Beyond the Ligament:

A "Whole Bone" Approach to Dentofacial Orthopedics and Falsification of Universal Alveolar Immutability ©

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INTRODUCTION

Clinical tissue engineering in dentofacial orthopedics is in its infancy; most research presently is *in vitro* and pharmaceutical. But the conceptual stage is set for *in vivo* bone tissue engineering by regenerative procedures in periodontology and modern medical orthopedics. However, the theoretical basis for manifestly successful clinical outcomes cannot be fortified by traditional orthodontic tooth movement (OTM) biology which focuses solely on the periodontal ligament as the operant organ. It is forces acting *beyond the ligament* which may be significant determinants of the alveolus and the consequent dentofacial form which lives, thrives and dies by the grace of dental root positions.(Moss, 1997) Specifically forces eliciting an osteogenic threshold of ~1,500-3,000 microstrain according to Professors Frost (2004) and Jee may stimulate appositional bone modeling.

A morphotype which nature initially "intended", before perverse environmental perturbations distorted its form, may be "recaptured" from an environmentally developed malocclusion. Of course this must occur within the range of physiologic potential but where etiologic agents such as chronic mouth breathing or premature tooth loss have caused abnormal distortion, that potential range is often quite obvious. Therefore, at the risk of overstating the theory of "alveolus development", this paper presents a modest synthesis of contemporary theories in cell biology to explain ostensible osteogenic activity, and alveolar phenotype alterations by ultra-low orthopedic force or by moving roots through a healing bone graft.

Dentofacial orthopedic physiology of the alveolus does not deny the relevance of periodontal 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, 1999) 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 (1969) has so eloquently 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 in all directions. Dental osteology which emphasizes the pressure-tension (PDL) model conflicts not only with logic but with medical long bone osteology as well, *viz*. pressure on long bones stimulates osteogenesis yet orthodontic pressure in the periodontal ligament is considered a stimulus for resorption.

We propose, not as a contentious polemic, but rather in the tradition of the Western dialectic, that this conflict may have derived from an ill-advised emphasis on the pressure-tension mechanism of the periodontal ligament (PDL). The original PDL model proposed by Schwarz and Oppenheimthe 1930's and expanded by Reitan in the middle of the 20th Century should be reconsidered in terms of 21st Century science. This paper aims to illustrate the practical application of alternative theories which help reconcile the inherent contradictions of the PDL model with demonstrations of surgical and non-surgical examples which support a "whole bone" perspective. Presently *in vitro* analyses of force distribution are being pursued by talented student research teams at the ULCA School of Dentistry in Los Angeles.

Not wishing to compound the semantic ambiguities in this science we use the words "remodel" and "model" indiscriminately to refer to architectural changes secondary to therapeutic mechanical stimuli. Finer distinctions between the terms is important but beyond the scope of this discussion. A clear contrast is made however among rapid *palatal expansion* (RPE) of the maxilla, *orthodontic* dental arch expansion and *orthopedics development* of the bony alveolus with direct continuous modulated force application. Since *wound healing recapitulates regional ontogeny** on a molecular level, regional alveolar ontogeny (development) 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 (e.g. >3,000 µE according to Frost). Thus, the alveolus is proposed herein as a separate ontogenic entity or "organ", capable of a singularly

* See: Murphy NC, 2006

active biological response to loading, irrespective of the subjacent maxilla or the subsumed dental matrix. In prior publications the term “maxillary expansion” has often been used in all three contexts without clear differentiation. (McNamara, 1999). 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. This concept is not new. Melsen (1999) spoke eloquently of it in her discussion of alveolar bone physiology and cited literature about 20 to 40 years old (Epker and Frost, 1965, Jee and Li, 1990, Burr et. al., 1985) in support of her discussion

Case examples and histological data demonstrate that both surgical and non-surgical tissue engineering cannot only produce manifestly stable alterations of alveolus form but also reflect abundant clinical evidence of molecular phenomena discovered by clinicians and researchers in the latter decades of the 20th Century. These observations are not intended to prove universality of our thesis, but rather, building on a rich theoretical heritage, to falsify presumptive concept of alveolar immutability. (See: Johnston, 1990, 1999, Ilizarov, 1969, 1989, Popper, 1971, 2002)

Clinical Demonstration: Patient E.R.

A non-compliant 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 Max 2000® palatal appliance was placed to treat a posterior cross bite as the anterior arch length deficiency was addressed by an 0.018 nickel titanium round wire in labial 0.022” slot brackets. This archwire was replaced with a 0.018” stainless steel archwire but no activation was made in the anterior or posterior sextants. The Max 2000® orthopedic expansion appliance was not activated upon insertion because the therapeutic mechanism is a self-activating, self-limiting continuous release of two transverse nickel titanium springs, each embedded in separate acrylic panels that deliver 150 grams apiece. **(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 one year.

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 sent to the Medical College of Georgia for fractal analysis, a biomathematical parameter diagnostic of bone remodeling. (Wagle, 2005)

Histological Analysis:

The specimen demonstrates young bone with conventional H & E stain in **Figure 4**.The same histological specimen, examined under polarized light demonstrates a “woven bone” or “reactive bone” pattern. **(Fig. 5)** The appearance of “woven bone” and confirmation of fractal patterns in the specimen **(Fig. 6)** are both important because they suggest immature bone remodeling; preexisting bone presumably would demonstrate a mature “lamellar” pattern.

Mechanical loading is thought to an increase fractal dimension at a bone interface which reflects mechanisms of cell- mediated remodeling presumably within regional deformations of 1,500-3,000 microstrain. 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.

DISCUSSION

Since no active adjustments were made by a clinician as the Max 2000® appliance worked in Case E.R. worked, it seems to have acted as a kind of “osteogenic machine”, altering the

palatal 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 **(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". (See: Enlow and Hans, 1996) 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 remodel 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 remodeling range.

Because the bone volume (BV) to total tissue volume (TTV) ratio is reduced from a normal 60% to ~30% (Ferguson, et. al., 2007) by surgical perturbation we conjecture that surgically-facilitated OTM accelerates bone remodeling in a similar and normal but amplified manner. There is no scientific evidence that pathological elements are operative or that any accelerated metabolic remodeling elicited either by bone grafts or threshold bone flexing (strain) is qualitatively different from standard orthopedic long bone remodeling concepts. Surgery merely adds speed, convenience, stability and a mitigated bacterial challenge.

Some experts claim surgically-facilitated OTM e.g. selective alveolar decortication (SAD) may be contraindicated in patients presenting with periodontitis. It is important to note that this may be a relative contraindication, not absolute. Case by case determination of indications and contraindications are often patient-specific and preference driven; while some risk-averse patients may elect to forgo surgical orthopedic care others can legitimately employ the SAD cost-effectively and with relative clinical impunity.

The Max 2000® Case also illustrates a paradoxical but important event where bone remodeling 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. (Longhurst, 1980). Thus, instead of mechanically moving teeth through the alveolus, it appears that palatal acrylic panels *biologically* "moved" the *whole alveolus bone*, remodeling the labial portion in contrast to simply and *mechanically* moving roots beyond the alveolar envelope presumably risking both bony dehiscence and gingival recession.

Conventional "Wisdom" and Innovation

Conventional wisdom based on works by Engelking and Zachrisson, (1982) and others (e.g. Thilander,et.al., 1983) seemingly 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 Wennström, et. al., (1993), Melsen (Cacciafesta, 2006) and others (Hom, et.al., 1984, Wilcko, et.al., 2001, Ferguson, et.al., 2007) suggest that the alveolar "envelope" or limits of alveolar housing may be more malleable than previously believed. The phenomenon of "phenotypic plasticity" explains this well. (Pigliucci, 2001) This plasticity is a well accepted concept in the field of developmental biology and is manifest only by various environmental or epigenetic perturbations. **(Fig. 7)** (Waddington, 1954, Siegal and Bergman, 2002, Stearns, 2002, and Slack JM, 2002) and may be engineered (Alperts, 2002, pp.536-545). The results of this philosophy are clearly demonstrated from the cellular and molecular level by the distorted cytoskeletal elements **(Fig. 8)** to the esthetic clinical outcome images. **(Fig. 9)**

In disease the perturbation may be infection, or pathological trauma. Therapeutic intervention may also be considered an epigenetic perturbation where chemical effects or orthopaedic force are sufficient to overcome buffering tendencies (canalization) that secure ontogeny on a fixed trajectory. The difference between pathologic changes and therapy is the ability to control and predict treatment outcome. This refined conceptualization of alveolus

physiology appears to be increasingly appealing to the enlightened clinicians and researchers alike.

This control is evident in the effect of the spring loaded Series 2000® appliances, presented here grossly and microscopically. Yet the manipulation of bony form is not the monopoly of dentofacial orthopedists. The histological actions of the Max 2000® (1997), appliance mimics the principles applied in the innovative philosophy of Professor Ponseti's treatment of *talipes equinovarus* (club foot) in that it attempts to redirect a pathologic growth trajectory toward a physiologic course. (Ponsetti, 2007, personal communication). Since facial morphotype evolves even throughout adulthood (Behrents, 1986) Dr. Williams' Max 2000 appliance may be a more benign alternative to surgically assisted rapid palatal expansion (SARPE) and certainly, considering relative morbidity, orthognathic surgery.

Generally, dentoalveolar orthopedists eschew traditional mechanical treatment philosophies and orthognathic surgery that attempt to rearrange physical components "from the outside in" instead of recruiting and engineering intrinsic biological forces "from the inside out". The latter explains, in a phrase of common parlance the dentoalveolar orthopedist's philosophy and the contrast illustrates why lock-step compliance to traditional paradigms may color the orthopedic concept as an anathema to conventional orthodontic thinking.

The presumed immutability of the alveolus has been historically problematic in that it can reduce treatment options to extraction or orthognathic surgery, conventional protocols which juxtapose "parts" instead of engineering physiologic "dynamics". In this regard any concept which emphasizes mechanical solutions can truncate intellectual growth and 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 et. al. (1990) indicate that routine extraction therapy to camouflage dysmorphic skeletal elements is neither a panacea nor guarantor of stability.

Molecular Biology

A further understanding of the molecular basis for alveolus physiology may take us closer to predictable modification of form by surgical, non-surgical 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 or "fail-safe" tactic. This is justified because since the time of Wolff and Roux bone has been considered a dynamic tissue adapting it form to its environment (form follows function).

For the modern dentofacial orthodontist, Moss elaborates that "roots are the functional matrix of the alveolar bone"* while some have dismissed the importance of this perspective as ontological *sine qua non* for the large bones of the craniofacial complex, it certainly makes good sense for the alveolus and a full 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 for specific anatomical areas, other ontogenic theories. Even the few critiques that the functional matrix theory has evoked admit that, despite its metaphysical vagaries, as a theory is not necessarily antithetical to other morphogenetic mechanisms, and can serve well as one essential *Weltanschauung* among others. (Johnston, 1976)

More recently, Professors Bidwell (Pavalko et. al., 2002) and Ingber (Maniotis et.al., 1997) join other mechano-biologists to illuminate this phenomenon further by suggesting that, on tissue, cellular and molecular levels, biochemical osteogenic functions such as morphogenesis can follow altered cellular form when bone is clinically "bent" **(Fig. 8)**.Thus, gross anatomical *form follows function* and intracellular *function follows form*.

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Moss, ML, personal communication, 2005.

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 determinate 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 analogue of the nephron. What Frost (2004) called the "nephron equivalent" is completely compatible with the principles of Wolff, Moss and contemporary cellular biology. This makes Frost-Jee concepts superior metaphors for the alveolus physiology and argues that this modern biological approach may deserve more attention as a functioning component in orthodontic therapy. We propose that the woven bone patterns seen in the presented cases exemplify these concepts. Melsen seems to argue this point from a rather parallax perspective (Cacciafesta, 2006) but has acknowledged that the concepts deserve greater research scrutiny, reminding us that explanations of the Utah Paradigm itself appeared in the orthodontic literature over 40 years ago. (Epker and Frost, 1965)

The "whole bone" paradigm essentially presents orthodontics "from the bottom-up", focusing on "optimal response" of alveolar bone instead of a "top-down" analysis of "optimal force". This is important because extraction in the prepubertal patient sacrifices developmental potential as it ablates part of a functional matrix critical to future facial development. This is basic developmental biology and classic ablation theory in chick embryology the alveolus in this respect is seen as a kind of "growth site" responding to tooth eruption and drift and negatively with extraction. As prudent clinicians we an never categorically rule out the need for tooth extraction for gaining arch length. However, injudicious bicuspid extraction ablates not only the tooth but all the future bone development and lip support that *might have developed*. In this respect tooth extraction is an *in vivo* ablation experiment in human children, especially prepubescent.

The problem for the injudicious clinician is that this pernicious sequella may not be evident for decades, a prevalence which only longitudinal twin studies over decades can explicate clearly. If alveolar development can call upon a strong foundation in basic osteology then the orthodontist is liberated from outdated strictures of traditional thought which 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* (Kuhn, 1970). 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 some suggest is painfully lacking in the orthodontic art. (Johnston, 1990, 1999). 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 the treated adolescent one may indeed notice a smile that is seemingly disproportionately large for the immature face. However, Figures 9A and 9B demonstrates 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. The figure and the histological documentation of supporting bone remodeling echoes the admonition of Dr. Williams that facial orthopedists should always try to "…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 so that the remaining dentition can fit into a manifestly inadequate alveolus deformed by the original malocclusion. The Series 200 attempts to do this by applying osteogenic forces from the palatal *alveolus* surface (not we did not say maxilla) transferred to the labial

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alveolus medulla and cortex. The treatment begins by measuring the available space from first molar to its contralateral antimere by calculating the circumference of the labial attached gingiva, rather than using cusp tips of obviously malaligned teeth or guessing whether a catenary curve or parabola might constitute the "best fit.

On a molecular biologic basis explanation for the Max 2000 effects may be found in the nascent science of mechanobiology (See: van der Meulen and Huskies, 2002) The literature on cell activity in fields of tensional stress may alter both extracellular and intracellular chemical activity by amplifying actions of membrane ion channels and secondary messenger cascades which can "reprogram" genetic expression.

Since morphogenesis is a transcription event of the nucleus dentofacial orthopedics qualifies as a "genetically engineered" phenomenon employing intracellular mechanisms well known to molecular biologists. Protein chemistry reminds us that changing the shape or appliances conformation of important cytosol proteins alters their reactivity in a way that adding radicals to an inorganic molecule alters chemical behavior. Moreover some researchers have actually identified specific complex proteins which transduce mechanical data directly to the DNA to alter genetic expression. (Pavalko, et.al., 2004). If the movement of the alveolus directly or indirectly through root movement can be seen as a flexure of the whole (alveolus) bone, it is no great logical leap to understand that "bending bone bends DNA" indeed. Already we know that bending bone creates a transduction candidate in the gap junctions **(Figs.10, 11, 12)** and "streaming potential" of ion flux of the osteocyte-canaliculi syncytium where bone is flexed. Is it not a mere logical extrapolation to conjecture that the bending of proteins and polarized genes may also play a synergistic contribution? Yet, clinically we seem to relish early 20th Century mechanical concepts despite a volcanic eruption of stem cell biology, cellular genetics and molecular biological science.

Indeed and in fact, on an intracellular level mechanobiologists have demonstrated in tissue culture that simply distortion of the cytoskeleton (Fig.6) of cultured osteoblast progenitor cells can elicit the releases calcium and nitric oxide (NO), both well known morphogens and stimulate differentiation and other physiologic functions *in vitro* in a number of tissue cultures besides bone. (Angele, 2006) It should not be surprising then that significant osteogenic morphogenesis occurs at the cellular level outside the periodontal ligament. It is important that residents and clinicians alike study the "new" biological sciences of cell genetics and molecular biology because what can be "seen" in the mind's eye, can be engineered by the clinician artistic view and shared by the specialty's wider vision.

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 during the transitional or mixed dentition. At this time phenotype changes dramatically. PAOO™ presents no age preference or restriction since surgical healing *per se* reverts all tissue to a kind of "neonatal" state.

Arch development from the palatal aspect may be employed simultaneously with conventional labial therapy. However, singular use of the Series 2000® appliance 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.

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* See Pigliucci, 2001

GENETIC EXPRESSION AND PHENOTYPIC PLASTICITY

It is also 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 n the biological system. Phenotypic plasticity is the "property of a given genotype to produce *different phenotypes* in response to *distinct (different) environmental conditions"* * (emphasis added) Pathosis and clinical therapy both qualify as determinate environmental conditions. In the case of 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 Max 2000 appliance. In the case of the PAOO™ procedures the surgical trauma itself and the actions of growth factors in the allograft qualify as environmental conditions sufficient to overcome canalization (buffering) of the developmental path to render a given clinical result, (alveolar bone *de novo*). Thus, it is quite logical and consistent with molecular biology and cellular genetics that different qualitative and quantitative perturbations would necessarily elicit different phenotypic clinical outcomes.

CONCLUSIONS

We have proposed that the ultra-light, self limiting force of the embedded nickel titanium springs in the appliance has activated a bone "mechanostat" phenomenon described by Melsen, the Frost-Jee collaboration(2002), and by others, Pavalko, 2002, Chung, 2003) in variable contexts. The appearance of woven bone in this E.R. case histological section and analysis of the fractal pattern therein suggest that remodeling of the alveolar bone was indeed occurring when the sample was taken.

This serendipitous observation gives serious pause to claims about the behavior of bone around teeth which are moved orthodontically. Specifically its immutability and the tendency of dental arch "expansion," to cause gingival recession must be reconsidered in light of this clinical demonstration. Some "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 to "recapturing" original phenotype with a Max 2000 or engineering it *de novo* with "bone morphing" and "face morphing" **(Figs. 13, 14)** the ambiguities of "expansion" always haunt us. Whether that be vexacious to the reader or enigmatic to the practicing clinician, this seems axiomatic:

"expansion" may "cause" bony dehiscence sometimes, but not forseeably in the individual and clearly not always (Djeu and Hayes, et. al., 2002)

The practical asset this appliance has is that it acts as an "orthopedic machine" eliciting "alveolus development" in an effort to obviate bony dehiscence and periodic adjustment pain associated with other RPE appliances. The problems with such appliances derive from their reliance upon *mechanical* ratcheting instead of *biological* engineering. In that respect the PAOO™ and Series 2000® orthopedic appliances are "not your father's orthodontics". 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 Series 2000® appliances and surgical orthopedic innovations of Wilcko-Ferguson may well emerge as progressive ideas whose time has come in 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 non-extraction preference. However, in respect to epistemic issues posed by Popper (1971, 2002)

a case of one or hundreds neither fully indemnifies a debt of uncertainty nor establish one perspective as intellectual coin of the realm. To the thoughtful facial orthopedist and modern biological 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 rethought, viz. 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 non-extraction alternative.

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 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.

Meanwhile, the fact remains: clinical evidence of phenotypic changes and labial alveolus remodeling have been associated with PAOO™ surgery and the Max 2000® appliance, clinical phenomena philosophically consistent with a “whole bone” approach to dentofacial orthopedics.

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Appendix I: Tissue Engineering: The Non-Surgical Alternative

Figures

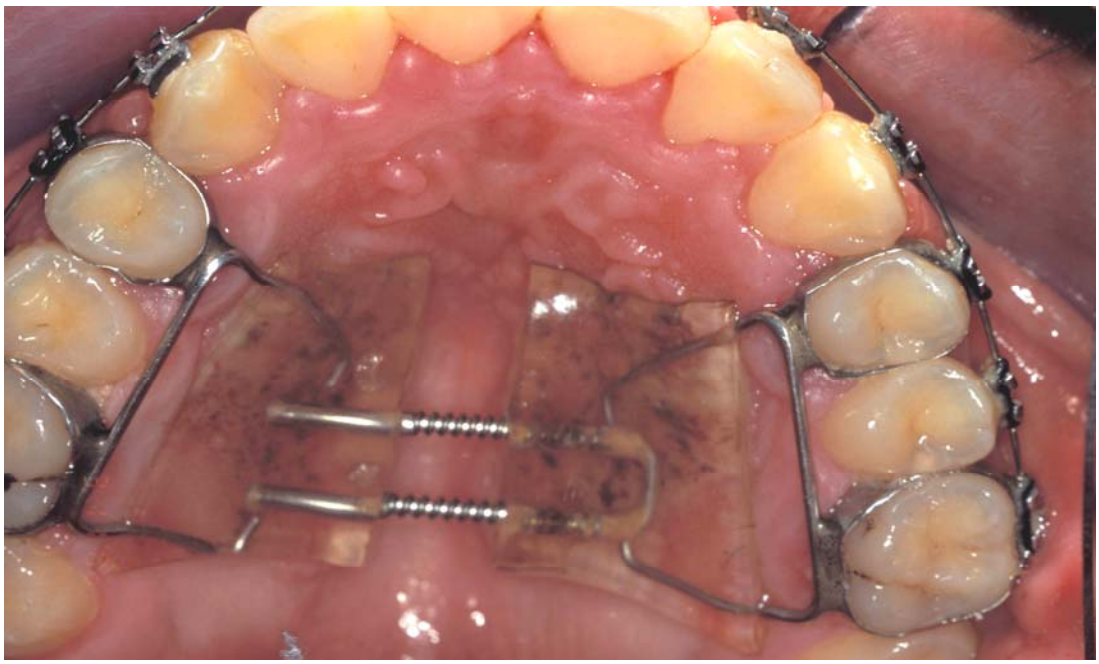


Figure 1 Max 2000® appliance applied ultra-light pressure to palatal alveolus. No attempt at maxillary expansion is made beyond the biologic signals transferred to the buccal plate through the alveolus spongiosa. The bands on teeth are for retention only and the buccal arch wire is passive. (Orthodontist: Neal C. Murphy, DDS, MS, Oxnard-Ventura, California, USA) (Max 2000® is a registered trademark of Dr. Michael O. Williams, Gulfport Mississippi.

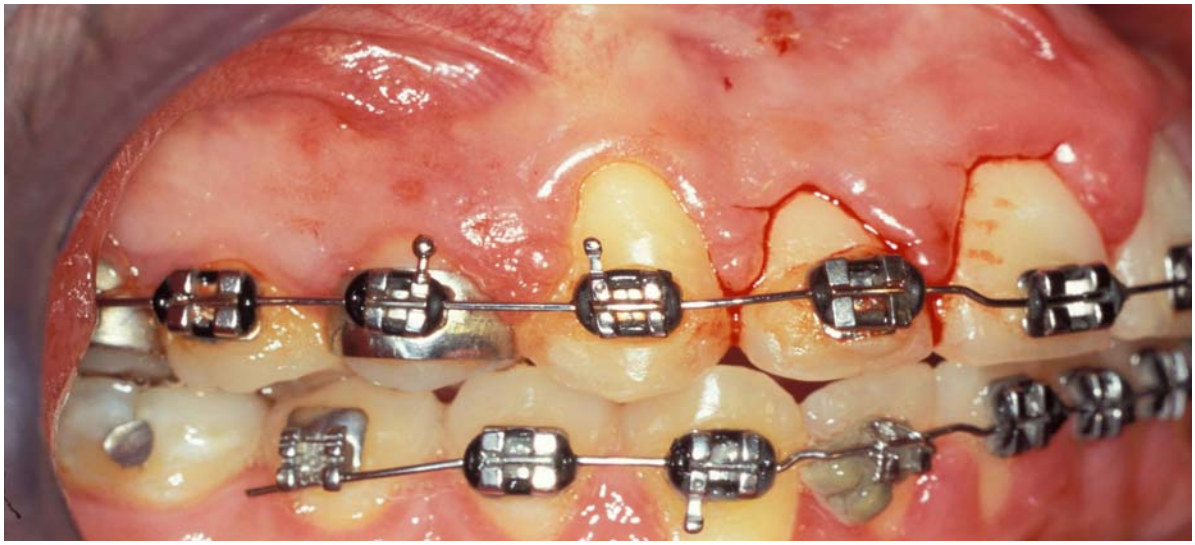


Figure 2 Case #1 E.R. Noncompliant 18 y.o. Hispanic male. Arch wire is passive.

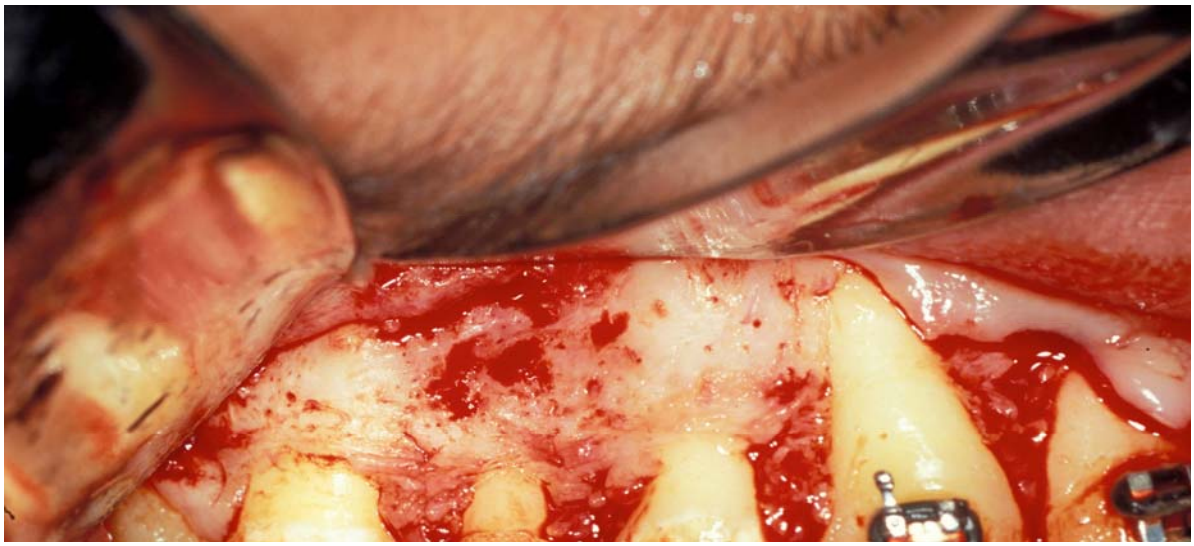


Figure 3 Case #1 E.R. Periodontal surgery reveals buccal bone where conjecturally palatal alveolus forces were transferred to buccal cortical plate, flexing the bone to stimulate osteogenesis in areas of periosteal compression. Note marked dehiscence where labial arch wire “pulled teeth beyond phenotypic range.
(Periodontal Surgeon: Dr. Neal C. Murphy)

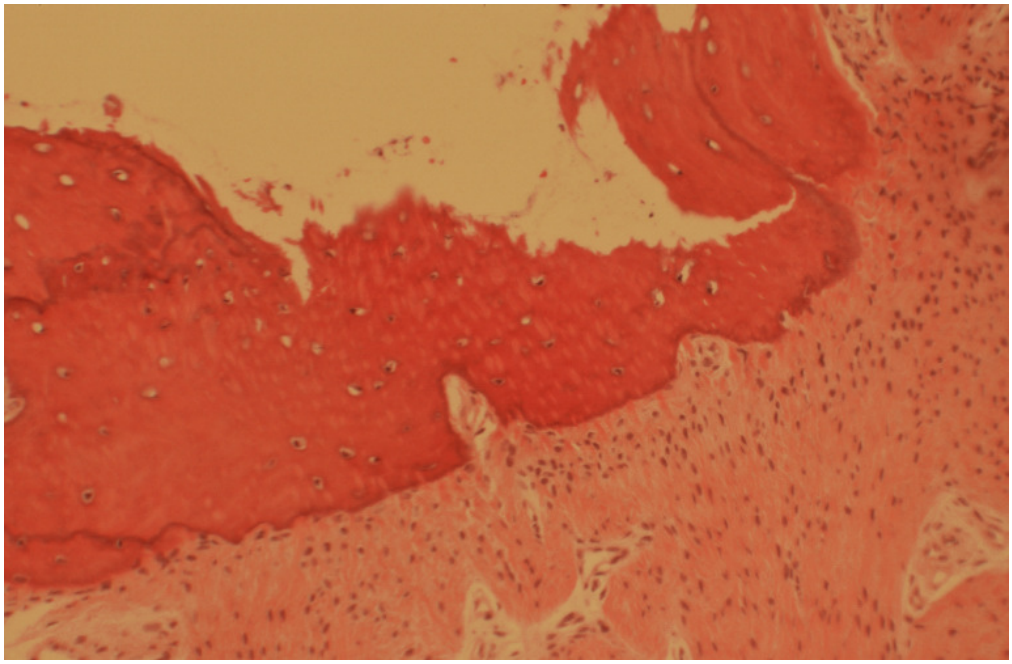


Figure 4 Routine H&E histological section at buccal aspect of tooth #5, labial to Max 2000® palatal alveolus development appliance. Note absence of lamellar pattern characteristic of mature bone.

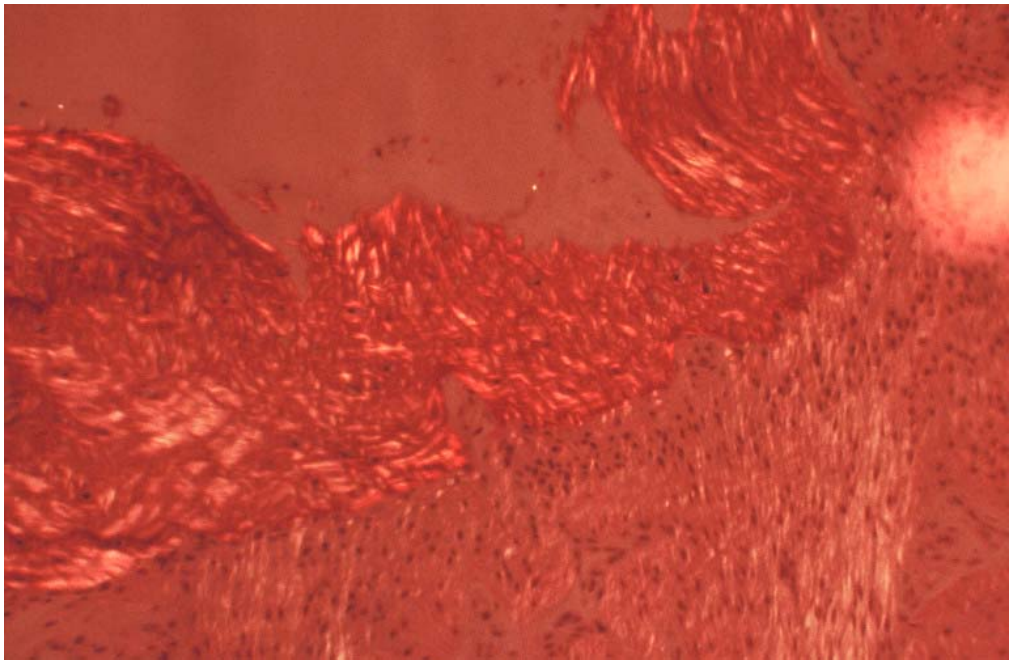
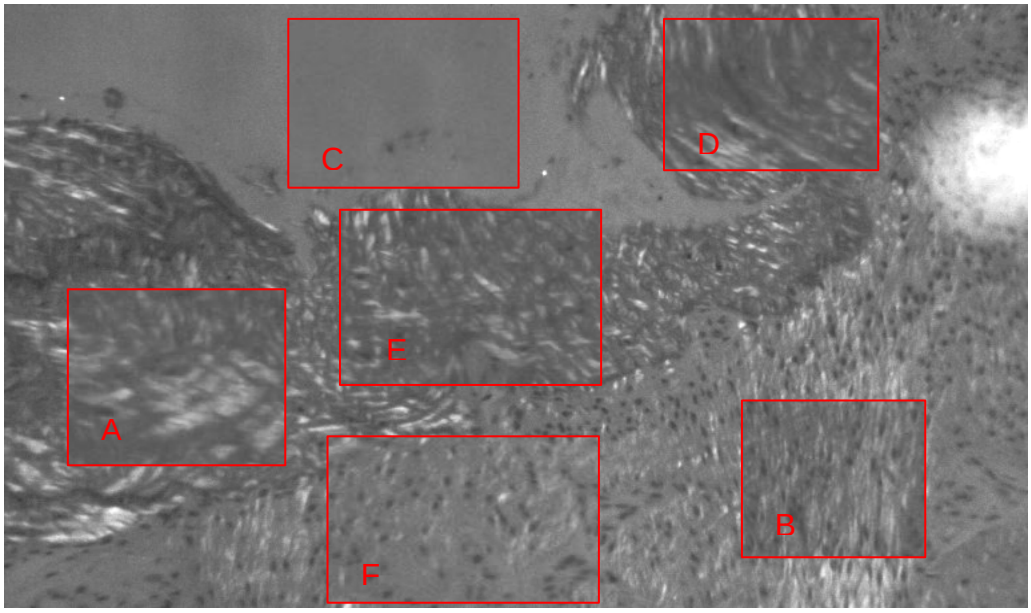


Figure 5 Polarized light section of specimen above. Note “woven bone” pattern characteristic of immature bone and regional osteogenesis.



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

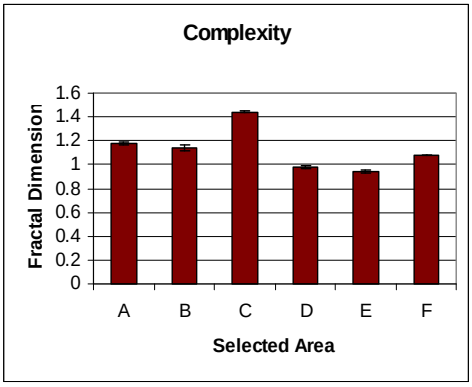


Figure 6 Fractal Analysis demonstrating bone remodeling. (Collegial gratitude is extended to James Borke, PhD, Medical College of Georgia for his consultation and the fractal analysis.)

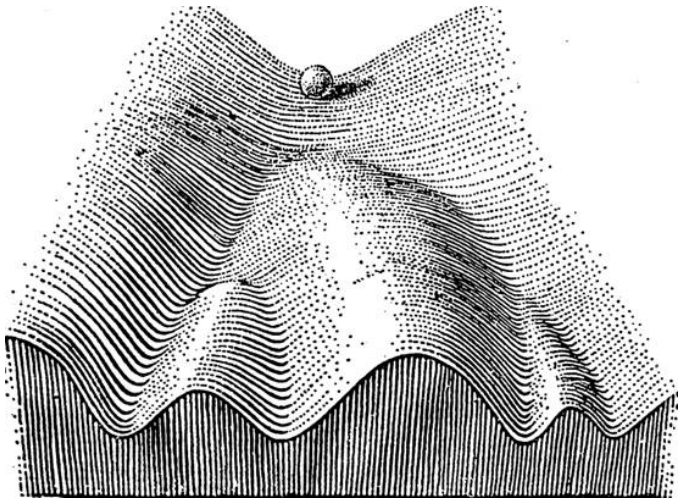


Figure 7 Waddington's Epigenetic Landscape metaphorically illustrates the fate of tissue development as a series of alternate ("canalized")fates buffered by variable heights of ridges that represent "environmental perturbations" altering the progress of a rolling ball the "genetic component" of morphogenesis. The height of each canalized path represents a kind of "energy of activation" threshold needed to alter the canalized" developmental path. Genetic expression interacts with and indeed is defined by environmental (epigenetic) influences. Genetic expression is not represented by a fixed phenotypic form directed by genotype. Thus the question is not, "…nature or nurture?", but rather "nature and nurture interacting together to manifest variable phenotypes. Thus, genotype is not so much a "blueprint" of phenotype but rather an "instruction manual" on how tissue should "act" in variable environments to manifest various phenotypic potentials.

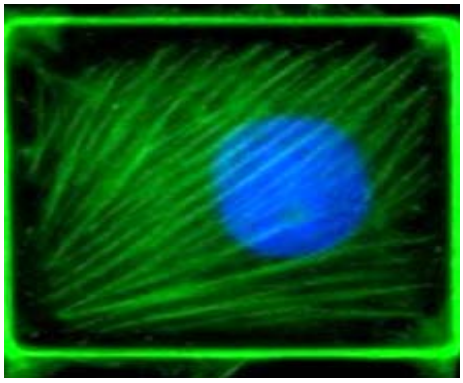


Figure 8 Demonstration of cytoskeleton deformation *in vitro*. Ho: this phenomenon in alveolar bone *in vivo* facilitates altered genetic expression as optimal response" is elicited by ultra-light orthopedic forces. Bending bone bends DNA and intracellular proteins altering genetic expression to change regional phenotype. With apologies to Wolff and his famous law, ("Form follows function.") it seems that on an intracellular level, "Function follows form". Green: actin filaments, Blue: nucleus (See Pavalko, 2002 and Pigliucci, 2001)

A. The Adolescent "Growing" Face

B. The Adult "Mature" Face
(The Same" Dental Entity" as Fig. 9A)

Figure 9 demonstrates the importance of developing a "large" smile that the adolescent can 'grow into" rather than a "small adolescent smile that the patient grows out of" The adolescent smile (above, A), seemingly disproportionate smile in youth is also compatible with the enlarged face (above, B) The pure "dental entity" is the same in both faces; the teeth have not changed but the face certainly has. We propose that the broad smile defines beauty in both age cohorts, and that extraction may very well have ablated any development of the adult alveolus. Further we suggest that the "larger smile" reflects an emerging Western archetype for facial esthetics in the 21st Century, a standard not coerced on patients by inveterate "non-extractionist" ideologues but rather a simple, natural and popular expression of cultural ethos.

(Photos and quote compliments of Dr. Michael O. Williams, Gulfport Mississippi, USA, inventor of the Series 2000® dentofacial orthopedic appliances. Used with permission. See: www.gulfcoastorthodontics.com)

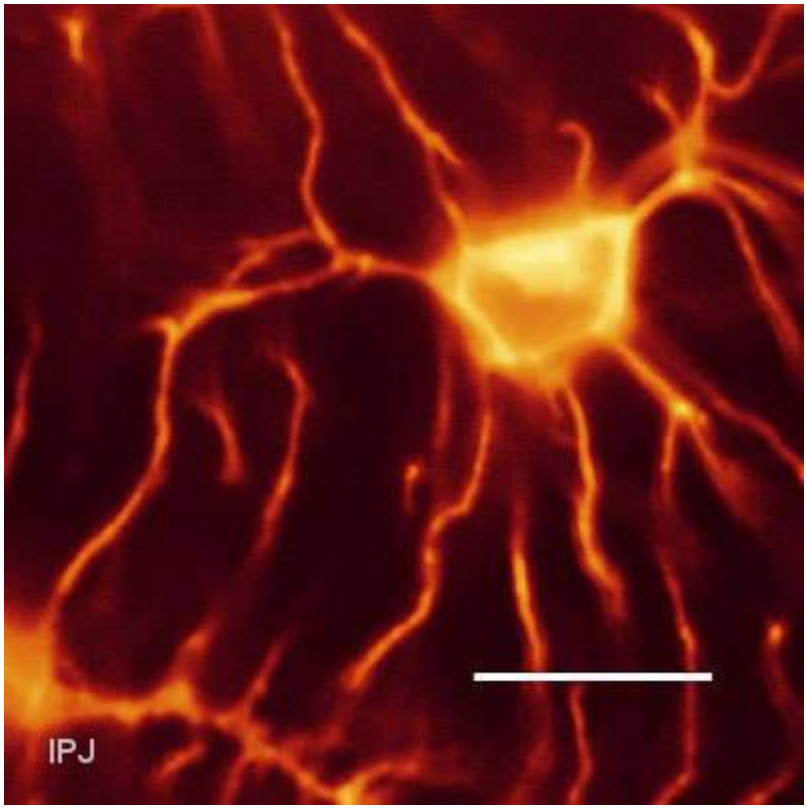


Figure 10 : Single osteocyte with cannaliculi. Note: Gap junction between two osteocytes in upper left quadrant of image. This suggest that bending the alveolus will alter ion flux within the osteocyte-cannaliculi syncytium acts as a kind of "neural network" transduction element changing mechanical energy to biochemical energy sufficient to alter regional alveolar phenotype. RH 414 staining and CLSM. Bar = 10 µm

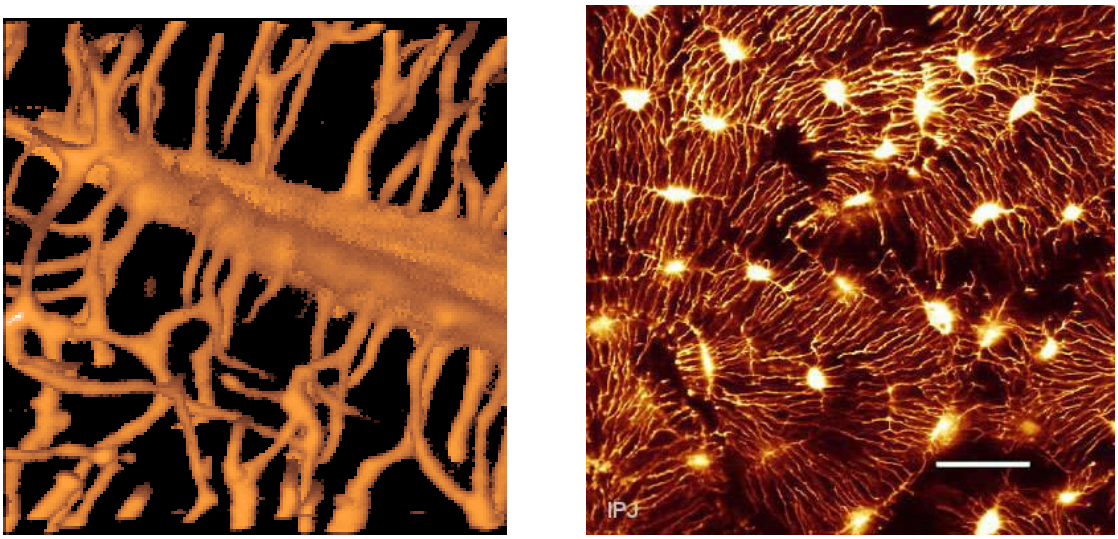


Figure 11 Left: A 3-D rendering of osteocyte with cannaliculi Right: Panoramic view of osteocyte-cannaliculi syncytium among osteons (Haversion systems)

Source: Poster No 64, International Poster Journal, 3(1): Poster No. 64, 3/15/01

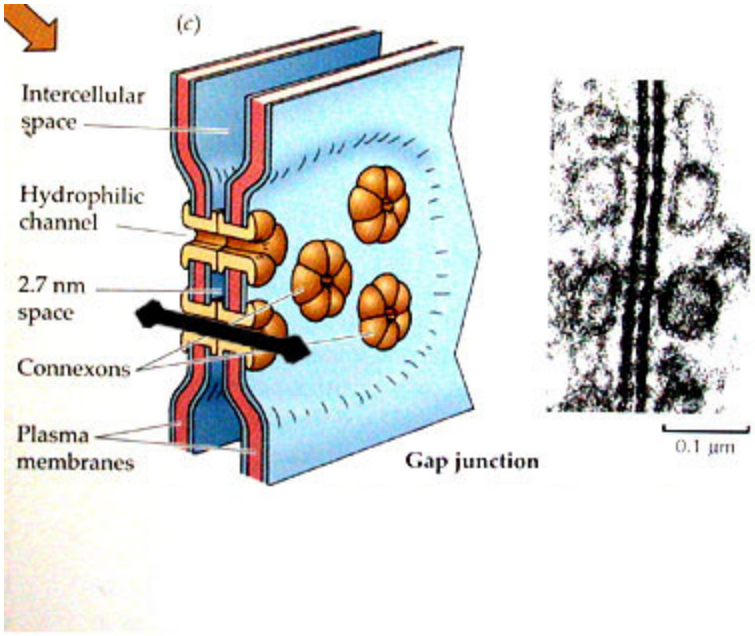


Fig.12 Schematic and photomicrograph renderings of a gap junction connection between cells. We hypothesize that gap junction between osteocytic cannaliculi in bone can act as a kind of neural network tansducing the mechanical energy of clinical force to the alveolus into biochemical morphogenetic factors that alter regional alveolar phenotype in young patients and in the healing periodontal wound of non-growers. If wound healing recapitulates regional ontogeny (Murphy NC, 2006) then this could be the cytoskeletal transduction mechanism.

Source: http://academic.brooklyn.cuny.edu/biology/bio4fv/page/gap-junctions.html

Appendix II: Tissue Engineering: The Surgical Alternative

PAOO™ 3x - 4x faster movement of teeth, less root resorption and better quality than conventional orthodontics, more stable because regional phenotype is altered by manipulation of genetic expression.

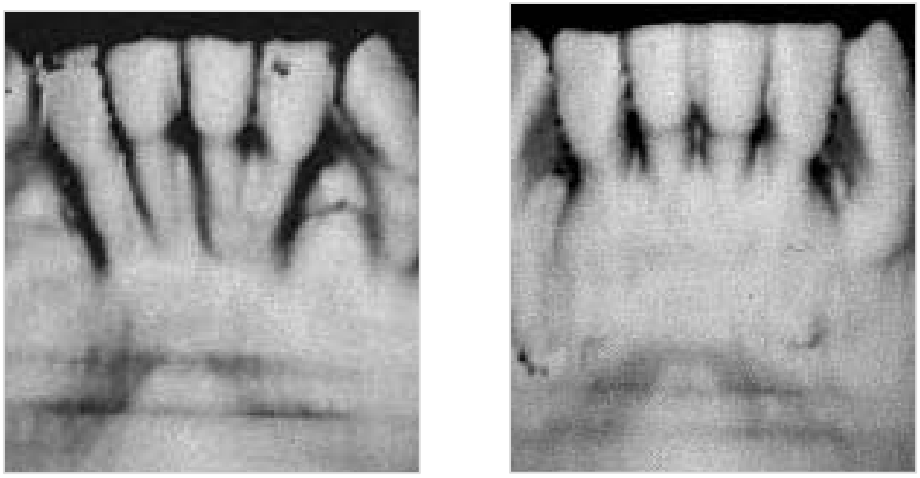


Figure 13 "Bone Morphing" altered regional phenotype after lower incisors were moved labially through a periodontal bone graft. Left is *before* orthodontic treatment; Right is *after* treatment. Most orthodontists would guess the reverse to be true but this reflects the popular conception that phenotype is immutable. The alteration of alveolar phenotype was possible because *bone healing recapitulates regional ontogeny.* (See Murphy, 2006)
(Surgeon: Dr. M. Thomas Wilcko, Orthodontist: William M. Wilcko, Erie, PA, USA, used with permission)

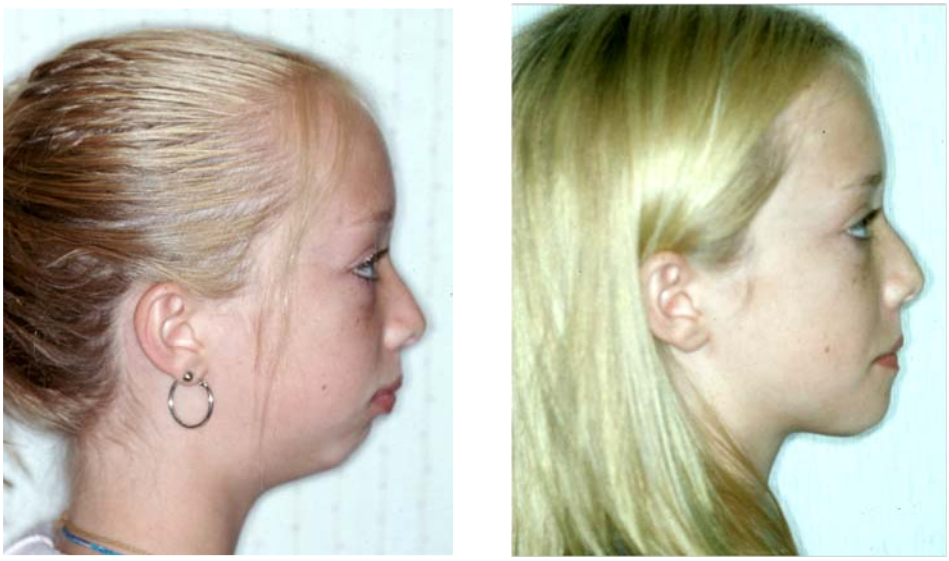


Figure 14 "Face Morphing" Note before and after facial esthetics when orthodontic forces are applied to bone as teeth roots (alveolus functional matrix) are moved through a healing bone graft. No orthognathic surgery was rendered in this case. Only simple periodontal surgery, invasive only to a depth of ~2mm was employed. Technically the surgery is described as *a full thickness mucoperiosteal replaced flap with osteoplasty (in this case "corticoplasty"* , or specifically, *selective alveolar decortication (SAD)* after Ferguson.

Surgeon: Dr. M. Thomas Wilcko, Orthodontist: William M. Wilcko, Erie, PA, USA, used with permission