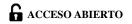
REVIEW ARTICLE



Clinical and experimental knowledge of photobiomodulation in accelerated orthodontics: A review

Conocimiento clínico y experimental de la fotobiomodulación en ortodoncia acelerada: Una revisión

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ABSTRACT

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acceleration of dental movement, methods such as low intensity vibrations, pulsed electromagnetic fields, and lowlevel laser therapy (LLLT). There have been multiple studies on the efficacy of LLLT in animal models, in vitro and in patients without conclusive results. **Objective:** Evaluate the state of the art on the use of LLLT to increase the rate of the orthodontic tooth movement to create a concise reference guide of the different laser and protocols available. Materials and Methods: The

Background: In recent years, there has been an increasing interest in finding a noninvasive method to induce the

to create a concise reference guide of the different laser and protocols available. Materials and Methods: The authors searched electronic databases (MedLine, Scopus and Semantic Scholar) for articles that evaluated the effects of low-lever laser therapy on the orthodontic tooth movement. Screening was performed at the title/ abstract and full-text level. Data extraction and quality assessment were performed by two reviewers independently. The reference lists of relevant studies were also screened for further relevant literature.

Results: We found conflicting information as to the efficacy of LLLT to accelerate the orthodontic tooth movement (OTM). There is no consensus in the way the irradiation should be performed.

Conclusions: The lack of a standardized irradiation protocol makes it hard to compare conflicting results, even in cases where the laser have the same technical specifications.

KEYWORDS

LLLT; OTM; Orthodontic Tooth Movement; GaAlAs Lasers; acceleration.

RESUMEN

Antecedentes: En los últimos años, ha habido un interés creciente en encontrar un método no invasivo para inducir la aceleración del movimiento dental, métodos como vibraciones de baja intensidad, campos electromagnéticos pulsados y terapia con láser de bajo nivel (LLLT). Se han realizado múltiples estudios sobre la eficacia de la LLLT en modelos animales, in vitro y en pacientes sin resultados concluyentes.

Objetivo: Evaluar el estado del arte en el uso de LLLT para aumentar la velocidad del movimiento dental ortodóncico para crear una guía de referencia concisa de los diferentes láser y protocolos disponibles. Materiales y métodos: Los autores buscaron en bases de datos electrónicas (MedLine, Scopus y Semantic Scholar) artículos que evaluaran los efectos de la terapia con láser de baja intensidad sobre el movimiento dental ortodóncico. La selección se realizó a nivel de título / resumen y texto completo. Dos revisores realizaron de forma independiente la extracción de datos y la evaluación de la calidad. También se examinaron las listas de referencias de estudios relevantes para obtener más literatura significativa.

Resultados: Encontramos información contradictoria en cuanto a la eficacia de la LLLT para acelerar el movimiento dental ortodóncico (OTM). No hay consenso sobre la forma en que se debe realizar la irradiación. **Conclusiones:** La falta de un protocolo de irradiación estandarizado dificulta la comparación de resultados, incluso en los casos en que el láser tiene las mismas especificaciones técnicas.

PALABRAS CLAVE

LLLT; OTM; movimiento dental ortodóncico; láseres GaAlAs; aceleración.

Clinical relevance

Scientific reasons for conducting the study. There is a lot of conflicting articles regarding the use of low-level laser therapy LLLT to accelerate the orthodontic tooth movement OTM, as well as an ever-increasing number of lasers, all claiming to have the right wavelength and power.

Main findings. There is a lack of standardization in the irradiation protocols, the efficacy of LLLT to accelerate the OTM is reported in a wide range of wavelengths, making it harder to discern which is the most effective protocol.

Practical implications. We urge the readers to review our chart to see the laser specs and protocols that more consistently reported gains in the rate of OTM, before acquiring a laser for their practice.

Introduction

The rate of tooth movement is an important factor in the duration of orthodontic treatment. This conventional treatment lasts about 2-3 years, this duration is linked to complications such as caries, root reabsorption, bone loss and non-compliance / abandonment of the patient. ^{1,2} Therefore, accelerating the orthodontic tooth movement (OTM) would be beneficial for the treatment and the oral health of the patient.

In recent years, the methods that have been studied for the acceleration of dental movement include corticotomies,³ low intensity vibrations,⁴ pulsed electromagnetic fields,⁵ pharmacotherapy ⁶ and low-level laser therapy (LLLT).⁷ There have been multiple studies on the efficacy of LLLT in animal models,⁸⁻¹¹ in vitro and in patients, so we felt it necessary to review the current literature regarding the effect of LLLT in the OTM, with an emphasis on the most recent human trials.

Materials and methods

Search criteria

MedLine, Scopus and Semantic Scholar databases were searched for literature until April 2020. A lateral search from the reference lists of eligible articles was also conducted.

Eligibility criteria

The inclusion criteria for eligibility for this review included randomized clinical trials (RCTs), prospective and retrospective controlled clinical trials (CCTs) descriptive studies and review articles. The exclusion criteria for this review included case reports, case series, opinion pieces, abstracts only, and articles in languages other than English or Spanish. Eligible studies needed to focus their intervention on LLLT-accelerated OTM. The results needed to be evaluated in comparison with a control group, be it either a discrete set of patients or a split mouth design in which each patient served as his or her control.

The science behind the LLLT & orthodontic tooth movement

The LLLT consists in exposing tissue to low levels of red and/or near infrared light, it takes its name from the fact that these wavelengths are considered to have a lower energy density when contrasted with ablation, cauterizing or cutting lasers. This low-level energy density also produces less heat, reason what sometimes the LLLT is referred to as cold laser. ¹²

The precise mechanism underlying the effects of LLLT are not yet fully elucidated. It has a wide range of effects at the tissular, cellular and molecular levels. There is strong evidence suggesting that within the cell, at the mitochondria level the LLLT increases adenosine triphosphate (ATP) production and modulates reactive oxygen species (ROS).^{12,13}

The LLLT acts by inducing a photochemical reaction in the cell. The photons from the laser are absorbed by chromophores inside the mitochondria of irradiated cells, electrons in the chromophores jump from a low-energy orbit to a higher-energy orbit. Thus, causes an increase in mitochondrial activity increasing production of ATP, NADH, proteins, and RNA, as well as an upregulation of cellular respiration all adding up to an increase in osteoclast genesis and with it, an increase in OTM.¹²

It's of particular importance for orthodontics the effect that the LLLT has on fibroblast, osteoblast and osteoclast, perhaps the 3 most important cells in the biomechanics of OTM. Multiple in vitro studies have found that LLLT increases the proliferation of human gingival fibroblast (HGF), basic fibroblast growth factor (bFGF), receptor of IGF-1 (IGFBP3) in HGF as well as insulin-like growth factor-1 (IGF-1) and the expression of collagen type I.^{1,14}

Dominguez *et al.* 2008 evaluated the effects of LLLT on periodontal and gingival fibroblasts, the irradiation was done with a 832.79-nm 808nm Ga-Al-As diode laser (Photon Lase III ,DMC Equipamentos; São Carlos, Brazil) keeping the power outoput at 37-mW, continuous mode for 32.45s, resulting in a 3.75 J/cm² energy flow. After irradiation, the plates were incubated, a non-significant increase was observed in the irradiated group of both cell lines at 24, 48, 72, 96, 120, and 148-h post irradiation. Experimental and control groups had no statistically difference on cell viability.¹⁵

Similarly, albeit finding statistically significance, Kreisler *et al.* 2003 studied the effects of LLLT on the proliferation of human periodontal ligament fibroblast.



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A 809nm Ga-Al-As diode laser (Oralaser voxx, Oralia GmbH, 78467 Konstanz, Ger- many) keeping the power outoput at 10-mW, continuous mode for 75, 150 and 300 s, resulting in a 1.96, 3.92 and 7.84 J/cm² energy flow respectively. They measured cell proliferation at 24,48 and 72 h after irradiation and found a higher cell proliferation on the experimental groups, the difference was significant up to 72h after irradiation, at which point cell activity reached a peak in all groups, irrespective of the incubation time and irradiation regimen.¹⁶

This is consistent with Pereira *et al.* 2002 study, they used a 904-nm Ga-Al-As diode laser, the power output was set at 120-mW during 8 and 24 s, with a energy flow of 1 and 3 J/cm² respectively. They found that the irradiated groups of NIH-3T3 fibroblasts (CRL 1658 from American Type Culture Collection, Rockville, MD) had a significant increase of cell numbers compared to the control groups without impairing procollagen synthesis.¹⁷

Likewise Almeida *et al.* 2001 also found that LLLT improved the in vitro human gingival fibroblast proliferation with nutritional deficit and that shorter exposure times lead to higher proliferation. For this, they used 4 lasers, with wavelengths and power output of 670 nm at 10mW, 780-nm at 50-mW, 692-nm at 30-mW, and 786-nm at 30-mW, manufacturers not disclosed. The energy flow was set at 2 J/cm² for all 4 lasers. Additionally, they found that the infrared laser (780-nm) induced significantly higher cell growth than the visible laser (670 nm) when set the same energy fluence (2-J/cm²).¹⁸

Aras *et al.* 2015 studied the effects of LLLT in an experimental rapid maxillary expansion model on female Wistar albino rats using an 808nm Ga-Al-As diode laser (Fotona XD-2 diode laser; Fotona, Ljubljana, Slovenia) applied with a 320 µm-diameter fiber handpiece. The rats were irradiated with 250 mW (0.25W) for 20 s, totaling 5 J/cm². They found that the LLLT group had significantly higher numbers of osteoclast cells when compared with the control group. (p= 0.036) There was no difference in the number of osteoblast cells, however histological analysis revealed the trabecular bone was larger and better ossified in the LLLT group indicating that the healing process was more advanced. They concluded that histologically, LLLT stimulated bone formation.¹⁹

The effects of LLLT can also be seen on human cells, Khadra *et al.* 2005 studied the effects of LLLT on attachment, proliferation and differentiation of human osteoblast-like cells cultured on titanium implant material using an 830nm Ga-Al-As diode laser. (Rønvig Dental AS, Denmark) Each culture dish was irradiated with 84mW at a dosage of 1.5 or $3J/cm^2$. They found no significant difference in the number of osteoblast cells at the 48h and 72h mark, but after 96h the number of osteoblast cells in the irradiated group was significantly higher. (p<0.05) They also found no significant difference on cell viability between the irradiated and control group.²⁰

However, significant difference in cell proliferation have observed as early as 24h post irradiation, Dominguez *et al.* 2008 evaluated the effect of LLLT on Normal Human Osteoblast cells (NHOs from Cambrex Bioscience, Charles City, IA, USA) using a 832.79-nm Ga-Al-As diode laser (Photon LASE laser, DMC Equipamentos; Sao Carlos, Brazil). The irradiation was performed keeping the energy output at 36.73 mW in continuous mode for 1131-s, resulting in an energy flow of 3.75 J/cm². They found that after the incubation periods (24, 48, 72, 96, 120, or 148-h.), the proliferation of NHOs, in the experimental group was statistically significant until the 5th day, when it reached contact inhibition.²¹

Sungsoo Na *et al.* 2018, studied the effect of LLLT on osteoblasts (MC3T3-E1,ATCC, Manassas, Virginia), osteocytes (MLO-A5), and osteoclasts (RAW264.7, ATCC, Manassas, Virginia) using a 940nm custom-made device delivering doses of 0, 1, 5, and 7.5 J/cm² After irradiation, cell activity was evaluated at 12, 24, and 48-h, while cell viability was evaluated at 12 and 24 h. They found that 24h after a 10 minute low-dose treatment ($1J/cm^2$ or 1.67 mW/cm²) proliferation of osteoblasts was substantially increased (p<0.0001), and unlike the osteoclast, irradiation did not affect viability of osteoblast cells which may positively affect bone formation.

This research revealed that osteoclast differentiation mainly occurs with low-dose treatments. The increase peaked at 12h (p<0.01) then it went down gradually until 48h post irradiation, at which point it was no different than the control group. Their results suggest that low-dose treatment stimulates osteoblast and osteoclast differently, LLLT effect on osteoblast can be seen 24 h after laser application, whereas the effect on osteoclast can be seen as early as 12 h.²² It's important to remark that this effect can no longer be seen after 48h for either the osteoblast or the osteoclast, and the clinical implications that this may pose when designing the irradiation protocols.

The evaluation of OTM and LLLT in human trials

As stated before, the average treatment time is 2-3 years, up to 8 months of that time is often used during the leveling and alignment phase, which makes it an ideal phase to study the effects of laser in the OTM.

There have been multiple human trials to evaluate the efficacy of LLLT on the OTM, with varying and conflicting results.²³⁻²⁵ In one side there are multiple clinical trials that found that the LLLT significantly improved the rate of OTM during the leveling and alignment phase when compared with the control group (Table 1). AlSayed Hasan *et al.* 2017 evaluated the effect of LLLT during the leveling and alignment phase in cases with crowded maxillary incisors, using a 830nm laser device (CMS Dental ApS, 55 Wildersgade, 1408 Copenhagen K, Denmark), the irradiation was done on day 0, 3, 7 and 14 for the first month and every 15 days from the 2nd month onwards.



First Author Publicatio n. Year	n			Lasei	ſ		Application			
		Laser type	Wave lenght	Power, Time	Dose (J/cm2)	Total Energy (J)	Irradiation Interval	Applied Tooth	Force (g) / Archsequence	Result Velocity Vs Control
Cruz (2004)	11	Diode Laser	780nm	20 mW, 10s	5 J/cm ²	0.2/Point 2.0/Session	4 days of each month	Canine	150 g	Increase 34% (2 Months)
Sousa (2011)	13	Diode Laser	780nm	20 mW, 10s	5 J/cm ²	0.2/Point 2.0/Session	0,3,7 Days of each month	Canine	150 g	2x Increase (4 months)
Genc (2013)	20	Diode Laser	808nm	20 mW, 10s	0.71 J/cm ²	0.2/Point 2.0/Session	0,3,7,14,21,28 Days	Upper lateral incisors	80 g	20-40% Increase (1 month)
Youssef (2008)	15	Diode Laser	809nm	100 mW, 10/20s	8 J/cm ²	8.0/Session	0,3,7,14 Days	Canine	150 g	2x Increase (6 months)
Isola (20019)	41	Diode laser	810nm	1W, 15s	66.7 J/cm ²	8J	Days 3, 7, and 14 days and every 15 days until the space closed	Canine	Force of 50/N was applied by a nickel-titanium (NiTi) closed coil spring	A shorter average time to complete space closure
Duan (2012)	44	Diode Laser	830nm	180 mW, 4s	3.6 J/cm ²	18/ point 54/session	Days 0,1,2	Upper 1st molar	10	Increase
AlSayed Hasan (2017)	26	Ga-Al- As	830nm	150 mW, 15s	2.25 J/cm ²	2 J/point	First month: 4 (d 0, 3, 7, 14); starting from the second month: every 15 days	Maxillary incisors	MBT prescription and 0.022-inch slot height, the archwire sequence used was 0.014-inch NiTi followed by 0.016 3 0.016- inch and 0.017 3 0.025-inch NiTi, and finally 0.019 3 0.025-inch stainless steel.	26% increase

They found a statistically significant difference between the irradiated group (150mW,2.25 J/cm²,15s) and the control group in the leveling and alignment improvement percentages at 1 month after the start of treatment (69.41% vs 48.85%,P=0.004) and 2 months (89.42% vs 71.7%,p=0.001) as well as in the overall treatment time (p<0.001).²⁶

The purported benefits of the LLLT are not limited to the leveling and alignment phase, studies have shown an improvement in the OTM when retracting canines following premolars extractions.²⁷⁻³⁴

Da Silva Sousa *et al.* 2011 evaluated the effects of LLLT during canine retraction with a nitinol coil spring with a constant force of 150g, reactivated after 30 and 60 days. 3D casts were taken at 0, 30, 60 and 90 days to measure the movement.

The irradiation was done with a 780nm Ga-Al-As diode laser (Twin Laser, MMOptics Ltda, Sao Carlos, Sao Paulo, Brazil) They found a statistically significant difference between the irradiated groups (20 mW, 5 J/cm²,10s for 3 days) and the control groups.²⁷



Genc *et al.* 2013 also evaluated the effect of LLLT on the rate of OTM during maxillary lateral retraction applying approximately 80g of force with nickel-titanium closed coil springs and using an 808nm Ga-Al-As diode laser (Fotona XD-2, USA) to perform the irradiation (20 mW, 0.71 J/cm²,10s) on day 0,3,7, 14, 21, and 28 days after the application of the nickel-titanium closed coil springs.

They found a statistically significant difference over time for the distances between the maxillary lateral incisors and the maxillary central incisors in comparison to the control group.³⁵

Youssef *et al.* 2008 evaluated the effects of LLLT using an 809 nm Ga-Al-As diode laser (Quanta, Italy) during space closure. Canine retraction was done with prefabricated 16×16 Blue Elgiloy Ricketts Springs (RMO) delivering 150g of force reactivated ever 21 days until space closure was achieved. The canines were irradiated (100mW,8 J/cm²,2×40 s) on days 0, 3, 7, and 14 after every activation. They reported an analgesic effect and a significantly increase in the rate of OTM during space closure when compared with the control group.²⁸

Yassaei *et al.* 2016 used a 980 nm Ga-Al-As diode laser (A.R.C. Laser GmbH, Nürnberg, Germany) to irradiate (100mW, 5.6 J/cm²,56s) the tooth during canine retraction, closed coil springs with a 150g force were used for the retraction on rectangular wires.

A light but not statistically significant improvement in the rate of retraction was observed, additionally the mean concentration of IL-6 was measured, finding there was no significant difference in the mean concentration of IL-6 between the groups during canine distalization and thus they could not provide conclusive evidence to support its efficacy.²⁹

Cruz *et al.* 2004 evaluated the effects of LLLT during canine retraction. A 12-mm Nickel-Titanium closed-loop coil spring exhorting 150g of force was used for the retraction. The irradiation was done with a 780nm Ga-Al-As diode laser (Twin Laser, MM Optics Ltda., Sao Carlos, SP, Brazil) ,the canines were irradiated (20mW, 5 J/cm², 10x10s) by the same operator, 5 points on buccal side and 5 by the palatal side.

A significantly higher rate of OTM was observed on the irradiation group. The accelerated OTM was achieved with a healthy response from periodontal tissue as confirmed by the radiographic images that showed no evidence of damage in the dental and periodontal tissue of the irradiated teeth.³⁰

Dominguez *et al.* 2015 evaluated the effect of the LLLT with a 670 nm laser (PeriowaveTM, Ondine Biopharma Corporation, Vancouver, Canada) the irradiation (200 mW, 6.37 W/cm², 540s on days 0, 1, 2, 3, 4, and 7) was done on the distal, buccal, and lingual side of the premolar for 3m on each side for a total of 9m.

For the space closure, the first bicuspids were distalized with a nitinol coil spring with a constant force of 150g, they found a slight improvement in the rate of OTM, after 30 days, the accumulated retraction was statistically significant.³⁶

Doshi-Mehta *et al.* 2011 evaluated the effect of LLLT during individual canine retraction by a nickel-titanium closed-coil. The laser used was an 800nm Ga-Al-As diode laser (LA3D0001.1; LAMBDA S.p.A., Vicenza, Italy) and the irradiation (100mW, 5J/cm², 80s) for bio-stimulation started 3 days after the nickel-titanium coil spring placement. The average time for complete canine retraction on the irradiated side was 4.5 months, showing a 30% higher OTM rate when compared with the control side.³¹

Qamruddin *et al.* 2017 evaluated the effects of LLLT during canine retraction using MBT self-ligating brackets. To retract the canines 6 mm nickel-titanium closed-coil springs were used, exerting a constant retraction force of 150g. A 940nm Ga-Al-As diode laser (iLas; Bio- lase, Irvine, Calif) was used to irradiate (100mW,7.5J/cm². 30s every 3 weeks) the canines on 10 points, 2 seconds per point.

The distance was measured digitally with CAD/CAM scanned models. A statistically significantly increase in the rate of canine retraction was observed, the rate on the experimental side was 2.02 times greater compared with the placebo side, thus it was concluded that LLLT can double the rate of OTM when applied in intervals of 3 weeks.³²

Varella *et al.* 2018 evaluated the effects of LLLT with a similar 940nm Ga-Al-As diode laser (Ezlase; BIOLASE Technology, Irvine, Calif) during canine retraction with a light nickel-titanium closed coil spring (9x12mm) exerting 150g of force between the canines and the first bicuspids. They also found a significant increase in the rate of OTM on the irradiated group (100mW ,8J/cm²,10x10s), twice that of the control group.³³

Isola *et al.* 2019 evaluated the effects of LLLT with an 810nm (Wiser Laser Doctor Smile, Brendola, Italy) during canine distalization using an orthodontic force of 50/N applied with a nickel-tatanium closed coil spring using a split-mouth design.



Table 2. Summary of studies where an effective protocol was used to accelerate the orthodontic movement.

	n		La	ser					
First Author Publication. Year		Laser type	Wave lenght	Power, Time	Dose (J/cm ²)	Irradiation interval	Applied tooth	Force (g) / Archsequence	- Result Velocity Vs Control
Heravi (2014)	20	Go- Al- As	810nm	30 secs	21.4 J/cm ²	Days 3, 7, 11, 15 over the first month	Canine	Distalizing with a nitinol coil spring with a constant force of 150 g	No significant difference on the rate of OTM
Limpanichkul (2006)	12	Diode laser 8	360nm	100 mW, 23s	25 J/cm ²	First 3 days of each month	Canine	150 g	No effect
Dalaie (2015)	12	Ga-Al-As diode laser	880nm ¹	00 mW, 80s	5 J/cm ²	Days 1, 3, 7, 30, 33, 37, 60, 63 and 67	Canine	Force 150 g was applied to each canine tooth via sectional closing loops (16x22 steel wire)	No stastically significant difference
Kansal (2014)	10	Gallium- Arsenide laser	904nm	12 mW, 10s	4.2 J/cm ²	Days 1, 3, 7, 14, 21, 28, 35, 42, 49, 56	Canine	MBT prescription-0.022 slot, force 150 g, 19x25 SS	No stastically significant difference
Yassaei (2016)	11	Ga-Al-As laser Diode laser	980nm	100 mW, 56s	5.6 J/cm ²	Days 0, 7, 14, 21, and 28 of each month during the canine retraction	Maxillary canine	150 g. A preadjusted 0.022 x 0.028" edgewise appliance was used for bonding and a transpalatal bar, NiTi closed coil springs on rectangular SS wire	No stastically significant difference

A shorter average time to complete space closure was observed on the irradiated (100mW,66.7J/cm²,15s,8J) side compared to the control side.³⁴ On the other side we have an equally important number of clinical trials that found that the LLLT does not improve the rate of OTM (Table 2).

Dalaie *et al.* 2015 evaluated the effect of LLLT on the OTM during space closure with loops, using a 810nm laser (Wiser Laser Doctor Smile, Lambda, Brendola, Italy) finding no significant difference between the irradiated group (100 mW, 5 j/cm², 80s) and the control group.³⁷

Heravi *et al.* 2014 evaluated the use of LLLT during canine retraction, with an 810nm Ga-Al-As diode laser, finding there was no significant difference on the rate of OTM or its degree of mesiodistal inclination between the irradiated (200mW,21.4J/cm²,30 secs) and control group.³⁸

Limpanichkul *et al.* 2006 is another study where the LLLT during canine retraction using a 860 nm Ga-Al-As diode laser (Top Laser 250 SIR 100, Medical Innovation, France) failed to produce an increase in the rate of OTM, the authors believe the energy density in their protocol (100mW, 25J/cm²,8 x 23s) was too low to induce any biological effect on the OTM.³⁹

Similarly Kansal *et al.* 2014 found that there was no statistically significant difference in the rate of OTM during canine retraction using a 904nm Ga-Al-As diode laser (ORALIA Dental Products, D-7750 Konstanz, Germany) between the irradiated group (12mW, 4.2/cm²,10 x10s) and the control group.⁴⁰

Conclusions

The varying and conflicting results can be explained by the equally diverse LLLT protocols used by each study. There is a broad range of laser types, laser colors, wavelengths, power levels, exposure times, doses and application methodology that vary from study to study.

More studies need to be done to assess the efficacy of LLLT in accelerating the OTM. The authors remark the need for a more technical approach when categorizing the lasers used in the LLLT and their effects in OTM, as well as the need to come up with a standardized point of application protocol, as it stands right now, every clinician irradiates the teeth as they see fit, making it impossible to compare their results with studies that used the same laser, but different protocol and vice versa.



Statement of Conflict of interest and waiver

All authors of the manuscript declare that they do not have competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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