How to Stimulate Orthodontic Tooth Movement in a non-invasive way: LLLT

Chung-Chen Jane Yao DDS, PhD
姚宗珍
Associate Professor
School of Dentistry
National Taiwan University
Taipei, Taiwan

New Development of Orthodontics

- Tools for records taking: digitalized
- Tools for diagnosis: radiographs with much less dosage, CBCT, MRI
- Tools for treatment: SLB, aligners, TADs
- Methods to shorten treatment time

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Efficient Orthodontic Treatment

- Appropriate and realistic treatment goals
- Sound biomechanical design
- Compliant patients

•Intrinsic limitation for some unknown biological factors: every one can respond to force but with individual variation

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Canine retraction and anchorage loss Self-ligating versus conventional brackets in a randomized split-mouth study

Andre´ da Costa Monini a; Luiz Gonzaga Gandini Ju´ niorb; R

from Angle Orthod. 2014;84:846–852

Table 7. Data From Articles on Maxillary Canine Retraction Velocity Comparing Self-Ligating Brackets (SLB) and Conventional Brackets (CB)

Reference	SLB, mm/mo	CB, mm/mo	*P*
Mezomo et al.[18]	0.90	0.84	.356
Burrow[11]	1.00	1.17	.0001
Oz et al.[16]	1.83	1.89	.77
Present study	0.71	0.72	.931

Table 8. Maxillary Canine Displacement Velocities/Month Demonstrated by Patients Divided in Two Groups Based on the "Speed of Movement"

	n	Mean, mm/mo	Difference, mm/mo
Slow movers	13	0.569	0.304
Fast movers	12	0.873	
Total	25	0.715	

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Table 1. Sample Characteristics

Mean age in T1, y	23.32 ± 5.08		
Age range, y	17.66–35.49		
Gender	Female	Male	Total
	16	9	25

- The rate of canine movement seems to be influenced by individual biological responses of patients, rather than by bracket type.
- Without management of the biological responses that occur after a force is applied to a tooth, it would be very difficult to observe a faster velocity of tooth movement in the future.

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How to stimulate bone turnover rate in dentoalveolar area

- Invasive
  - Corticotomy
  - Corticision, puncture of alveolar bone, flap surg
  - RAP for 4-6 months
- Non-invasive
  - Ultrasound
  - Vibration
  - Low level laser

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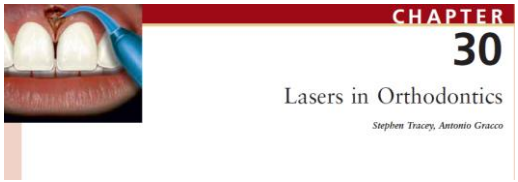
LASERs in Orthodontics
5th edition of Orthodontics—
Current Principles and Techniques



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OUTLINE

They focus on most ablation of tissues and only some healing for ulcers and herpes lesions.

The effects on OTM are not mentioned!

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LLLT in all medical fields

- power density usually at 1 mW-5mW/cm^2.
- The treatment usually lasts for one minute and is performed for days or weeks.
- Instead of cauterization or heating, light energy is transformed to chemical energy as photosynthesis.
- The chemical energy will then affect cellular activity and metabolism.

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How?

- When given mono-wave red light or ultrared light, mitochondria rat hepatocytes will increase ATP synthesis and oxygen consumption (Kato, Shinzawa et al. 1981).
- Increased level of ATP help to generate cAMP and sustain the membrane bound ATP-dependent Calcium pump, providing secondary messengers for multiple signaling pathway.

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Possible roles of mitrochondria playing in LLLT

- Action spectrum in HeLa cells was identified to increase DNA and RNA synthesis significantly at 620 nm, 680 nm, 760 nm, and 820 nm when 560-960 nm range tested (Karu and Kolyakov 2005).
- These wavelengths are corresponding to the spectrum of metal ligands in electron transport chain. Cytochrome C oxidase requires metal ligands to function.

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Low Level Laser Treatment in Medicine

facilitate wound healing, reduce inflammation and pain

- treat tendonitis, back pain, neck pain, muscle fatigue, peripheral nerve damages and stroke
- increase rate of bone repair during fracture healing

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Low Level Laser Treatment in Dentistry

- TMJ arthritis
- decrease post operative pain and healing time
- treating facilities
- reducing dentin hypersensitivity
- treating Herpes virus infection, repetitive ulceration or mucositis, allodenia and trigeminal neuralgia
- facilitating treatment treating bisphosphonate related osteonecrosis of jaws (BRONJ)

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LLLT to Accelerate OTM?

- Cellular levels
- Animal levels
- Patient levels

- Is it effective?
- Is it safe?

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Fundamentals of bone biology

- Activation of Ob and Oc
- Via biochemical signaling
- Via mechanical signaling

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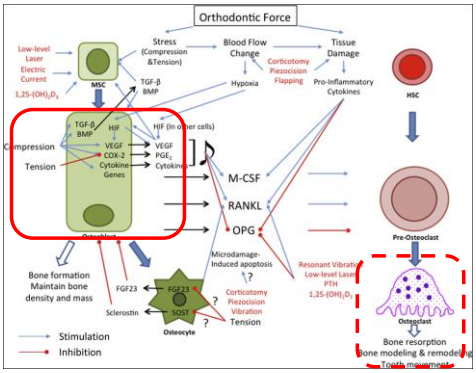

Summary of cellular and molecular mechanisms underlying accelerated orthodontic tooth movement.
From **Accelerated orthodontic tooth movement: Molecular mechanisms**
American Journal of Orthodontics and Dentofacial Orthopedics, Volume 146, Issue 5, 2014, 620 – 632
Hechang Huang , Ray C. Williams , Stephanos Kyrkanides

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Dosage of LLLT

- 1) Radiance: i.e., power density; power in unit area; watt/cm^2
- 2) Radiant energy: J, joule; power x time of exposure
- 3) Total radiant energy: total energy under the same operation; collective from different points of radiance
- 4) Radiant exposure: energy density; energy per unit area, joule/cm^2

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At Cellular Level

- In vivo experiments were carried at 0.5-4 J/cm^2, 10-900 mW.

- Ob cells: activity increased! BONE HEALING FASTER!!
  higher proliferation and better differentiation (850 nm, Ozawa et al. 1998)
  higher osteopontin, and bone sialoprotein expression (632 nm, Stein et al. 2005)

- Oc cells: differentiation better!
  9.33, 27.99, 55.98, 93.30 J/cm^2
  TRAP(+) cells more in 9.33, 27.99, 55.98 J/cm^2
  Less TRAP (+) at 93.30 J/cm^2 compared to control
  more RANK, RANKL expression than control
  (810 nm, Aihara et al, 2006)

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From animal experiments

- Where do we start?
- Borrow the lessons from literature

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The Literature Review

-about LLLT and Tooth Movement in Japan

- In Kawasaki's study in 2000, diode 830 nm 100 mW laser applied for three spots with 3 min per site around the moving molars did increase moving rate up to 1.3 folds which effectively shortened the lag phase (Kawasaki and Shimizu 2000).
- From immunohistochemistry, number of osteoclasts at pressure site was 1.6 folds higher than control group at initial stage, and cells were more differentiated at tension side.

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The Literature Review

-about LLLT and Tooth Movement in Japan

- Similar study design by Yamagushi using 810 nm 100 mW applied every day for 7 days showed accelerated OTM as previously found (Yamaguchi, Hayashi et al. 2010). With more extended experimental duration up to 21 days, acceleration of OTM and decreased BMD were significant under similar exposure to LLLT (Yoshida, Yamaguchi et al. 2009).

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The Literature Review

-about LLLT and Tooth Movement in Japan

- In these two studies, more RANK/RANKL positive cells were noticed one or two days following laser exposure, more MMP-9, cathepsin K and intergrin on osteoclasts were found. Therefore, these data suggest more degradation of bone at pressure side upon LLLT.
- It also was found that although light emission diode may emit light with fixed wavelength, it is incoherent in nature and did not give similar increase of OTM rate in rats under the same total energy density.

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The Literature Review

-about LLLT and Tooth Movement in Brazil

- Habib used 790 nm 40 mW laser with total 20 Joule every other days in rats (Habib, Gama et al. 2010).
- He demonstrated significant increasing number of osteoclasts at compression side compared to the control group in histological analysis.
- However, the total movement rate did not reach statistical significance in another paper from this same group (Gama, Habib et al. 2010).

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The Literature Review

-about LLLT and Tooth Movement

- In Brazil

  780 nm 70 mW

  5.25 J/cm^2 increased

  but 35 J/cm^2 decreased.

Goulart et al.

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Amdt-Schultz Law states that for every substance, small doses stimulate, moderate doses inhibit, and large doses kill.

阿爾恩特-舒茲法則

- There is positive correlation between the dosage to its effect until reaching a threshold. Once beyond the threshold, higher dosage will not promote but only inhibits.
- The more, the better only until certain level!
- Once beyond that level, it is worse!

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Amdt-Schultz Law

- Diode laser with 780 nm, 70 mW every seven days on dogs for 63 days, 5.25 J/ cm^2 showed acceleration of OTM from day 0-day 21 but not with higher power density at 35J/ cm^2, which did inhibit the OTM from day 0-day 42 (Goulart, Nouer et al. 2006).
- Inhibition of OTM was also found by Seifi in rabbits with 606 nm 10 mW 9 Joule daily and 850nm 5 mW 3 joule daily (Seifi, Shafeei et al. 2007).

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Research Goal

- To determine efficacy of 970 nm diode laser in orthodontic treatment, including
  - facilitate tooth movement rate
  - reduce relapse rate after treatment

Acceleration of OTM Conclusion

- 970 nm low level can accelerate OTM by almost 2 folds
  - decrease bone volume
  - increase bone turnover rate
- With the same setting, low level laser can decrease relapse rate
  - increase bone formation in furcation area

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Briefing for Animal Experiments

- Either 810-830 nm , 780-790 nm , or 970 nm can all accelerate OTM.
- Even though those two studies without significant increasing of rate of OTM, obvious histological changes on LLLT sides were shown.
- Since these two studies measured directly between incisors and molars, this might add more measurement errors.
- More accurate results were obtained by measuring dental casts, micro-CT by using second molar as a reference point.

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Briefing for Animal Experiments

- The most striking inhibition of OTM came from the high power density at 35J/cm^2 which warrants caution
- However, since the small size of it oral cavity compared to the available hand piece, the energy density used was much higher than those at cell culture level in vitro.

  Cells: at 0.5-4 J/cm^2, 9.33 (+), 27.99 (+), 55.98 (+), 93.30(-) J/cm^2

  Rats: 7.5 J/mm^2 (-), 12.5 J/mm^2 (+), 150 J/mm^2 (+)

Briefing for Animal Experiments

- Surprisingly, there was no tissue damages reported throughout the literature. These variable results may arise from intervals of exposure.
- Once per month was not able to show its stimulation and this may lead to insignificant results on overall rate of OTM.
- On the contrary increased cell numbers and more vessels have been a common finding to show its biostimulatory effect in histological analysis.

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Clinical Trials on Patients

- A great deal of individual variations among our patients from clinical experiences
- Adopted split mouth design to avoid individual variations

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Clinical Trials on Patients

- Hard to compare
  - Different orthodontic appliances (minor)
  - mechanical design with different anchorage (minor)
  - Waiting period before retraction (minor)
  - methods of measurements (minor)
  - Using different laser and parameters of application (major)

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Clinical Trials on Patients

- From 2004 until now (Cruz, 2004), there are at least 7 papers found on PUBMED published regarding LLLT applied for accelerating canine or premolar retraction.
- Only one study from Limpanichkul et al (2006) did not show positive result.

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Clinical Trials on Patients

--Review papers--

- **Influence of Low-Level Laser Therapy on the Rate of Orthodontic Movement: A Literature Review**
  Torri S, Weber JB. Pontifícia Universidade Católica do Rio Grande do Sul (PUCRS), Porto Alegre, RS, Brazil
  Photomed Laser Surg. 2013 Sep;31(9):411-21
  include: 3 clinical studies, 6 rats studies, 2 dogs studies
- **Efficacy of low-level laser therapy for accelerating tooth movement during orthodontic treatment: a systematic review and meta-analysis**
  M. K. Ge, W. L. He, J. Chen, C. Wen, X. Yin, Z. A. Hu, Z. P. Liu and S. J. Zou From State Key Laboratory of Oral Diseases, Department of Orthodontics, **West China** School of Stomatology, **Sichuan University**,
  Published online: 20 February 2014 **Lasers in Medical Science**
  10.1007/s10103-014-1538-z
  Include: 6 RCTs and 3 quasi-RCTs (nonrandomization allocation)-1 Japan separator study-3 China regional articles=5 RCTs

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Efficacy of low-level laser therapy for accelerating tooth movement during orthodontic treatment: a systematic review and meta-analysis

M. K. Ge, W. L. He, J. Chen, C. Wen, X. Yin, Z. A. Hu, Z. P. Liu and S. J. Zou
2014 **Lasers in Medical Science**

- This systematic review and meta-analysis demonstrated that LLLT might speed up the tooth movement in orthodontic treatment.
- The results showed that the LLLT could accelerate OTM in 7 days (mean difference 0.19 mm, p=0.03) and 2 months (mean difference 1.08 mm, p=0.02).

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- It seemed that this accelerating effect showed no statistical difference between upper and lower jaws.
- No obvious adverse effect was detected in this review.

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- A relatively lower energy density (2.5, 5, and 8 J/cm2) was seemingly more effective than 20 J/cm2, 25 J/cm2, and even higher ones, although the optimal dose remained undetermined.

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The unresolved but most important issue--

- One important and difficult issue for LLLT is to define the optimal dose or energy density in orthodontic treatment.

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7th RCT-premolar retraction + laser probe into pocket
6 applications in 45 days,
RANKL/OPG in GCF, pain reduction

Dominguez, 2013 N=10 12-16 y/o in Spain	Hilgers bracket 18-slot Nance holding arch	Extract upper second premolar 14 days before treatment Working wire: 016 SS sectional wire between first premolar to first molar NiTi spring to retract first premolars	670 nm, 200mW continuous wave, 6.37 W/cm^2, Total 9 min, 108J Days 0, 1, 2, 3, 4, 7 At distal, buccal, lingual side as a periodontal probe	Impression on days 0, 2, 7, 30, 45 3.73±1.08 mm (laser) vs. 2.71±0.90 mm (control) after 45 days

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Laser parameters high energy density

Study ID	Type of laser	Wavelength/energy density	Power output/total time per tooth(s)	Frequency of laser treatment
Limpanichkul 2006 Thailand	GaAlAs semiconductor diode laser	860 nm	100 mW	Days 1, 2, 3 of every month
		25 J/cm^2	184 s/tooth	For 3 months
Gui 2008[a] China	GaAs semiconductor laser	650 nm	20 mW	Once a week
		25 J/cm^2	1,200 s	For 4 weeks
Doshi-Mehta 2012[a] India	GaAlAs semiconductor diode laser	810 nm	80 mW	Days 0, 3, 7, 14 of every 15 days
		20 J/cm^2	100 s/tooth	For 4.5 months
Dominquez 2013 Spain		670 nm ?	108J, 9 min/tooth	For 45 days

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Laser parameters low energy density

Youssef 2008[b] Syria	GaAlAs semiconductor diode laser	809 nm	100 mW	Days 0, 3, 7, 14 of every stage(3 weeks)
		8 J/cm^2	80 s/tooth	For 3 stages
Cruz 2004[b] Brazil	GaAlAs semiconductor diode laser	780 nm	20 mW	Days 0, 3, 7, 14 of each month
		5 J/cm^2	100 s/tooth	For 2 months
Wang 2007[b] China	GaAlAs semiconductor diode laser	780 nm	20 mW	Once a week
		5 J/cm^2	100 s/tooth	For 8 weeks
Sousa 2011[b] Brazil	GaAlAs semiconductor diode laser	780 nm	20 mW	Days 0, 3, 7 of each month
		5 J/cm^2	100 s/tooth	For 4 months
Xu 2006 China	He–Ne laser with CO_2 laser assisted	632 nm 2.5 J/cm^2	20 mW	Days 1, 2, 3, 4, 5 in 21 days
Fujiyama 2008 Japan	CO_2 laser, 5 pulses per 1,000 s	Not specified	2 W	Once (immediately after separation)

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Clinical Trials under Taking at NTUH
weekly application of LLLT

- Canine retraction
- Molar uprighting
- Pain reduction
- Retention

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Clinical Trials under Taking at NTUH
weekly application of LLLT

- Canine retraction—until completing canine retraction; split mouth study
- Molar uprighting-different individual
- Pain reduction—one side after AW changes
- Retention--two months before D&D: 4 application of LLLT at one side, holding for one month, then D&D

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Clinical Trials under Taking at NTUH
weekly application of LLLT

- IRB/Clinical Trial Registration
- LASER purchase
- Intra-oral scanner

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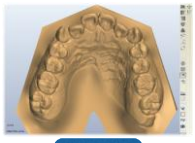
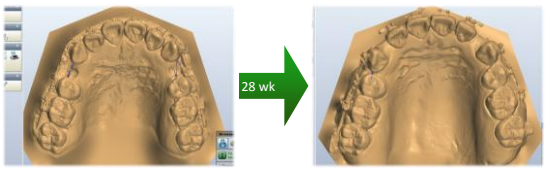
A-03
- experimental side: L't

	103.04.25	103.11.06	Rate (mm/wk)
R't	6.39 mm	0.81 mm	0.20
L't	6.82 mm	0.00 mm	0.24



Pre-treatment



103.04.25 103.11.06

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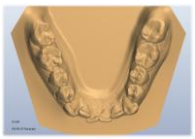
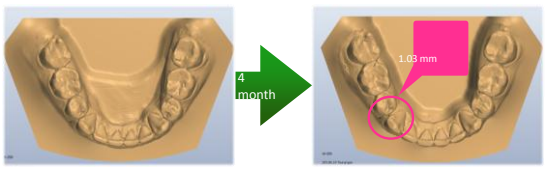
D-01
- experimental side: L't



Pre-treatment



103.06.10 103.10.09

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Take home message: YES!!!
From well controlled split-mouth study

- Which type of laser?
- When? Timing, frequency, duration
- Cost and benefit

Advantage
- Not invasive, multiple application, less chair time
- Selective sites of activation
- Control by dentists
- Possible control pain simultaneously (add-on value)

Disadvantage
- Expense of equipment
- Frequent office visit (due to the expense of LASER); More applicable for high density population in city

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Which one matters the most?

- Total energy or power density? Energy/cell
- The minimal frequency to stimulate?

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Advantage of LLLT compared to other methods for accelerating OTM

Booster the biological bone turnover in a non-invasive way (no bleeding, no pain)

- Especially for those slow movers!
- Any time during treatment period repetitively!
- At selective sites of activation, not the whole arch!
- Simultaneous pain reduction?

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