Laser-Assisted Periodontal Regeneration and Human Histology

This article presents 2 case studies that demonstrate the human histological evidence required to make the claim of true periodontal regeneration using the laser-assisted regeneration (LAR) protocol.

Scientific evidence to support a treatment modality is the hallmark of the ethical practicing clinician. Human histology is the highest form of scientific analysis for proving the truth of a complex healing event such as periodontal regeneration. To date, hundreds of positive patient outcomes using the laser-assisted regeneration (LAR) protocol have been published by various authors in numerous peer-reviewed and non-peer-reviewed publications and in 2 International Association for Dental Research abstracts.1-11

Periodontal regeneration on a previously diseased tooth root surface is a unique, challenging, and elusive healing event to obtain in humans.12-14 True periodontal regeneration requires the 3 original components of the periodontal apparatus to arise anew and eventually form into new cementum, a new periodontal ligament (Sharpey's fibers), and new alveolar bone.15 The health of the attachment apparatus can be assessed by measuring the clinical attachment level (CAL) (the distance from the cemento-enamel junction to the tip of a periodontal probe during periodontal diagnostic probing).

Typically, the realization of complete regeneration of the 3 tissues of the periodontal attachment apparatus has required extensive surgical site preparation to allow for instrumentation sufficient for the addition of exogenous materials such as growth factors, bone grafts, and biologics. Proving a claim for true periodontal regeneration in humans requires that histologic, microscopic analysis be conducted in living human beings.

In this article, 2 examples from 2 different human histology studies are presented—one for a single-rooted tooth5 and the other for a molar tooth.8 The studies were conducted by 2 separate principal investigators that were included in 2 separate submissions to the US Food and Drug Administration (FDA) over a period of 12 years. As a result of these submissions, the FDA issued a clearance (March 2016) for the claim of “true periodontal regeneration” using the PerioLase MVP-7 pulsed Nd:YAG Dental Laser System (Millennium Dental Technologies) with the LAR protocol. These cases included clinical assessments, radiographic evidence, microcomputed tomography (microCT), light microscopy, and backscatter scanning electron microscopy together with a human histological evaluation of 3 months duration in one study5 and 9 months duration in the more recent study.8

The objective of this article is to demonstrate the histological evidence required to make the claim of true periodontal regeneration, based on the FDA clearance noted above.

Evidence-Based Dentistry

Evidence-based dentistry (EBD) has become a buzzword in certain arenas of academia and organized dentistry. Not all who use the term are defining EBD the same way. Some define EBD in ways that fit their personal perspectives, such as only what the literature states in a systematic review, but that is not EBD. EBD integrates 3 important components:

1. the most current, clinically relevant scientific evidence;
2. a dentist’s clinical expertise; and
3. clinical judgment.
Periodontitis is an infectious disease that progressively destroys the alveolar bone, periodontal ligament (PDL), and root cementum that attach the teeth to the bone. Destruction of this attachment apparatus results in the loss of teeth. New attachment may be created in normal anatomic relationships and function.15

Kao et al14 point out that various approaches have been developed in attempts to achieve periodontal regeneration, among them the use of a demineralized freeze-dried bone allograft, guided tissue regeneration with the use of barrier membranes, the application of biomimetic agents such as enamel matrix derivative, and the LAR technique. Of these, the laser protocol is the least invasive.13

The AAP’s Position Paper on Periodontal Regeneration (2005)16 defines terms relevant to this discussion:

- **New attachment** is defined as the union of connective tissue or epithelium with a root surface that has been deprived of its original attachment apparatus. This new attachment may be an epithelial adhesion and/or a connective tissue adaptation or attachment and may include new cementum to which periodontal ligament fibers are attached.

- **Bone fill** is defined as the clinical restoration of bone tissue in a treated periodontal defect. Bone fill does not address the presence or absence of histologic evidence of a new connective tissue attachment or the formation of a new periodontal ligament.

- **Regeneration** refers to the reproduction or reconstitution of a lost or injured part, in contrast to repair, which describes the healing of a wound by tissue that does not fully restore the architecture or function of the part.

- **Periodontal regeneration** is defined histologically as regeneration of the tooth’s supporting tissues, including (1) alveolar bone, (2) the periodontal ligament, and (3) cementum over a previously diseased root surface.

The ultimate aim of periodontal regeneration techniques is to induce or guide healing to regenerate the morphology back to its original configuration. In order to evaluate a regeneration technique experimentally, a notch is made on the root surface at the bottom of a periodontal pocket to provide a histologic landmark for the apical extent of the destruction and determination of subsequent coronal periodontal wound healing. True periodontal regeneration is then defined by histologic evidence of new bone, a periodontal ligament, and cementum appearing above the notch on a previously diseased root surface.17

Yukna et al15 wrote in their peer-reviewed and published manuscript:

*The 1996 World Workshop in Periodontics established specific histologic criteria for proof of regeneration. Experimental teeth must have loss of connective tissue attachment (CTA) and alveolar bone*
(AB) associated with periodontitis. In addition, subgingival and/or subcrestal calculus must be present at the time of surgery so that a [bur] notch can be made into the root at the apical extent of calculus (into the calculus and beyond its apical boundaries). Proof of new attachment is demonstrated by new cementum (CEM) and CTA; and regeneration is evidenced by the presence of new CEM, PDL, and AB coronal to the apical extent of the notch.

According to Yukna et al, “The three most central 200-μm serial step sections were blindly and randomly evaluated for the nature of the healed tissues—specifically the presence and length of new CEM, new CTA, new AB, and healed junctional epithelium relative to the apical extent of the calculus notch.”

LAR Protocol
A near-infrared, variable pulsed dental laser specifically designed and optimized for the LAR protocol was utilized in both studies (PerioLase MVP 7 pulsed Nd:YAG Dental Laser System). In the LAR protocol, no exogenous materials of any sort are used. The true periodontal regeneration achieved with LAR is accomplished by using the patient’s own blood proteins that contain the stem cells, fibroblasts, native growth factors, and blood constituents. The blood is thermally affected in LAR in such a manner that the regenerative factors are trapped within a red thrombus that is formed using scientifically determined algorithms of optimal laser operating parameters (Figure 1). In LAR, there is a lack of any wide surgical access outside of the bony housing, a lack of deep dissection into the vestibule or across the palate, and a lack of extensive vertical releasing incisions. The protocol uses a minimally invasive periodontal flap to enable access under the perioseum and directly into bone for ostectomy and/or ostotomy. The soft tissues are thereby easily approximated and stabilized without the need to suture with tension to adapt the margins of the flaps together. It is essential to provide a sealed system of unviolated and unmoleseted external periodontal tissues for the regenerative growth factors to be contained within for protection of the regenerative cells and process.

CASE 1
Human Canine Histological Study
Figure 2 demonstrates the histological evidence of periodontal regeneration for tooth No. 6 using the LAR protocol.5

From the histological data, clinicians can extrapolate from scientific research on the LAR protocol to clinical expectations when following the strict LAR protocol and treatment algorithms.

SUMMARY
The restoration of destroyed periodontium and re-creation of its normal anatomic relationship and function is the ultimate aim of periodontal regeneration methodologies. One particular well-defined LAR technique has been shown to regenerate the attachment apparatus (new cementum, periodontal ligament, and alveolar bone) on a previously diseased root surface. Published histological evidence from human studies provides the scientific authentication of true periodontal regeneration achieved through the minimally invasive surgical LAR protocol. These investigations confirm the clinical findings and radiographic evidence reported by clinicians who...
The two techniques with the most guided tissue regeneration (GTR) are
migration.

ing a new level of attachment to the new cementum, establish-
to the root dentin (D), with
cementum (NC) is adjacent (NB), and a thick layer of new
There is an island of new bone 9 months following treatment.
of the supracrestal environment 6
Figure 15. Inset 3 (from Figure 6) shows continued regeneration of the supracrestal environment 9 months following treatment. There is an island of new bone (NB), and a thick layer of new cementum (NC) is adjacent to the root dentin (D), with interconnecting fibers of the PDL. Sharper’s fibers perpendicular to the new cementum, establishing a new level of attachment and presenting a barrier to JEP migration.

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Footnotes

1. “Currently, osseous grafting and guided tissue regeneration (GTR) are the two techniques with the most histologic documentation of periodontal regeneration. Other regenerative therapies have also provided a promising potential for significantly improving clinical parameters and demonstrating substantial ‘fill’ of treated defects. However, only limited histologic evidence of true regeneration has been demonstrated with the majority of these therapies.”

2. “Regeneration refers to the reproduction or reconstitution [restoration] of a lost or injured part, in contrast to repair, which describes healing of a wound by tissue that does not fully restore the architecture or the function of the original part. Periodontal regeneration is defined histologically as regeneration of the tooth’s supporting tissues, including alveolar bone, periodontal ligament, and cementum over a previously diseased root surface. New attachment is defined as the union of connective tissue or epithelium with a root surface that has been deprived of its original attachment apparatus. This new attachment may be epithelial adhesion and/or connective tissue adaptation or attachment and may include new cementum. It is to be distinguished from reattachment, which describes the reunion of epithelial and connective tissue with a root surface. Bone fill is defined as the clinical restoration of bone tissue in a treated periodontal defect. Bone fill does not address the presence or absence of histologic evidence of new connective tissue attachment or the formation of new periodontal ligament.”

3. Kao et al14 is the most recent of a long series of systematic reviews of published methods to achieve periodontal regeneration.18-27 Current approaches include a demineralized freeze-dried bone allograft (DFDBA), guided tissue regeneration (GTR), bone fill with enamel matrix derivative (EMD), recombinant human platelet-derived growth factor BB (rhPDGF-BB), and open flap debridement (OFD). Kao et al14 have included a new category of regenerative approaches, termed laser-assisted regeneration (LAR), which is specifically identified by the authors as the Millennium Dental Technologies’ LANAP protocol that uses the Perio-Lase MVP-7 pulsed Nd:YAG Dental Laser System. Based on the review of 2 peer-reviewed studies of human histology,5,8 following LAR, Kao et al14 conclude, “Using the Nd:YAG laser with this procedure, periodontal regeneration is achievable on a previously diseased root surface.”

4. “This technique is intriguing in that it is another approach to minimally invasive surgical therapies as reviewed by Cortellini.18 A minimally invasive surgical approach may offer advantages in regeneration of defects in the esthetic zone in which minimal soft tissue change is required. Additionally, because of the minimally invasive nature and expendable surgical materials required, this approach may be appropriate for multiple defects as a first line of management.”

5. Regarding other laser devices, one cannot extrapolate regenerative findings to other laser devices or treatments that have no defined protocols, operating parameters, or treatment algorithms and have no documentation of healing events from human histologic studies.
1. What are the components of the periodontal attachment apparatus?
   a. Fibroblasts, junctional epithelium, and lamina propria.
   b. Cementum, periodontal ligament, and alveolar bone.
   c. Sharpey’s fibers, bone marrow, and dentin.
   d. Odontoblasts, gingival epithelium, and enamel.

2. What is the main function of cementum?
   a. To provide anchorage for periodontal ligament fibers.
   b. To protect the predentin from periodontopathogens.
   c. To generate fibroblasts for collagen bundles.
   d. To remodel alveolar bone through an osteoclastic process.

3. Which of the following fiber types insert into alveolar bone and cementum?
   a. Von Korff fibers.
   b. Alveologingival fibers.
   c. Circular fibers.
   d. Sharpey’s fibers.

4. Which of the following regenerative procedures is the least invasive?
   a. A demineralized freeze-dried bone allograft.
   b. A guided tissue regeneration via membranes.
   c. A laser-assisted new attachment procedure.
   d. The application of an enamel matrix derivative.

5. What is the definition of “clinical attachment level”?
   a. The measurement from the crest of the gingival margin to the base of the pocket.
   b. The distance between the apical extent of the calculus notch and the basement membrane.
   c. The measurement from the dentoenamel junction to the marginal ridge.
   d. The distance from the cementoenamel junction to the tip of the periodontal probe.

6. What is the rationale for performing decortication to treat intrabony defects?
   a. To enhance the bone-healing process by increasing revascularization.
   b. To facilitate bone remodeling by conventional instrumentation.
   c. To establish histological landmarks to evaluate new attachments.
   d. To remove overlying necrotic osseous tissue and lipopolysaccharides.

7. What is the primary justification for performing occlusal adjustment during a laser-assisted regeneration procedure?
   a. To minimize patient discomfort during the healing event.
   b. To ensure an optimum aesthetic result post-healing.
   c. To reduce traumatic forces that cause the breakdown of supporting structures.
   d. To provide unobstructed excursive glides of the mandible.

8. Rete ridges strengthen the attachment of epithelium to which structure(s)?
   a. Tooth cementum.
   b. Connective tissue.
   c. Salivary glands.
   d. The trigeminal nerve.

9. In a human histological study, what is the purpose of placing a calculus notch on a root surface?
   a. It inhibits the apical migration of long junctional epithelium.
   b. It enables the assessment of subsequent periodontal wound healing coronally.
   c. It releases the tension of circumferential periodontal fibers for greater access.
   d. It increases the surface area for a stronger retention of splints in mobile teeth.

10. In periodontal tissues, how is regeneration differentiated from repair?
    a. Regeneration re-adapts tissue to periodontal defects.
    b. Repair re-establishes the function of the injured tissue.
    c. Regeneration restores lost or diminished periodontal tissue.
    d. Repair restores the architecture of original tissue.

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