Innovations with lasers could lead regenerative dentistry

Praveen R. Arany

With this year, 2015, being designated as the year of light, the acknowledgment for the key role of light in multiple areas of our very existence and more specifically, in areas of human health are being widely promulgated.1 Many references to the beneficial effects of light and specifically sunlight are relentless in the literature across ancient civilisations.2 Notably, the ability of concentrated light radiation in the management of lupus vulgaris by Niels Helyg Finsen received the Nobel Prize in Medicine and Physiology in 1903.3 The all-pervasive nature of infrared and near-infrared optoelectronics in our current society is readily evident such as the simplest supermarket laser scanners and optical communications to precision medical lasers and more recent laser weapon systems. This is also perhaps best highlighted by this year’s Nobel Prize in Physics to the inventors of the blue light emitting diodes (LEDs), a simple invention with profound impact on our current society.3

Clinical laser application

Dentistry has historically been a leading clinical specialty in adoption of new technologies. Light has been a central part of clinical dentistry through innovations of operating lights and fibre optic illuminations to light cured restorations and more recently, optical imaging. Although lasers were commercially available since 1960’s, the first dental laser for hard tissue applications was approved by the US FDA in 1987. Adoption for high power soft tissue applications has always been popular in many medical fields such as surgery, oncology, dermatology and ophthalmology.

First discoveries

Following the invention of this exciting new tool, early biological concerns focused around the safety of this new device with natural comparisons being drawn to ionizing forms of electromagnetic radiation. Among the early pioneering studies, Anderson and Matson reported a peculiar phenomenon—high doses destroyed tissue in a precise and predictable manner but very low doses produced a startling improvement in wound healing and promoted hair growth.4–7 This was a surprising discovery on many accounts.

While high energy electromagnetic radiation, such as Gamma, X-rays and Ultraviolet, were able to achieve significant linear energy transfer generating biological damage (nuclear acid strand breaks), the effects of visible (and later infra-red) lasers did not appear to fall entirely post treatment and at 14 days.19 The increase at 14 days correlated well with an increase in monocyte-macrophage influx, well-known cellular sources of TGF-1. We next looked into the increased early expression of active TGF-1 in these wounds. TGF-1 secretion resulted in a change in its conformation, to a latent TGF-1 complex that was shown to have a pivotal role in dentin physiology.16–18 We noted the ability of low power lasers to promote dentin regeneration using human dental stem cells. To validate these observations, rodent pre-odontoblasts (MDPC-25) cells grown in a polymeric scaffold, simulating a 3-D niche were treated with low power lasers.

Laser treatments were able to induce dentin differentiation as evidenced by increased dentin-specific mineralization and tissue remodelling. To confirm the role of TGF-β in vivo, transgenic mice with lack of TGF-β receptor in all cells capable of inducing dentin (utilizing a Dentin Nailsphosphoprotein specific transgene) were generated. Experiments in these mice did not demonstrate any significant dentin induction following laser treatment validating the critical role of TGF-β activation in mediating its effects.

Previous studies have shown the therapeutic benefits of supplementing exogenous (recombinant) TGF-β for reparative...
dentin, this study suggests the use of low power lasers can activate andodentous latent TGF-β1 present naturally in the pulp-dentin complex to drive differentiation of resident dental stem cells (Fig. 2). Thus, this therapy can utilise the inherent repair-regenerative responses naturally present in native tissues.

Clinical Applications of Laser-Dentin induction

These observations have potential clinical implications where dentin would need to be therapeutically generated. The two directly relevant clinical scenarios are for pulp capping following deep carious lesions and for dentin desensitisation. In the former case, removal of decayed or damaged tooth structure approximating the pulp (close to or clear exposure) that requires the use of pulp capping agents (such as Calcium hydroxide) could be potentially replaced with low power laser treatments.

In the second scenario, the use of low power laser treatments on exposed dentinal tubules could potentially generate an intrinsic dentin barrier that would relieve tooth sensitivity. This would be more effective than our current approach to extrinsically occlude exposed tubules modes.

The two major limitations of the current study were that we noted calcifications interspersed throughout the pulp chamber, spatially distinct from the laser-biological tissue interface. We believe this is perhaps a combination of the inherent near-infrared laser wavelength that readily permeates throughout biological tissue as well as the soluble nature of the activated molecules. This could be potentially addressed by better optical focusing techniques and use of specific reagents that absorb the radiant energy and spatially restrict the biological interphase.

A second limitation in this study was the observation that laser-generated dentin was a tertiary or reparative form that lacks pristine tubular structure. It appears that additional cues both biophysical (architecture) and biochemical (soluble, organisational) are necessary to promote morphodifferentiation of the newly induced dentin.

In attempts to further explore these molecular mechanisms, we have more recently extended developed a polymeric scaffold system with precise morphogen fields. Using this model, we were able to extend our observations with dental stem cells and laser-activated TGF-β1 mediated dentin differentiation to mesenchymal stem cells suggesting this approach could have significant potential with other stem cell types as well.

Conclusion

Both ROS and TGF-β are central biological mediators in a wide range of biological responses. The ability to selectively activate them in a spatiotemporally defined manner in vivo using low power lasers provides a significant clinical tool for various therapeutic interventions.

Questions on precise wavelengths, clinical protocol (delivery and dose ranges) and context of the pathophysiological response are all critical issues that need to be explored rigorously to enable further effective clinical translation of this therapy.

Further, the ability to effectively move this therapy into mainstream clinical dentistry will require more basic research, development of robust clinical standards and education at various levels (basic dental training and continuing education) (Fig. 3).

In the current era of personalised medicine and strategies to utilise sophisticated technologies and pharmaceuticals to individualise health care, the significant promise of lasers in clinical dentistry may indeed be the leading, pivotal technology that ushers in the new era of regenerative dentistry.

Acknowledgement

This work was supported by the intramural research program of the National Institute of Dental and Craniofacial Research, National Institutes of the Health.

Editorial note: A list of references is available from the publisher.