $p<0.005$) after phototherapy with no significant heterogeneity ($I^2=0$ %) when compared to placebo control. The number of repetitions (Fig. 3) also increased by 5.47 (95 % CI 2.35–8.59, $p<0.0006$) after phototherapy with no significant heterogeneity ($I^2=0$ %) when compared to placebo control. Other measures of muscle performance (1RM, maximal voluntary contraction, peak force, and work performed), showed similar results with 10 out of 15 comparisons significantly in favor of phototherapy groups.

For CK activity, which may be suggestive of an increased risk for muscle damage, results were too heterogeneous to perform a meta-analysis. However, phototherapy groups had significantly lower CK activity in six out of six comparisons with placebo control. For other outcomes with biochemical markers (LDH, lactate, and CRP), seven out of ten comparisons were significantly in favor of the phototherapy groups when compared to placebo.

The positive and consistent results were obtained using phototherapy sources (laser and LED) with 640, 655, 660, 808, 810, 830, and 850 nm wavelengths, doses from 0.3 J to 41.7 J per point or site, and power output from 10 to 200 mW per spot. The most significant results were achieved with higher power outputs (100 and 200 mW) and energy doses between 5 and 41.7 J per site irradiated. The improvement in performance was 2 % up to 57 %, and CK activity decreased from 11.6 % to 83.2 % with active phototherapy.

Discussion

Phototherapy effects have been investigated in several biological processes such as analgesia, inflammation, and tissue healing [29]. Previous systematic reviews in this area are few, and they have not quantified main outcome measures by meta-analyses or investigated dose–response relationship or optimal doses [30]. Since the first finding of LLLT on muscle damage and fatigue development in rats by Lopes-Martins et al. [8], several studies have been published investigating its effects on exercise performance and post-exercise recovery.

The large amount of studies included in this systematic review shows consistent positive results of LLLT and LEDT in delaying muscle fatigue, mainly when pre-exercise treatment is performed. On the other hand, Ferraresi et al. [26] irradiated post exercise with LLLT and found an increase of 28.76 % in muscle performance (1RM test) in the laser-treated group compared to training group. This suggests that strength training may be successfully combined with post-exercise LLLT as well.

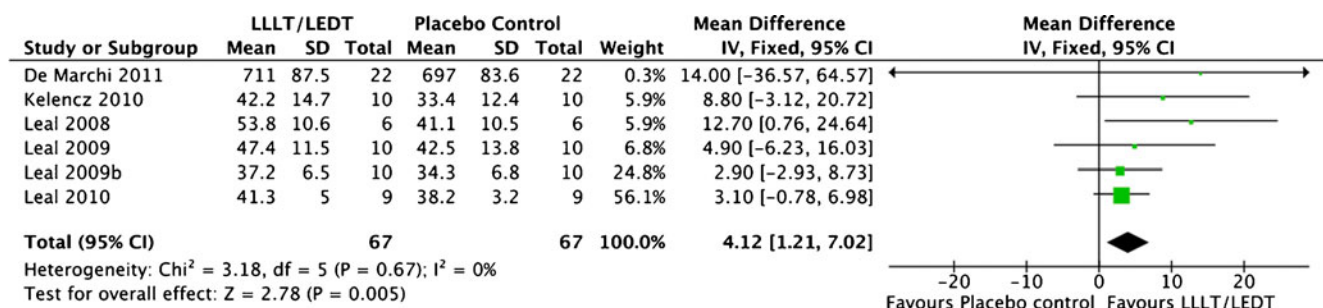


Fig. 2 Relative risk of increase time to exhaustion in phototherapy-treated versus placebo-control groups in six trials reporting categorical data

In one of the trials that did not find positive results for LLLT [17], neuromuscular electrical stimulation was employed to induce skeletal muscle contractions, and pre-exercise phototherapy treatment was applied with LLLT scanning, which dilutes energy density and could explain their absence of positive results. The scanning application method implies greater energy loss by refraction, and consequently lower absorption of light by increasing angle and relative large distance between laser beam and human skin (and also the target tissue: quadriceps muscle). The area of irradiation was about 50 cm^2 , and consequently, the beam angle exceeds 15 deg and, therefore, a considerable amount of light would be reflected and consequently not absorbed in half of the irradiated area. In addition, the scanning method implies that muscle cells only get irradiated for some tenths of a second every 20 s, which is clearly insufficient. The trial was also underpowered with a small sample of five participants, and type II error cannot be excluded.

Leal Junior et al. [19], in a study comparing the effects of a single diode LLLT with a cluster of LEDT before high intensity exercise, found decreased levels of CK after exercise only when subjects were irradiated pre-exercise with LEDT, but with no changes in blood lactate levels or performance in both groups. The nonsignificant results may be explained by the small irradiated area in the rectus femoris muscle and several large muscle groups involved in a Wingate test. It is noteworthy that the main outcome of this study was decreased levels of CK, an important marker of muscle damage that is linked to muscle recovery.

The vast majority of LLLT studies show positive results if applied stationary for at least 30 s of irradiation. This seems to

be crucial for achieving positive effects from phototherapy. It has been suggested that phototherapy has a biphasic dose–response pattern. This means that low energy doses lead to no effect, intermediate energy doses lead to stimulatory effect, and high doses lead to inhibition of cellular activity [4].

On one hand, it can be argued that the observed effects from phototherapy in muscle performance are small. But it is interesting to note that the positive effects of phototherapy seem to be even more consistent for surrogate outcome measures like the biochemical markers. This increases the credibility of the positive outcomes seen for muscle performance measures, because it strengthens the notion that there are underlying photochemical processes responsible for the observed effects. In addition, several of the nonsignificant results can be explained by insufficient irradiation either from too low doses or too small areas covered by irradiation. For other conditions like tendinopathies and arthritis, several authors have found correct dosing to be crucial for achieving effects [31–33]. It is important to highlight that the majority of the included studies (92 %) used phototherapy before exercise [16–25, 27, 28]. The positive effects of the phototherapy application prior to exercise seem not only to improve muscle performance but also to prevent injuries due muscle fatigue and improve post-exercise recovery.

The most common hypotheses for LLLT mechanisms are increased mitochondrial activity and ATP synthesis, acceleration of the resolution of inflammation [16, 18, 20, 22, 26]. But integration between the production of ATP aerobically and anaerobically involving phosphocreatine resynthesis, and removal and oxidation of lactic acid by

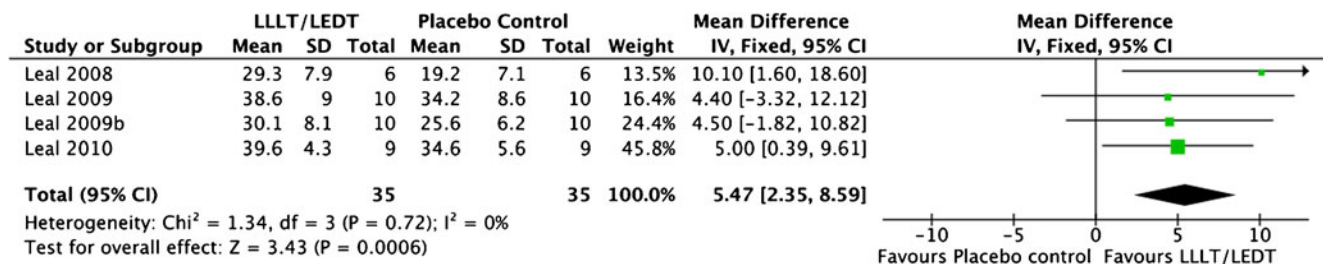


Fig. 3 Relative risk of increase repetitions in phototherapy-treated versus placebo-control groups in four trials reporting categorical data

increasing the local microcirculation have also been suggested to be stimulated by phototherapy [26–28]. Other effects of phototherapy on performance and recovery have been proposed and are still being investigated [34, 35].

The wavelength and the optimal dose are items of important questions both in research and in clinical use. It is necessary to define the optimal therapeutic window for achieving positive results in improvement of exercise performance and recovery. Therefore, it is important to develop more studies to understand the physiological mechanisms of action of phototherapy and to standardize the parameters of laser and LED. In the same way, it is important to standardize exercise protocols employed and outcomes assessed, trying to optimize the use of phototherapy in clinical practice.

Conclusion

Irradiation with phototherapy employing LLLT and LEDT with red or near-infrared wavelengths seems to induce a dose-dependent effect in improvement of performance in skeletal muscle during exercises. There are also indication that phototherapy may preserve tissue against exercise-induced muscle damage and speed up recovery when applied before exercises. The optimal dose seems to be identical for the three purposes, and irradiation should be delivered stationary to points for every 5 cm² of muscle tissue with a dose of 5–6 J per point (spot); however, when cluster probes are employed, a smallest dose per diode must be considered to avoid an overdose per area irradiated (site). Further studies are still needed to establish precise dose range and other optimal parameters for phototherapy in this promising research area.

Contributorship statement ECPLJ participated in the literature search, development of inclusion and exclusion criteria, selection of trials for inclusion in the analysis, methodological assessment, data extraction and interpretation, writing of the report, and supervised writing of the report as a whole. AAV and EFM participated in the selection of trials for inclusion in the analysis, methodological assessment of RCTs, and data analysis. SDC and PTCC participated in data interpretation and analysis and critically reviewed the report. JMB participated in development of inclusion and exclusion criteria, data analysis and interpretation, writing of the results section of the report, and supervised writing of the report as a whole. All authors read and approved the final manuscript.

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References

- Weir JP, Beck TW, Cramer JT et al (2006) Is fatigue all in your head? A critical review of the central governor model. *Br J Sports Med* 40: 573–586
- Al-Mulla MR, Sepulveda F, Colley M (2011) A review of non-invasive techniques to detect and predict localized muscle fatigue. *Sensors (Basel)* 11:3545–3594
- Bibikova A, Oron U (1993) Promotion of muscle regeneration in the toad (*Bufoviridis*) gastrocnemius muscle by low-energy laser irradiation. *Anat Rec* 235:374–380
- Huang YY, Chen AC, Carroll JD et al (2009) Biphasic dose response in low level light therapy. *Dose Response* 7:358–383
- Lin F, Josephs SF, Alexandrescu DT et al (2010) Lasers, stem cells, and COPD. *J Transl Med* 8:16
- Mester E, Szende B, Gärtner P (1968) The effect of laser beams on the growth of hair in mice. *Radiobiol Radiother (Berlin)* 9: 621–626
- Karu TI (1987) Photobiological Fundamentals of low-power laser therapy. *IEEE J Quantum Electron* 23:1703–1719
- Lopes-Martins RA, Marcos RL, Leonardo PS et al (2006) Effect of low level laser (Ga-Al-As 655 nm) on skeletal muscle fatigue induced by electrical simulation in rats. *J Appl Physiol* 101: 283–288
- Almeida P, Lopes-Martins RA, Tomazoni SS et al (2011) Low-level laser therapy improves muscle performance, decreases skeletal muscle damage and modulates mRNA expression of COX-1 and COX-2 in a dose-dependent manner. *Photochem Photobiol* 87:1159–1163
- Cheung K, Hume P, Maxwell L (2003) Delayed onset muscle soreness: treatment strategies and performance factors. *Sports Med* 33:145–164
- Centre for Evidence Based Medicine (1999) The physiotherapy evidence database (PEDro) scale items. University of Sydney, New South Wales, Australia
- Verhagen AP, de Vet HC, de Bie RA et al (1998) The Delphi list: a criteria list for quality assessment of randomized clinical trials for conducting systematic reviews developed by Delphi consensus. *J Clin Epidemiol* 51:1235–1241
- Paolillo FR, Milan JC, Aniceto IV et al (2011) Effects of infrared-LED illumination applied during high-intensity treadmill training in postmenopausal women. *Photomed Laser Surg* 29:639–645
- Vieira WH, Ferraresi C, Perez SE et al (2012) Effects of low level laser therapy (808 nm) on isokinetic muscle performance of young women submitted to endurance training: a randomized controlled clinical trial. *Lasers Med Sci* 27:497–504
- Paolillo FR, Corazza AV, Borghi-Silva A et al (2013) Infrared LED irradiation applied during high-intensity treadmill training improves maximal exercise tolerance in postmenopausal women: a 6-month longitudinal study. *Lasers Med Sci* 28:415–422
- Leal Junior EC, Lopes-Martins RA, Dalan F et al (2008) Effect of 655-nm low-level laser therapy on exercise-induced skeletal muscle fatigue in humans. *Photomed Laser Surg* 26:419–424
- Gorgey AS, Wadde NA, Sobhi NN (2008) The effect of low level laser therapy on electrically induced muscle fatigue: a pilot study. *Photomed Laser Surg* 26:501–506
- Leal Junior EC, Lopes-Martins RA, Vanin AA et al (2009) Effect of 830 nm low-level laser therapy in exercise-induced skeletal muscle fatigue in humans. *Lasers Med Sci* 24:425–431
- Leal Junior EC, Lopes-Martins RA, Baroni BM et al (2009) Comparison between single-diode low-level laser therapy (LLLT) and LED multi-diode (cluster) therapy (LEDT) applications before high-intensity exercise. *Photomed Laser Surg* 27:617–623
- Leal Junior EC, Lopes-Martins RA, Rossi RP et al (2009) 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* 41:572–577
21. Leal Junior EC, Lopes-Martins RA, Baroni BM et al (2009) Effect of 830 nm low-level laser therapy applied before high-intensity exercises on skeletal muscle recovery in athletes. *Lasers Med Sci* 24:857–863
 22. Leal Junior EC, Lopes-Martins RA, Frigo L et al (2010) 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* 40:524–532
 23. Kelencz CA, Muñoz IS, Amorim CF et al (2010) Effect of low-power gallium–aluminum–arsenium noncoherent light (640 nm) on muscle activity: a clinical study. *Photomed Laser Surg* 28:647–652
 24. Baroni BM, Leal Junior EC, Geremia JM et al (2010) Effect of light-emitting diodes therapy (LEDT) on knee extensor muscle fatigue. *Photomed Laser Surg* 28:653–658
 25. Baroni BM, Leal Junior EC, De Marchi T et al (2010) Low level laser therapy before eccentric exercise reduces muscle damage markers in humans. *Eur J Appl Physiol* 110:789–796
 26. Ferraresi C, de Brito OT, de Oliveira ZL et al (2011) Effects of low level laser therapy (808 nm) on physical strength training in humans. *Lasers Med Sci* 26:349–358
 27. De Marchi T, Leal Junior EC, Bortoli C et al (2012) Low-level laser therapy (LLLT) in human progressive-intensity running: effects on exercise performance, skeletal muscle status and oxidative stress. *Lasers Med Sci* 27:231–236
 28. Almeida P, Lopes-Martins RA, De Marchi T et al (2012) Red (660 nm) and infrared (830 nm) low-level laser therapy in skeletal muscle fatigue in humans: what is better? *Lasers Med Sci* 27:453–458
 29. Tam G (1999) Low power laser therapy and analgesic action. *J Clin Laser Med Surg* 17:29–33
 30. Borsa PA, Larkin KA, True JM (2013) Does phototherapy enhance skeletal muscle contractile function and postexercise recovery? A systematic review. *J Athl Train* 48:57–67
 31. Bjordal JM, Couppe C, Chow RT et al (2003) A systematic review of low level laser therapy with location-specific doses for pain from chronic joint disorders. *Aust J Physiother* 49:107–116
 32. Chow RT, Johnson MI, Lopes-Martins RA et al (2009) 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* 374:1897–1908
 33. Jang H, Lee H (2012) Meta-analysis of pain relief effects by laser irradiation on joint areas. *Photomed Laser Surg* 30:405–417
 34. Leal Junior EC, de Godoi V, Mancalossi JL et al (2011) 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* 26:493–501
 35. Miranda EF, Leal-Junior EC, Marchetti PH et al (2013) Acute effects of light emitting diodes therapy (LEDT) in muscle function during isometric exercise in patients with chronic obstructive pulmonary disease: preliminary results of a randomized controlled trial. *Lasers Med Sci*. doi:10.1007/s10103-013-1359-5, Published Online first: 7 June 2013