Non-Surgical Alveolus Development and Tissue Engineering for Dentofacial Orthopedics: Clinical and Histological Evidence of Efficacy of Series 2000® Appliances

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PREFACE

Clinical tissue engineering in dentofacial orthopedics is in its infancy; most research presently is *in vitro* and pharmaceutical. But the stage is set for *in vivo* bone engineering by the efficacy of regenerative procedures and contemporary medical orthopedics. The alveolus and consequent dentofacial form lives, thrives and dies by the grace of dental root positions (see: Moss[1]); *ergo* physiological forces applied to the alveolus as teeth roots move labially conceivably stimulate labial bony remodeling sufficient to reduce or obviate indications for bicuspid extraction therapy. Yet the conventional wisdom based on work by Zachrisson[2] et al. suggests that the labial alveolus is immutable and labial movement causes bony dehiscence. Data in this case study and the work of Wilcko-Ferguson[3], Fuhrmann[4] and others suggests that the alveolar "envelope" or limits of alveolar housing may be more plastic than previously thought. Phenotypic plasticity is manifest by epigenetic perturbations during development and genotype promises a myriad of forms; not a singular fixed phenotype.

By definition, all scientific truth is tentative, thus any 21st Century "breakthroughs" in both surgical and non-surgical approaches merely refine existing orthodontic treatment protocols based upon prior, but evolving knowledge; that knowledge is power and modern biotechnological power proffers the ability to "engineer" many alternative phenotypic potentials. The difference between pathologic form and therapy is the ability to control and predict treatment outcome. The therapy herein mimics the principles applied in the treatment of *talipes equinovarus* (club foot) in that it attempts to redirect a pathologic epigenetic growth trajectory[5]. Since facial morphotype evolves even throughout adulthood (see: Behrents, R. et. al.[6]) it may be logically conjectured that a threshold microstrain applied to bone, even in adults, can be osteogenic; in that respect one must ask if the alveolus is different than long bones and if manipulated to an alternate form will it revert to original morphotype or remain as a "buffered" form of original epigenetic "intent". (see Waddington[7]) Certainly from the studies of Little et al,[8] routine extraction therapy 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 than previously thought. This case of one proves such therapy, via continuous low- force magnitude may be an appropriate starting point.

And if this case is indeed an exemplar of such labial bone osteogenesis then the rationale for routine therapeutic or serial bicuspid extraction may need to be refined or categorically rejected in some cases. The extraction of bicuspids is well established in contemporary orthodontic protocols but has remained controversial for over 100 years. Nonetheless, it represents an anathema to non-extraction purists who compare extraction to ablation experiments in classic embryology. The "truth", as usual, lies in rational, moderate, and prudential consultation with patients, a respect for individual biodiversity and the patients (or parent) preeminence the final arbiters of facial esthetics. Technically, whether data are anecdotal, intuitive, empirical, or controlled in vitro, all modest scientists must admit that experimental data often fail to capture the entire heterogeneous domain of mechanisms responsible for facial morphogenesis. That is to say, epistemologically one cannot "prove" something does not exist'; one may only "prove" that any given hypothesis has failed to document existence (i.e. one fails to disprove a null hypothesis). Yet an example of one "proves existence". However prediction and quantization of truth, in this case the potential to stimulate labial bone growth with palatal pressure, may never be fully knowable for any given individual patient. Nonetheless if such osteogenic development is possible, all the clinicians can and should, we contend, approximate a stylistic "form" appropriate to each individual patient not an arithmetic mean derived from a Gaussian frequency distribution.

Finally, where belief values are dynamic in the flux of a postmodern pluralistic culture, accommodation to individual psychosocial needs may actually trump any scientific basis for clinical care. That is, a plethora of treatment styles, successful on an empirical basis Enhanced conceptual development of this clinically successful, evidence-based, and popular regimen of bone tissue can precede and even appear to contradict any scholastic apologia with impunity.

An Old Concept; a New Scientific Rationale

Over the course of a century a major philosophical schisms has served as an abiding source of intellectual dialogue (and unfortunately even devolved into occasional ad hominem diatribes which this presentation endeavors to avoid). On one side of the debate many 20th Century orthodontists limited their mission to tooth movement and extraction of teeth. This reflects one popular philosophy that supporting bone is immutable and necessitates the sacrifice of teeth to "fit" into a fixed phenotype of bone. (e.g." You have too many teeth for such a small jaw.") A pernicious side effect of this philosophy, routinely or injudiciously applied are: significant relapse after 20 years and unaesthetic flattening of the lower facial profile, which produces a premature aging appearance in the 3rd and 4th decades of life. Another philosophy (Moss's Functional Matrix Hypothesis) contends that the bone follows the movement of teeth in health as water conforms to the matrix in which it is contained. Indeed, within reason, standard bone ontogeny itself developed from the times of Wolf[9]and Roux[10] suggests that the dental roots can be seen conceptually as both functional and spatial matrices for alveolar morphogenesis.

We propose that on a molecular biological basis, threshold microstrain releases endogenous growth factors including not only bone morphogenetic protein (BMP) in stressed bone but also a number of other complex proteins referred to as "mechanosomes"[11]. This may occur by altering mechanosensitive ion channels in the cell membrane or even induce nuclear events since morphogenesis has been cited as a transcription level phenomenon. If indeed an "optimal osteogenic response" is elicited by the appliance in question it may up-regulate mesenchymal cells to differentiate into osteoblasts when placed in a field of applied orthodontic (dentofacial orthopedic) force rather than merely recruiting osteoblasts in situ. This (therapeutic) epigenetic perturbation may be facilitated by alterations in intracellular tensegrity (see: Ingber et. al.)[12] and integral to altering stable alveolar form. Yet the underlying molecular biologic mechanisms are still not as clearly defined as they should be. Thus, impetuous abandonment of traditional extraction therapy in severe Class II maxillary saggital excess or bimaxillary protrusion is imprudent at best. Hence we note the manifest need for wider dissemination of data among basic scientists, biomedical engineers and experts in molecular, genetic and cell biology working in synergy with progressive, thoughtful clinicians.

Fig. 1 Above left shows a palate we propose is pathologically altered during development through the transitional dentition. Above center demonstrates how a growth trajectory can be altered with continuous ultra -light force conceivably transferred to the labial alveolus with a
Series 2000® appliance, (See: Melsen, 2002, citing Frost and Epker). Figure far right illustrates at the cellular level how an altered cytoskeletal tensegrity is effected when cells are manipulated by an external matrix in vitro.[13] (See: http://www.childrenshospital.org/research/ingber)

CONCLUSIONS & QUERY

Subjectivity is the essence of art, partially explained by science but ultimately intuitive and largely inviolable by scientific reductionism. This case merely presents histological evidence of alveolar osteogenesis and suggests that the art of one practice style (viz.Dr. Williams') has a basis in scientific fact. We posit that the ultra-light, self limiting force

of the Series 2000®, in concert with the "mechanostat principle" of Utah paradigm, may have captured the threshold microstrain (500-1,000) necessary to differentiate mesenchymal stem cells to functional periodontal and periosteal osteoblasts capable of altering regional alveolus phenotype. Clinical tissue engineering will render 21st Century dentofacial orthopedics more discrete, predictable and professionally rewarding. This presentation clearly demonstrates that such a hypothesis has some empirical basis and represents a kind of serendipitous "proof of principle". The burden to disprove universality now lies with academics and intellectual clinicians, who, through a dialectical synthesis, may embellish, refine, truncate or flatly reject the legitimacy of the conjectures herein. Only time will tell how prescient these concepts will eventually prove to be. Meanwhile, the fact is: clinical evidence of remodeling of labial bone has been associated with the Series 2000® appliance. It is ironic that emerging concepts in molecular biology may simply explicate molecular biologic mechanisms which Edward Angle could only intuit a century earlier when he advocated non-extraction therapy.

MATERIALS AND METHODS

Fig 2: (Right) A Series 2000® appliance was removed after 15 months in a noncompliant hygiene patient. Since no active adjustments were made by a clinician during that time, the appliance acted as a kind of osteogenic "machine", widening the dental arch without producing any expected bony or soft tissue dehiscence. Indeed the bone biopsy below actually demonstrated woven bone characteristic of active remodeling.

TREATMENT TIMING

Optimal times to treat the growing child, measured in dental age not chronology, for optimal effects, is during the transitional or mixed dentition. 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 load (dental plaque) and addresses orthopedic problems directly instead of camouflaging dysmorphic alveolar form with altered tooth positions.

Fig. 3 Above Left: Clinical appearance of inflamed gingiva after noncompliant hygiene with a Series 2000® appliance for 15 months. Above Right demonstrates bone formed on the labial surface of the teeth subjected to ultra-light force and presumptive "mechanostat"-induced microstrain sufficient for osteogenesis. Biopsy was taken from the labial surface of the bicuspid alveolus and periodontal membrane for microscopic analysis with conventional and polarized light by an independent and unbiased oral and maxillofacial pathologist.

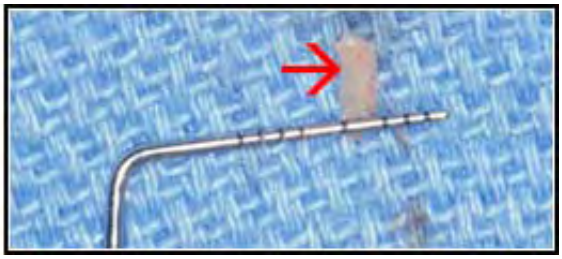
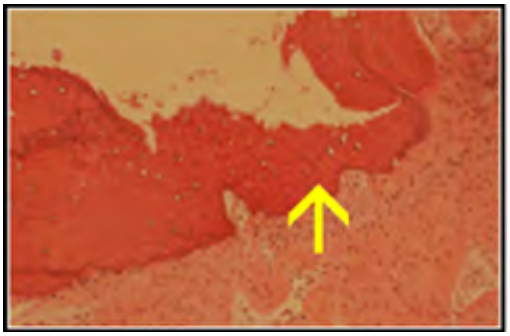


Fig. 4 Above Left: Arrow indicates location of labial alveolar bone specimen subjected to microstrain sufficient to simulate osteogenesis by the Series 2000® Appliance. Pay particular attention to the bony dehiscence of the canine which was not part of the Series 2000® treated tissue. The philosophy of the Williams' protocol is based on research which contends that expansion is best performed in the bicuspid/molar arch segments and that the principle of inviolable transverse intercanine dimension is neither denied nor affirmed. Above Right: Specimen ready for fixation and microscopic analysis. (Orthodontist and surgeon: Dr. Neal C. Murphy, Los Angeles)

BELOW: Histological Analysis of Biopsy Specimen from Series 2000®

Non-surgical dentofacial orthopedic appliance



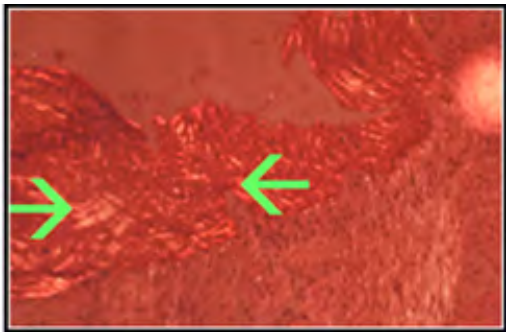


Fig. 5 Above Left : demonstrates young bone (yellow arrow) with conventional H & E stain. Above Right: Same histological specimen under polarized light demonstrating "woven bone" pattern (green arrows). The appearance of "woven bone" is important because it suggests immature remodeling; preexisting bone would demonstrate a mature "lamellar" pattern.

“Face Morphing”

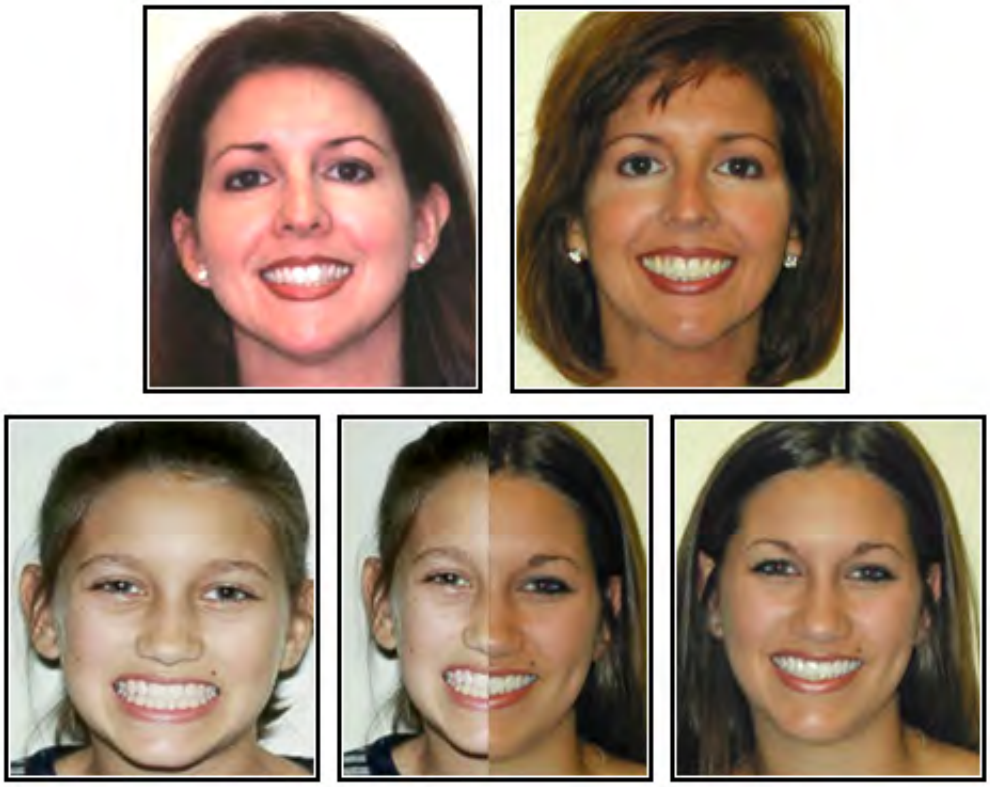


Fig. 6 Top: Note changes in facial appearance after treatment with the Series 2000®. This change may be due to labial alveolus remodeling, not just tooth movement; the case study is representative of other facial orthopedic treatment outcomes.

Ho: development of the dentoalveolar complex with physiologic force produces the threshold microstrain as described by the Frost-Jee “Utah Paradigm” eliciting an elusive but “optimal response” of alveolar bone justifying non-extraction therapy.

Fig 6 Bottom Comparison: Note how the absolute dimension of the smile defines the adolescent face yet also fits esthetically well with the more mature adult face. This illustrates the maxim of Dr. Michael O. Williams that facial orthopedists should “create an adult smile the adolescent can grow into, not an adolescent smile the adult grows out of.“ (Orthodontist: Dr. Michael O. Williams, Gulfport, Mississippi USA)

ADDENDUM

From a psychosocial perspective it is important to remember that subtle changes in facial form, strongly affected by the lower face, are often noticed by patients and peers only subliminally .Once sensitize to the issues of facial development patients may report “fuller lips”improved nasal respiration and “better cheek bones” (zygomatic processes). These are common unsolicited observations made by patients and parents alike which are not inconsistent with facial orthopedic principles. Facial orthopedic research is ripe for studies to clarify exact causal connection within the non-extraction protocols because this case suggests that alveolar bone remodeling and even patient testimonials may have a basis in biologic fact.

Quo vadis?

REFERENCES AND SUGESTED READING

Help yourself to the attached list of references. Contact Dr. Williams or Dr. Murphy personally for a more academic and comprehensive list concerning dentofacial orthopedics and/or in vivo tissue engineering for 21st Century dentistry

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