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

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

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

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

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.
They focus on most ablation of tissues and only some healing for ulcers and herpes lesions. The effects on OTM are not mentioned!

**LLLT in all medical fields**

- power density usually at 1 mW-5mW/cm².
- 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.

**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.

**Possible roles of mitochondria 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.

**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
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, alodenedia and trigeminal neuralgia
- facilitating treatment treating bisphosphonate related osteonecrosis of jaws (BRONJ)

LLLTT to Accelerate OTM?

- Cellular levels
- Animal levels
- Patient levels
- Is it effective?
- Is it safe?

Fundamentals of bone biology

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

Dosage of LLLT

- 1) Radiance: i.e., power density; power in unit area; watt/cm²
- 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/cm²

At Cellular Level

- In vivo experiments were carried at 0.5-4 J/cm², 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/cm²
  TRAP(+) cells more in 9.33, 27.99, 55.98 J/cm²
  Less TRAP (+) at 93.30 J/cm² compared to control
  more RANK, RANKL expression than control
  (810 nm, Alhara et al, 2006)
From animal experiments

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

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.

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).

• 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.

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).
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!

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

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.

• The most striking inhibition of OTM came from the high power density at 35J/cm² 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/cm², 9.33 (+), 27.99 (+), 55.98 (+), 93.30(-) J/cm²
  Rats: 7.5 J/mm² (-), 12.5 J/mm² (+), 150 J/mm² (+)
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.

Clinical Trials on Patients

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

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)

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. Pontificia Universidade Cato´lica 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
  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

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

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

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.

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

<table>
<thead>
<tr>
<th>Study ID</th>
<th>Type of laser</th>
<th>Wavelength/energy density</th>
<th>Power output/total time per tooth(s)</th>
<th>Frequency of laser treatment</th>
<th>Laser parameters low energy density</th>
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<tbody>
<tr>
<td>Limpanichkul 2006 Thailand</td>
<td>GaAs semiconductor diode laser</td>
<td>860 nm</td>
<td>100 mW</td>
<td>Days 1, 2, 3 of every month for 3 months</td>
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<td>Gui 2008 China</td>
<td>GaAs semiconductor laser</td>
<td>650 nm</td>
<td>20 mW</td>
<td>Once a week for 4 weeks</td>
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<tr>
<td>Doshi-Mehta 2012 India</td>
<td>GaAs semiconductor diode laser</td>
<td>810 nm</td>
<td>80 mW</td>
<td>Days 0, 3, 7, 14 of every 15 days</td>
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<tr>
<td>Dominquez 2013 Spain</td>
<td>670 nm</td>
<td>?</td>
<td>108J, 9 min/tooth for 45 days</td>
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<td>Youssef 2008</td>
<td>GaAs semiconductor diode laser</td>
<td>809 nm</td>
<td>100 mW</td>
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<td>Cruz 2004 Brazil</td>
<td>GaAs semiconductor diode laser</td>
<td>780 nm</td>
<td>5 J/cm²</td>
<td>100 s/tooth for 2 months</td>
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<td>Wang 2007 China</td>
<td>GaAs semiconductor diode laser</td>
<td>780 nm</td>
<td>5 J/cm²</td>
<td>100 s/tooth for 8 weeks</td>
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<td>Sousa 2011 Brazil</td>
<td>GaAs semiconductor diode laser</td>
<td>780 nm</td>
<td>5 J/cm²</td>
<td>100 s/tooth for 4 months</td>
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<tr>
<td>Xu 2006 China</td>
<td>He-Ne laser and CO₂ laser assisted</td>
<td>632 nm</td>
<td>20 mW</td>
<td>Days 1, 2, 3, 4, 5 in 21 days</td>
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<td>Fujiyama 2008 Japan</td>
<td>CO₂ laser, 5 pulses per 1,000 s</td>
<td>Not specified</td>
<td>2 W</td>
<td>Once (immediately after separation)</td>
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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.

Laser parameters high energy density

- Doshi-Mehta 2012 India
- Dominquez 2013 Spain
- Limpanichkul 2006 Thailand
Clinical Trials under Taking at NTUH
weekly application of LLLT

• Canine retraction
• Molar uprighting
• Pain reduction
• Retention

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

Clinical Trials under Taking at NTUH
weekly application of LLLT

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

A-03

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<td>R’t</td>
<td>6.39 mm</td>
<td>0.81 mm</td>
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<tr>
<td>L’t</td>
<td>6.82 mm</td>
<td>0.00 mm</td>
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Rate (mm/wk)

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
Which one matters the most?

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

**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?**