Beyond the Ligament: A Whole-Bone Periodontal View of Dentofacial Orthopedics and Falsification of Universal Alveolar Immutability

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When a theoretical basis for manifestly successful clinical outcomes cannot be fortified by traditional orthodontic tooth movement (OTM) biology that focuses solely on the periodontal ligament as the operant organ, a new hypothesis should be built on the old concepts by synthesizing new biological data with it. This article presents a modest synthesis of contemporary theories in cell biology to explain ostensible osteogenic activity and alveolar phenotype alterations by ultra-low orthopedic force from an alveolar development appliance (ADA). Histological appearance of biopsy specimens demonstrate a "reactive" woven bone pattern, dramatically illustrated under polarized light, where the alveolar development appliance puts labial forces on the palatal alveolus via acrylic panels and 300 *g* of force induced by coiled nickel titanium springs. "Internal control" biopsy specimens taken from nontreated alveoli show normal lamellar pattern in histological sections. The behavior of the bone cannot be explained totally with a periodontal pressure-tension model. Molecular biological concepts and the Utah Paradigm of Bone Physiology are recruited to explain how ultra-light forces applied to the palatal alveolus might stimulate "compensatory periosteal apposition" on the labial alveolus, thus developing a new alveolar phenotype through bony developmental "drift." (Semin Orthod 2008;14:246-259.) © *2008 Published by Elsevier Inc.*

When a theoretical basis for manifestly successful clinical outcomes cannot be fortified by traditional orthodontic tooth movement (OTM) biology (that focuses solely on the periodontal ligament as the operant organ) a new hypothesis should be built on the old. It is forces acting beyond the ligament that may be significant determinants of the alveolus and the consequent dentofacial form, which lives, thrives, and dies by the grace of dental root positions.[1]

Specifically, an osteogenic threshold of ~1500 to 3000 microstrain according to Frost[2] and Jee and Li[3] may stimulate appositional bone modeling, reflecting the morphogenetic threshold range of therapeutic "optimal" force that elicits what should be called an "optimal response." It is this concept that Burch[4] paraphrasing Reitan alluded to with their term "compensatory periosteal apposition."

Therefore, at the risk of overstating the theory of "alveolus development," this article presents a modest synthesis of contemporary theories in cell biology to explain ostensible osteogenic activity and alveolar phenotype alterations by ultra-low orthopedic force from an alveolar development appliance (ADA).

Dentofacial orthopedic physiology of the alveolus does not deny the relevance of peri-

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odontal ligament phenomena but merely goes beyond the ligament to analyze the alveolar response to orthopedic force from a "whole bone" perspective. This whole bone—or "all-bone" according to Melsen[5]—paradigm is an important complement to the classic pressure-tension model because it lends a consistency with medical orthopedic and contemporary osteology literature. As Baumrind[6] has proposed in the past, the periodontal ligament is best characterized, not as a pressure-tension sling, but rather as a contained viscoelastic gel where forces are distributed equally in all directions, and this has some merit for bone as well.

A clear contrast is made, however, among rapid palatal expansion (RPE) of the maxilla, orthodontic dental arch expansion and orthopedic development of the bony alveolus with direct continuous modulated force application. If wound healing recapitulates regional ontogeny, a molecular level event, then tissue may be engineered in a similar manner whether the wound is surgical or simply microfracture "healing" of the alveolar osteon (Haversian system) from excessive force (eg, $>3000\ \mu E$ according to Frost).

Thus, the alveolus is proposed herein as a separate ontogenic entity or "organ," capable of a singularly active biological response to loading, irrespective of the subjacent skeleton (maxilla and mandibular corpus) or the subsumed dental matrix. In prior publications the term "maxillary expansion" has often been used in all three contexts without clear differentiation.[7] This is unfortunate yet ubiquitous in the literature, and it would be most fortunate indeed for students and other neophytes in craniofacial orthopedics if more nuanced distinctions could be articulated. The concepts herein discussed are not totally new. Melsen spoke eloquently of them in her discussion of alveolar bone physiology, citing literature as old as 20 to 40 years ago,[8,9] which has been echoed in modern tissue engineering dialogues as late as 2006.[10]

The Mechanobiology of the Alveolus

A novel "bottom-up" approach has evolved from biomedical engineering and it is wise to review the perspectives of sister sciences before we pronounce certitude on any field of natural scholarship. In this regard, van der Meulen and Huskies' definition of "mechanobiology" is interesting.[11] In a defining article they propose a different approach for studying the effects of force on tissue and human cells.

Applied to the dentofacial orthopedic realm, mechanobiology proffers the integration of these sciences into a kind of "new biology" for the orthodontic specialty. As old as it is new, this new biology is articulated well within the intelligent and compelling perspectives posited by Singh's spatial matrix hypothesis,[12] which point out, through the use of finite element analysis, that the tissue constantly regresses to homeostasis.

Specifically, mechanobiology studies most fundamentally how bone is regulated by signals to cells generated by variable degrees and directions of loading. The questions that mechanobiology investigates are most compatible with constructs defined by Frost and Jee in the activity of bone's basic multicellular unit (BMU). In a phrase, mechanobiology picks up, in a traditional reductionist progression, where Frost's tissue-level nephron equivalent left off.

Case Examples

Case examples and histological data demonstrated are not intended to prove universality of a "whole bone" thesis, but rather the contrary, namely building on a rich theoretical heritage,[13,14] and medical concepts of osteogenesis,[15,16] it seeks to falsify presumptive concepts of universal alveolar immutability.[17]

Clinical Example #1: Patient E.R.

A noncompliant 18-year-old Hispanic-American male presented with hemorrhagic hyperplastic gingivitis and incipient periodontitis after a protracted period of inadequate oral hygiene. Approximately 15 months earlier a fixed "alveolar development appliance" (ADA; Max 2000 DynaFlex Orthodontic Laboratory, St. Louis, MO) was placed to treat a posterior cross bite as the anterior arch length deficiency was addressed by an 0.018-inch nickel titanium round wire in labial 0.022-inch slot brackets. This archwire was replaced with a 0.018-inch stainless steel archwire, but no activation was made in the anterior or posterior sextants. The ADA was not periodically activated after insertion because it is self-activating

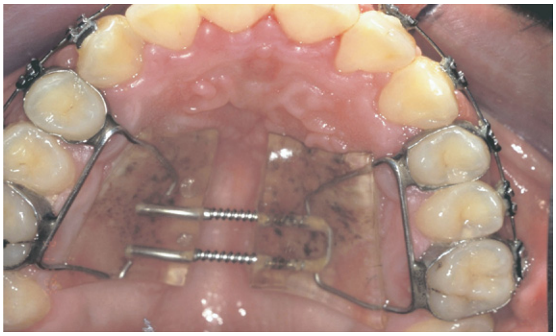


Figure 1. Max 2000, an alveolar development appliance (ADA) applied ultra-light pressure to the palatal alveolus. (Orthodontist: Neal C. Murphy, CWRU, UCLA; Max 2000® is a registered trademark of Dr. Michael O. Williams, Gulfport, MS.) (Color version of figure is available online.)

and self-limiting. Two transverse nickel titanium springs, each embedded in and connecting separate acrylic panels, deliver 150 *g* apiece for a total appliance force of 300 g (Fig 1). The bands on first molars and first bicuspids are for retention only. The active force solely lies on the palatal alveolus. No archwire adjustment or palatal appliance adjustments were made for 1 year.

Figure 2. (A and B) Case #1 E.R. Periodontal surgery reveals buccal bone where, conjecturally, palatal alveolus forces were transferred to buccal cortical plate, flexing the bone to stimulate osteogenesis in areas of periosteal compression. Note marked dehiscence where labial archwire "pulled" teeth beyond phenotypic range. (Color version of figure is available online.)

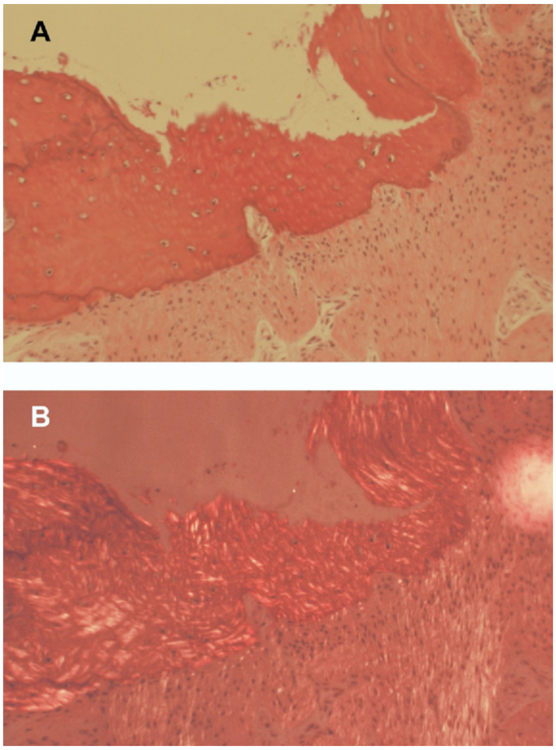
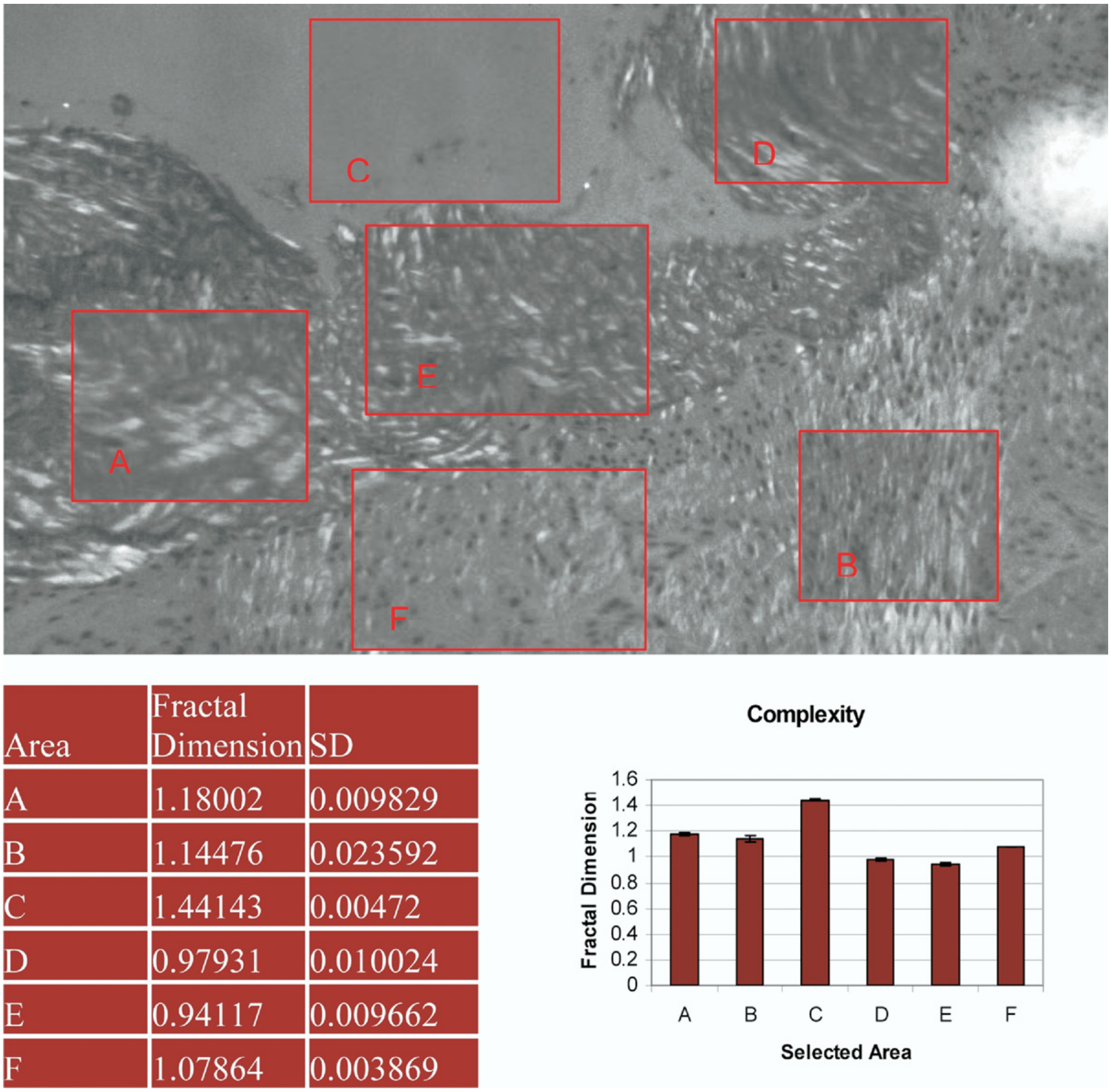


Figure 3. (A; top) Routine hematoxylin and eosin histological section at buccal aspect of tooth #5, labial to Max 2000 palatal alveolus development appliance. Note absence of a "lamellar" pattern that is characteristic of mature bone. Panel B (bottom) is a polarized light section of specimen. Note "woven bone" pattern characteristic of immature bone. (Color version of figure is available online.)

Fifteen months after the appliances were placed they were all removed and the patient was treated with periodontal flap surgery to regain periodontal and gingival health. During the surgery a biopsy specimen was taken from the labial alveolar crest of the maxillary right first bicuspid (Figs 2, 3) and sent to a university oral pathologist for blinded microscopic examination. An image of the specimen was then subjected to fractal analysis, a biomathematical parameter diagnostic of bone modeling.[18]

Histological Analysis: Patient E.R.

The specimen demonstrates young bone with hematoxylin and eosin (H&E) stain in Fig 4. The same histological specimen, examined under polarized light, demonstrates both a woven confirmation and fractal patterns (Figs 5 and 6). These patterns are important because they sug-



Area	Fractal Dimension	SD
A	1.18002	0.009829
B	1.14476	0.023592
C	1.44143	0.00472
D	0.97931	0.010024
E	0.94117	0.009662
F	1.07864	0.003869

Figure 4. Fractal analysis demonstrating bone remodeling. Fractal geometric patterns are characteristic "footprint" of remodeling and provide biomathematical of the reductionist histological morphological pattern. Biology is characterized by a reductionist analysis of smaller and smaller "stuff" (gross anatomy to histology, a kind of microscopic anatomy). How the stuff functions through time is a mathematical function and the "geometric footprint" of cell proliferation creates a pattern referred to as a "fractal," a pattern common to dissipative systems. Analogously, a point moving in time on one coordinate defines a line, a line defines a plane, and a plane moving through time on a perpendicular coordinate defines a cube or rectangular solid. (Thanks to James Borke, PhD, Medical College of Georgia, for his consultation and the fractal analysis.) (Color version of figure is available online.)

gest immature bone modeling in response to therapy; preexisting bone presumably would demonstrate a mature "lamellar" pattern.

Mechanical loading is thought to be an increased fractal dimension at a bone interface that reflects mechanisms of cell-mediated remodeling presumably within regional deformations of 1500 to 3000 microstrain.[19,20] These changes in fractal dimension appear to be proportional to loading and are thought to provide a new parameter for force determination in orthodontic tooth movement.

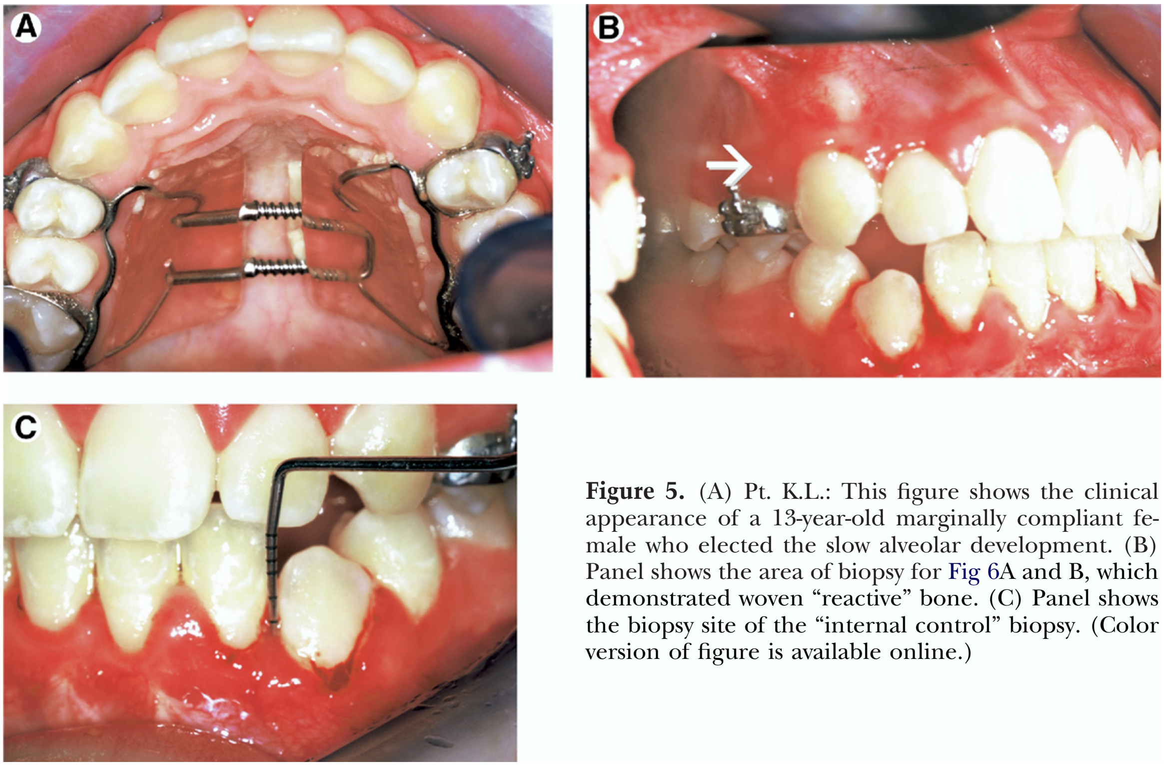


Figure 5. (A) Pt. K.L.: This figure shows the clinical appearance of a 13-year-old marginally compliant female who elected the slow alveolar development. (B) Panel shows the area of biopsy for Fig 6A and B, which demonstrated woven "reactive" bone. (C) Panel shows the biopsy site of the "internal control" biopsy. (Color version of figure is available online.)

Clinical Example #2: Patient K.L.

A marginally compliant 13-year-old white female presented with a posterior cross bite. The patient was hypersensitive to discomfort associated with strong mechanical manipulation of her dentition so rapid palatal expansion was declined in favor of slow palatal alveolar development. Approximately 2 months before biopsy an ADA identical in design to that used with clinical example #1 (patient E.R.) was placed to treat a posterior cross bite. No labial archwires were employed (Fig 7A and B).

Histological Analysis: Patient K.L.

After securing full informed consent, 2 months after insertion of the maxillary appliance, sections of the interdental bony septa were taken for microscopic examination. The specimens were obtained with a hand instrument on reflecting a labial full thickness (mucoperiosteal) flap and examined "blind" by a university oral and maxillofacial pathologist. With a healthy respect for scientific skepticism, an additional "internal control" specimen was taken from interseptal bone between the patient's ipsilateral mandibular first bicuspid and canine (Fig 5A-C). The specimens displayed in Fig 6A-C demonstrate standard H&E-stained histological sections (with and without polarized light respectively) of interseptal alveolar bone. The histologic pattern of woven (immature modeling) bone is almost identical to that secured from patient E.R. In this case #2 (L.K.), however, the sample was taken from the interseptal bone between teeth numbers 5 and 6, the patient's right maxillary first bicuspid and canine, an area that was influenced directly by the palatal alveolus' acrylic panels.

Figure 7A and B demonstrate a contrasting pattern in the internal control specimens taken from the mandibular alveolus between teeth numbers 22 and 23 (the patient's mandibular right canine and first bicuspid), which were not subjected to orthodontic or orthopedic stimulation. This internal control is typical of the pattern in patients' alveolar bone presenting in steady-state equilibrium suggesting that the maxillary alveolus woven bone pattern was not due to inflammation or normal function but rather by putative alveolar "bending" to the labial alveolus

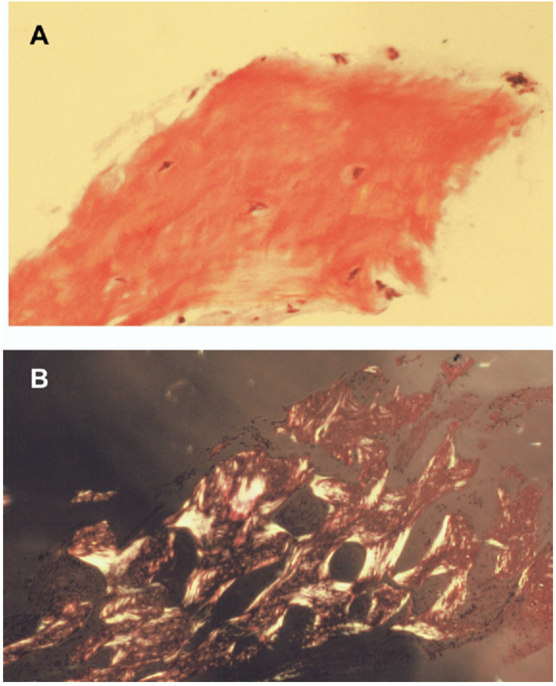


Figure 6. (A) Pt. K.L.: This figure shows the histological pattern of the biopsy specimen in Fig 5A. There is no evidence of an organized pattern normally seen with mature bone. This standard hematoxylin and eosin-stained specimen suggests the woven, or "reactive," pattern of physiologic bone remodeling in response as described by Frost's minimal effective strain. (B) Panels shows woven bone image, with polarized light, of interseptal alveolar bone biopsy between teeth #5 and 6. This appearance demonstrates a pattern typical of that where ultra-low stress delivered to the palatal alveolus (compare palate per se). The woven bone pattern is similar to that seen in Fig 3 (Pt. E.R.) and that secured in most patients treated with this appliance. (Color version of figure is available online.)

as the bone is physiologically yet therapeutically bent (strained).

While these interesting specimens suggest the possibility of labial osteogenesis with palatal alveolus stimulation, we do not claim universality. We modestly propose a hypothesis to be refined by meaningful professional dialogue in the tradition of the Western dialectic. Only time will reveal how prescient our nascent theories will ultimately prove to be as we present these findings in an attempt to falsify the notion of universal alveolar immutability; Popper's falsification principle is a more profound epistemological criterion for truth and a rigorous test of veracity greater than the more standard method of independent corroboration.[17]

Discussion

Since no active adjustments are necessary with a spring-loaded alveolus development appliance (ADA), it worked in cases E.R. and K.L. as a kind of "osteogenic machine," altering the palatal and labial alveolus form biologically without producing any expected bony or soft tissue dehiscence. Indeed the only area of bony dehiscence appeared where the labial archwire may have mechanically "pulled" the roots labially in case E.R. (Fig 3). This clinical picture suggests that continuous ultra-light loads directly on the palatal alveolus may have modeled labial bone as a tooth-alveolus complex "moves" labially through remodeling "drift." Some theorists speculate that the alveolus is immutable and "expansion" of the dental arch inevitably produces bony dehiscences or fenestrations and gingival marginal recession ("stripping," "runners"). The case of E.R. ostensibly suggests that bone may model to preclude these complications if two conditions are met: (1) the movement occurs without active periodontitis, and (2) the internal strain falls within a threshold modeling range.

The creation of woven bone in Fig 3 is interesting because woven bone is characteristic of bone modeling following an injury. For example, after a fracture (and callus formation) bone responds first by depositing "woven bone." Woven bone is a disorganized structure with a high proportion of osteocytes. Weaker than fully mature bone, it exhibits a small quantity of randomly oriented collagen fibers, but forms quickly at the site of injury. Later in the maturing process woven bone develops to lamellar bone, which exhibits a highly organized pattern of concentric sheets and a relatively low proportion of osteocytes (see Fig 7, Pt. K.L.). Lamellar bone is stronger than woven bone and is characterized by a greater number of collagen fibers running in opposite directions in alternating layers, much like plywood. This contributes a quality to the bone that is relatively more resistant to torsional and tensional stresses. What is interesting in these examples is easily repeated by the reader by taking biopsies of the alveolus during and after the ADA appliances have been removed and the alveolus reverts to a steady-

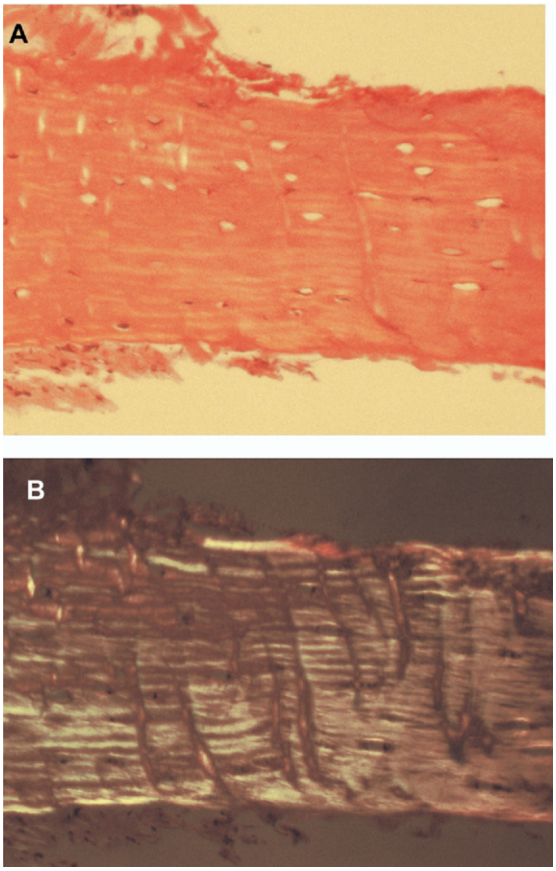


Figure 7. (A; top) Pt. K.L.: The panel shows a control specimen taken from the mandibular alveolus between teeth numbers 22 and 23, which were subjected to no orthodontic or orthopedic stimulation. This internal control demonstrating steady-state lamellar bone serves as contrast to the typical histological pattern of "reactive, woven" bone modeling pattern as dramatized in Fig 6A and B. (B; below) Internal control specimen shows, with polarized light, a normal mature lamellar bone pattern. "Reactive" woven bone does not appear in this polarized section because it is in a "steady state" of osteoclastic-osteoblastic dynamic equilibrium with a highly organized Haversion systems (osteones) characteristic of relatively unstressed bone. This contrasts with the "reactive and woven bone" appearance in the same patient in Fig 6A and B, where the Max 2000 appliances applied force to the palatal alveolus, through the spongiosa to the labial cortex, which appears in patients subjected to ultralight force-induced alveolus development. (Color version of figure is available online.)

state equilibrium of "remodeling." To our knowledge this is the first time a woven bone pattern suggesting therapeutic modeling has been demonstrated with this kind of appliance.

The ADA case examples also illustrate a paradoxical but important event where bone modeling occurred even in a field of infection. The reasons that infection has not complicated the remodeling are that the force magnitude was low and unidirectional, not oscillating ("jiggling"), as is generally evident in cases of occlusal trauma. In case E.R. the infection qualitatively defined gingivitis, not periodontitis; the distinction between these entities is critical for the uninitiated clinician but often problematic to diagnose.[21] Thus, instead of mechanically moving teeth through the alveolus, it appears that palatal acrylic panels biologically "moved" the whole alveolus bone by resorption/osteogenesis "drift." This type of modeling of the labial portion contrasts sharply with mechanically movements of roots beyond the alveolar envelope, a procedure that traditionally has been associated with putative bony dehiscence and gingival recession.

Conventional "Wisdom" and Innovation

Conventional wisdom based on works by Engelking and Zachrisson[22] and others[23] intimate that the labial alveolus is immutable and labial movement "causes" bony dehiscence (the implicit epistemological ambiguity of causality is typically unclarified). However, contrasting data and comments by Lindskog-Stokland and coworkers,[24] Melsen,[25] and others[26-30] suggest that the alveolar "envelope" or limits of alveolar housing may be more malleable than previously believed and can be virtually defined by the position of the roots. Thus, the concept of dental roots as a functional matrix for bone is often validated implicitly in the works of many independent authorities. Indeed the explanation of biological mechanisms of alveolus bone modeling has been cited as one mechanism to explain the effects of some functional appliances.

Specifically, referring to a subset of functional dentofacial orthopedic appliances, Norton suggests that some "create a space or vacuum into which teeth moved and the alveolar process followed . . . ."[31] The phenomenon of "phenotypic plasticity," when applied to the genetic expression of a single generation organism, explains this well.[30] This plasticity is a well-accepted concept in the field of developmental biology[31,32] and is manifest only by various environmental or

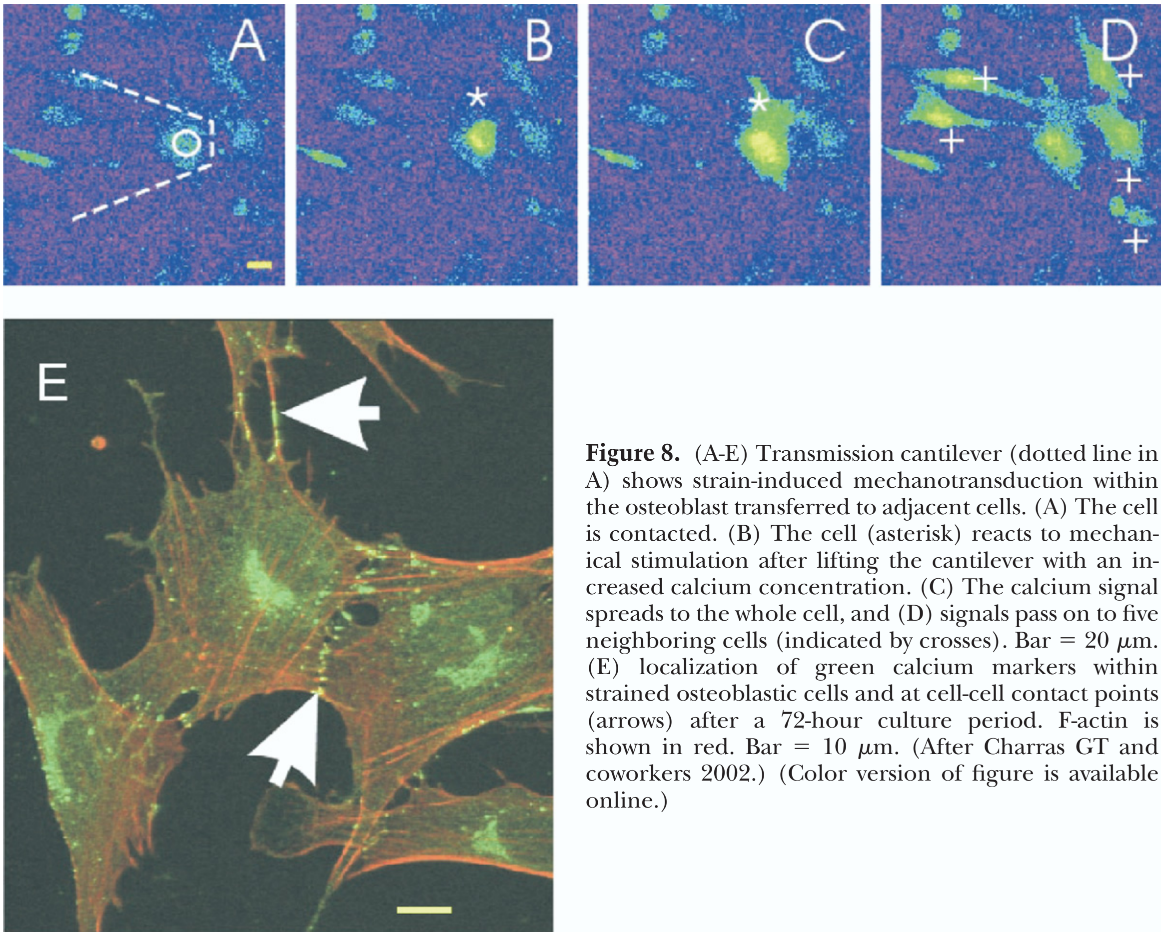


Figure 8. (A-E) Transmission cantilever (dotted line in A) shows strain-induced mechanotransduction within the osteoblast transferred to adjacent cells. (A) The cell is contacted. (B) The cell (asterisk) reacts to mechanical stimulation after lifting the cantilever with an increased calcium concentration. (C) The calcium signal spreads to the whole cell, and (D) signals pass on to five neighboring cells (indicated by crosses). Bar = 20 μm. (E) localization of green calcium markers within strained osteoblastic cells and at cell-cell contact points (arrows) after a 72-hour culture period. F-actin is shown in red. Bar = 10 μm. (After Charras GT and coworkers 2002.) (Color version of figure is available online.)

epigenetic perturbations[33-37] and may be engineered. Whether surgical or nonsurgical, these examples argue for the malleability of even adult bone in general and against alveolar immutability in particular.

This control is evident in the effect of the spring-loaded ADA, presented here grossly and microscopically. Yet the domain of nonsurgical alveolar bone engineering is not the monopoly of dentofacial orthopedists. The histological actions of the ADA mimics the principles applied in the innovative philosophy of Ponseti's treatment of talipes equinovarus (club foot) in that it attempts to redirect a pathologic growth trajectory toward a physiologic course.[38] Since facial morphotype evolves even throughout adulthood, the ADA appliance may be a more benign alternative to surgically assisted rapid palatal expansion (SARPE) and, certainly, considering relative morbidity, orthognathic surgery.

The presumed immutability of the alveolus has been historically problematic in that it can reduce treatment options to extraction or orthognathic surgery, conventional protocols that juxtapose "parts" instead of engineering physiologic "dynamics." In this regard any concept that emphasizes, or worse on occasion dogmatically defends, mechanical solutions as "inviolable art" can eclipse emerging biological imperatives. This is a needless and unfortunate limitation because many patients disdain major surgical alternatives categorically and even preemptively. Moreover, the studies of Little and coworkers[39] indicate that routine extraction therapy to camouflage dysmorphic skeletal elements is neither a panacea nor guarantor of stability.

A further understanding of the molecular basis for alveolus physiology may take us closer to predictable modification of form by surgical, nonsurgical, or pharmaceutical means. For now, these cases prove the principle that immutability of alveolar bone is not universal and alveolar surgery or continuous ultra-low force magnitude may indeed be an appropriate starting point from which orthognathic surgery or extraction may be deferred as a reasonable second choice, a "fallback" or "fail-safe" tactic that ensures that inevitable error will fall on the side of tissue maintenance. This is justified because since the time of Wolff and Roux bone has been considered a dynamic tissue adapting its form to its environment (form follows function).

For the modern dentofacial orthodontist, Moss elaborates through his perennial missives on the functional matrix hypothesis (FMH) that "dental roots are the functional matrix of the alveolar bone" (Moss ML, personal communication, 2005). While some have dismissed the importance of this FMH perspective as merely an ontological sine qua non for the large bones of the craniofacial complex,[40] it certainly makes good sense to apply it to the human alveolus as well. A fully integrated, comprehensive, and intellectual context of facial growth and development is incomplete without it. For, after all, if theory is merely a convenient intellectual construct to predict or explain an observed phenomenon, its modest application here certainly goes beyond simplistic explanations based on ligament histology and supplements other ontogeny theories. Even the few critiques that the functional matrix theory has evoked admit that, despite its metaphysical vagaries, as a theory it is not necessarily antithetical to other morphogenetic mechanisms, and can serve well as a modest but logically essential *Weltanschauung* among others.[39]

More recently, some molecular biologists are suggesting that, on cellular and biochemical levels, osteogenic morphogenesis should be considered as a transcriptional event. Altered extracellular matrices, cellular form, and internal cytoskeletal elements when bone is clinically stressed can manifest within an optimal range. Thus, gross anatomical form follows function and intracellular function follows form.

The Utah Paradigm in Dentofacial Orthopedics

The Utah paradigm of bone physiology is also an instrumental element in explaining a "whole bone" approach to alveolar bone modeling. It proposes that a tissue-level entity (termed the "mechanostat") is a definitive but neglected functional determinant of bone physiology in steady-state homeostasis or remodeling. Structurally a basic multicellular unit (BMU) is a collection of regional osteons that act as the bone analog of the nephron. What Frost called the "nephron equivalent" is completely compatible with the principles of Wolff, Moss, and contemporary cellular biology.

In this regard, the natural eruption, guided eruption, and even the "forced eruption" of fractured teeth can be easily seen as "growth sites" responding positively to drift and guidance, yet negatively with premature loss and serial extraction. As prudent clinicians we may never categorically rule out the need for tooth extraction for gaining arch length. However, we are wise to recall Pascal's wager if injudicious bicuspid extraction ablates not only the tooth but all the future bone development and lip support that might have developed.

The problem for the injudicious clinician is that this pernicious sequella may not be evident for decades, a prevalence that only longitudinal twin studies over decades can explicate clearly. If alveolar development can call on a strong foundation in basic osteology, then the orthodontist is liberated from strictures of traditional thought that accepts pernicious side effects by default.

New ways of thinking ("NewThink"), of course, often cause some consternation and even fundamental existential angst among those comfortable with the *status quo*.[41] But change is integral to the very fabric of science, and the reconciliation of clinical expediency with new-science conjecture is an intellectual imperative that may be too rare in the art of orthodontic treatment.

Often the developed alveolus is somewhat shocking to a clinician who is used to seeing small smiles in small children. Indeed, where alveolus development can help define eruption trajectories in the treated adolescent, one may indeed notice a smile that is seemingly disproportionately large for the immature face. However, Fig 9A and B demonstrate how a smile that defines the face of youth also fits esthetically well with the more mature adult face. Regardless of historical guidelines we believe that the emerging esthetic standard for a so-called full smile must be recognized and justified scientifically. It seems that the histological docu-

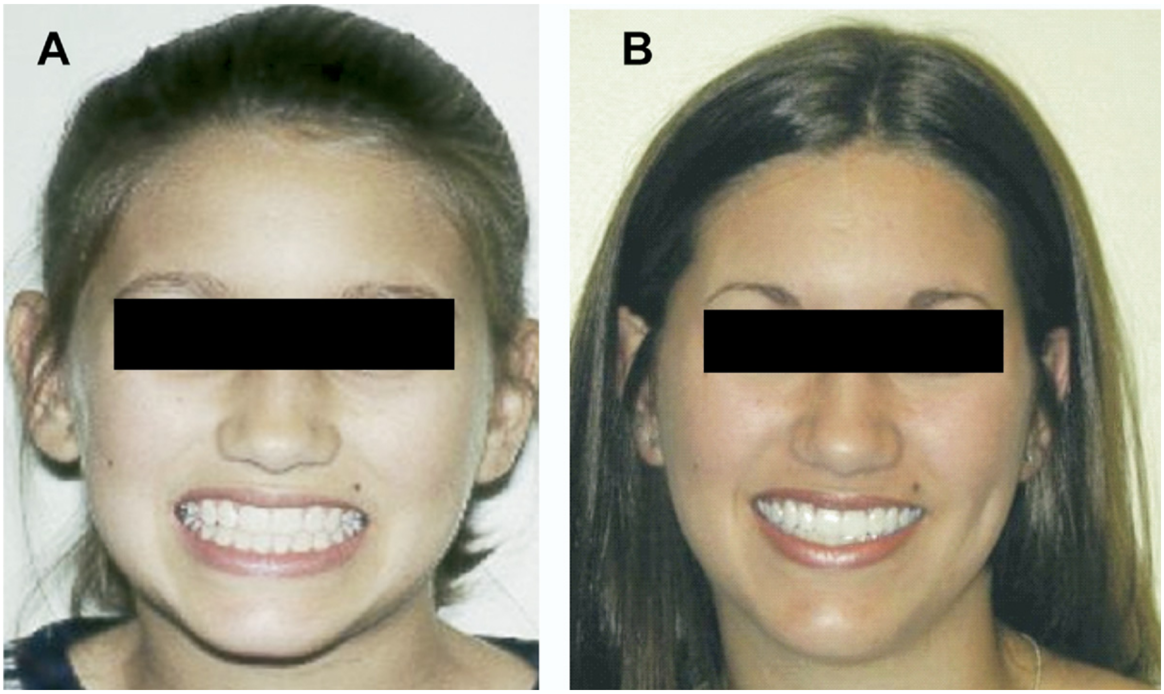


Figure 9. (A) Panel shows the esthetically pleasing treated adolescent "growing" face. (B) Panel shows the same smile, esthetically appropriate in the adult face. (Color version of figure is available online.)

mentation of supporting bone modeling may justify the admonition of that facial orthopedists should "create an adult smile which the adolescent can grow into, not an adolescent smile the adult grows out of."

This philosophy suggests that if the alveolus can be orthopedically engineered to an alternate phenotype by biological engineering, instead of mechanical manipulation, it is preferred to extracting teeth where a remaining dentition is mechanically fit into a manifestly inadequate alveolus, deformed by the original malocclusion.

Treatment Timing

It is important to understand that the scientific literature contains compelling and ample justification for redirecting growth trajectories in prepubescent humans. Therefore, the best time to treat the growing child with this self-limiting "machine" is measured in dental age not chronology. Generally, optimal effects are elicited from these kinds of ADA during the transitional or mixed dentition. At this time phenotype changes dramatically. Periodontally accelerated osteogenic orthodontics (PAOO) surgery, in contrast, presents no age constraints since surgery per se reverts healing tissue to a kind of "neonatal" state of morphogenetic development.

Arch development from the palatal aspect may be employed simultaneously with conventional labial therapy. However, singular use of the ADA sans labial archwires reduces the risk of bracket breakage, pernicious increases in pathogenic bacterial biofilm (dental plaque) load, and addresses orthopedic problems directly instead of camouflaging dysmorphic alveolar form with altered tooth positions.

Genetic Expression and Phenotypic Plasticity

It is important to note that phenotype is not a one-to-one manifestation of genotype. While genotype has often been defined as a "blueprint" for tissue form, this allusion is simplistic to the point of gross misrepresentation and leads to frankly erroneous thinking. In fact the genotype is more akin to an "instruction manual" directing tissue development to a myriad of forms depending on the degree of phenotypic plasticity inherent in the biological system and epigenetic influences, be they pathologic, therapeutic, or neutral. In this sense, the case examples of the orthodontist's gentle root manipulation of bone resemble the rationale medical orthopedist, Dr. Ignacio Ponseti, in his attempts to obviate surgery for talipes equinovarus (Ponseti I, personal communication, 2007). In the therapeutic realm, the "biological message" sent by the dentofacial orthopedist can be seen as a more complex alteration of the alveolus, similar to that seen with the periodontist's attempts to alter alveolus form by equilibration when traumatic occlusions causes a pathognomonic alveolar "hourglass" cribriform plate profile. Pigliucci defines phenotypic plasticity as the "property of a given genotype to produce different phenotypes in response to distinct environmental conditions."

In the case of example #1, E.R., the "pull" of the labial arch wire is purely orthodontic. This "environmental condition" (perturbation) is quantitatively and qualitatively distinct from the alveolar orthopedic "push" of the acrylic panels in the ADA. Thus, it is quite logical and consistent with epigenetic principles that different perturbations would necessarily elicit different phenotypic clinical outcomes because pathoses and clinical therapy both qualify as determinate environmental perturbations; the latter is just more predictable.

Conclusions

When the patient says, "I prefer nonextraction care," he or she is making a statistical forecast. That is to say, the patient is saying in effect, "I forecast in a field of future uncertainty, that I will experience greater "utility" (subjective sense of worth, value, or satisfaction) if teeth are not extracted." In the absence of logical or empirical scientific certitude that extractions are absolutely contraindicated (a rare event), the preference should be in the decision process that evolves with each patient visit.

Moreover, the authors suggest that the patient is implicitly employing a variant of Pascal's wager by "hedging the bet" and the authors propose that such a choice, when given to patients, empowers them with a commitment to participation in the decision making and management, including a reasonable assumption of risk that is rightfully shared. After all, the role of science is to solve problems for individuals, not statistical cohorts, samples, corporations, arithmetic means, or professional organizations. Clinicians are for the benefit of patients, and not patients for clinicians. It is imperative to view each patient as an individual and not as a mean. The art and science that the authors propose are simply methods for the benefit of the patient.

The relationship between alternatives is a variant of Pascal's wager wherein the patient, selecting a nonextraction alternative, for example, falsifies the notion that extraction therapy will deliver a superior future utility "payoff" (maximum esthetic form and function) and minimizes the chances of irreversible "damage." This "criterion of preference" by an enlightened patient in the 21st century is just as important to the informed consent of the patient as cephalometric tracings of statistical norms. It is also satisfying on a practical level because, by including the patient in the "committee" of stakeholders, it technically employs patient preference as a so-called Bayesian prior, a well-known and acceptable component of health care quality derived from the mathematics of decision theory, where progressive data accumulations make forecasting more robust.

The histological data, easily replicated by every private practitioner, suggest that ultra-light, self-limiting force of an embedded nickel-titanium spring appliance can ostensibly activate the bone as a "mechanostat" mechanism—as developed by the Frost-Jee collaboration and described for dentofacial orthopedics so well by Melsen. Perhaps soon the exact biochemistry will disclose that it activates architectural transcription factors, as explained by molecular biologists in variable contexts. The appearance of woven bone in clinical demonstration cases E.R. and K.L. histological sections and analysis of the fractal pattern therein suggest that modeling of the alveolar bone can indeed occur where the sample was taken. This serendipitous but consistent observation gives serious pause to claims about the behavior of bone around teeth that are moved orthodontically. Specifically the immutability of the dental alveolus and the tendency of dental arch "expansion" to cause gingival recession must be reconsidered in light of the scientific rationale provided and clinical demonstration. Further, engineering the alveolus by ultra-light force directed to the alveolus, periodontal surgically facilitated OTM, or *in situ* pharmacologic management[42] is a clinical reality that suggests routine bicuspid extraction to avoid putative but often illusory "periodontal problems," or to lend stability to long-term clinical outcomes, may be questioned. Moreover, the authors suggest that traditional biologic rationales for bicuspid extraction (beyond "increased efficiency") where they exist should be subjected to the same caliber of scientific scrutiny that is leveled on new or novel variations of traditional themes.

"Arch expansion" is a dangerously vague term, subsuming flattening of the curve of Wilson, separating the maxillary palatal and pterygomaxillary sutures, flaring incisors labially to original positions, tipping or bodily moving molars buccally. Whether one is physiologically "recapturing" original phenotype with an appliance or creating a novel phenotype, the ambiguities of "expansion" always haunt us. Whether that be vexatious to the reader or enigmatic to the practicing clinician, this seems axiomatic: "expansion" may "cause" bony or bony dehiscence sometimes, but not foreseeably in the individual and clearly not always.[43]

The practical asset the spring appliance has is its "orthopedic machine" mechanism, self-limiting and mildly self-adjusting, to elicit "alveolus development" and obviate bony dehiscence and periodic adjustment pain associated with other RPE appliances. The problems with grossly mechanistic appliances derive from their reliance on mechanical ratcheting instead of biological engineering. In that respect, the philosophies implicit in both PAOO surgery and ADA appliance protocols and design of the orthopedic appliances, if we may condescend to popular contemporary parlance, are clearly "not your father's orthodontics." Thus, the rationale for their clinical efficacy should at least dispel any fear or loathing that theory in the orthodontic specialty is moribund or dead. The ADA, like the Wilcko-Ferguson collaboration, may well emerge as the singularly most progressive synthesis in this first decade of the "Century of the Biologist."

For the sake of intellectual integrity it should be stated that this discussion neither condemns bicuspid extraction as an acceptable modality nor contradicts the claim that some patients may wish the expedient care it facilitates. In addition, although one may claim that side effects of injudicious bicuspid extraction are unpredictable, too small to be perceived, or, even in the worst case, reversible later in life, it is the very unpredictability itself that argues for a prudent nonextraction preference. However, in respect to the rigorous scientific criterion of truth as proposed by Popper,[17] one or two examples that contradict a scientific theory's claim (so-called counterfactual) can weaken or even disprove the theory as legitimate universal law. The authors consider that their examples appear to be counterfactual to the claim of universal immutability.

To the thoughtful facial orthopedist and modern, even dogmatically strict clinical empiricist steeped in modern biologic theory, however, what is demonstrably obvious in the case presented, and arguably valid deductively from the emerging science, is that any universal claim of alveolar immutability must be seriously rethought, in terms of contemporary periodontal regenerative science and tissue engineering, namely the demonstrated clinical phenomena falsify the idea of universal alveolus immutability.

The philosophy implicitly expressed by these words does not contradict bicuspid extraction but complements it with a scientific basis and epistemological argument supporting a cogent nonextraction alternative acknowledging that for some patients a fixed alveolus deformity can no more define normal than a short leg can be the standard to pathologize the other longer leg. The argument that remediable hearing loss in children should be maintained as a legitimate physiologic variant also echoes the immutable alveolus contention. Yet there are clinicians who, subscribing to such apostasies, will defend alveolus immutability despite an infinite number of counterfactuals. In a sadly droll sort of way, intransigent doctrinaire clinicians and dogmatic protocols are their own worst enemies. Yet for the thinking clinician one need only quote Williams James, "if you wish to upset the law that all crows are black . . . it is enough if you prove one single crow to be white." This article has presented two.

On a practical level bicuspid extraction will probably be around for some time. However, to the extent that an individual patient must be fully informed of all alternatives, the malleability of the alveolus irrespective of its skeletal bases falsifies any claim of that bicuspid extraction therapy may be either universally necessary or sufficient. With the presentation of these cases the burden to disprove universality now lies with academics and intellectual clinicians, who, through further research may confirm, refine, falsify, or reject the legitimacy of these conjectures. Only time will tell how prescient these proposals will prove to be. Future research, both in vitro and in vivo, should concentrate on defining the exact amount of microstrain range that stimulates compensatory periosteal appositional osteogenesis of the alveolus. We know from craniofacial biology that the microstrain of cranial sutures of approximately 500 to 1000 microstrain[44] will elicit evidence of bone modeling, a much lower range than that usually found for long bones. There is no reason to believe that the alveolus should behave exactly like a suture, yet despite its critical importance in orthodontics it has been largely uninvestigated using principles of the Utah paradigm as suggested in 1965 by Epker and Frost. Investigations are ongoing at University of California in Los Angeles (UCLA) on exactly this topic. How the dynamics of the alveolus are ultimately defined will take decades but some significant biologic data are already here.[45,46]

Meanwhile, the fact remains: clinical evidence of phenotypic changes and labial alveolus modeling have been associated with ultralight forces with a novel alveolar development appliance, as demonstrated in Figures 3, 4, and 6, a clinical phenomenon consistent with a "whole bone" approach to dentofacial orthopedics. (Fig 8).

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"As the twig is bent, so inclines the tree" (Virgil, 70-19 BC).

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