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Orthodontics at a Pivotal Point of Transformation

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Abstract

The profession of orthodontics is projected to face a multitude of challenges. Do cyclic forces accelerate the rate of tooth movement and hence the speed of orthodontic treatment? Would bioengineered cementum and dentine be a solution to root resorption? What would orthodontics be like when bioengineered periodontal ligament and alveolar bone become clinical practice, or one day, entire teeth are bioengineered? Would it be possible to selectively differentiate stem cells into osteoblasts or osteoclasts by either static or cyclic forces? What is the new demand on orthodontic expertise with increasingly automated appliances? What will be the impact of the next generation of dental implants or rapid prototyped crowns on orthodontics?

A century ago, Edward Angle's practice of fixed appliances, along with other seminal contributions, such as functional appliances, established the profession of orthodontics. Today, the biophysical principles of orthodontics remain largely unchanged from Angle's era, despite incremental refinements of brackets and wires. The paucity of fundamental innovations in orthodontics for decades presents intrinsic risks for the profession. This review will identify challenges for contemporary orthodontics and delineate strategies for the profession to evolve in an era of unprecedented scientific and technological advances, and serve as a call to action for the orthodontic profession.

1. Orthodontic forces since Angle's era - force frequency yet to be considered

Orthodontic forces delivered today by Ni-Ti springs are based on the same principle as forces delivered in Angle's Ribbon arches - i.e. static forces that are constant over time until decay¹. A series of experiments with data published in peer-reviewed literature in orthodontic, orthopaedic, and bone biology journals over the past decade, indicate unequivocally that cyclic forces, with oscillatory magnitude, accelerate the rate of bone modelling and remodelling at rates that are far greater than static forces^{2–10}. Recently, data

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from another laboratory further support the notion that bone remodeling and tooth movement can be accelerated by cyclic forces ¹¹.

Cyclic forces differ from, and should not be confused with, intermittent forces. Intermittent forces, as defined in the orthodontic literature, are static forces applied for some time and then removed for some other time ¹². Cyclic forces, on the other hand, change magnitude rapidly. Cyclic forces have also been referred to as pulsatile forces or oscillatory forces. The frequency of both intermittent forces and static forces is zero at all times. The frequency of cyclic forces is always greater than zero. Why does force frequency matter? To answer this question, an appreciation of the fundamentals of mechanics is necessary. Force = mass $\times$ acceleration. Counter-intuitively, force is not a measurable property. One can only measure the effects of force such as strain, defined as changes in a structure's deformation over its original state. The definition of strain can only be satisfied by a change in the structure's length, which is only inducible repeatedly by a change in force magnitude (cyclic forces), instead of a constant or static force. A physical force has a total of five fundamental properties: magnitude, direction, frequency, point of application and duration. All properties of forces have been studied extensively in orthodontics, albeit that many aspects are still poorly understood, with the exception of force frequency. With frequencies greater than zero (e.g. 1 Hz, 30 Hz to the infinite), cyclic forces impact cells multiple times. Static or intermittent forces have zero frequency, and therefore impact cells only once, regardless of the duration of force application ¹³. When a static force is removed and applied again, it provides another stimulus to a cell. This seemingly trivial difference in force frequency between cyclic forces and static forces leads to drastic differences in cellular and tissue responses ⁶⁻⁸. This has been demonstrated in both orofacial bones and long bones ^{7,8,14,15}. Multiple cycles of change in force magnitude or cyclic forces are of significance because cells respond more readily to rapid oscillation in force magnitude, than to a constant force ¹⁵. A force propagating through a biological tissue is transduced as tissue-borne and cell-borne mechanical stress which in turn induces interstitial fluid flow ¹⁶. Although fluid flow is a current focus of the mechanotransduction pathways, its anabolic or catabolic effects rely upon deformation of extracellular matrix molecules, transmembrane channels, cytoskeleton and intranuclear structures ^{15,16}.

Why does the average orthodontic treatment take 1.5 to 2.5 years to complete, whereas a typical bone fracture heals in 1–2 months, and involves a far greater amount of bone modeling and remodeling than orthodontic tooth movement? The answer to this question is currently unclear. Nonetheless, one must have a clear understanding of modeling and remodeling inducible by static and cyclic forces, along with wound healing, before attempting to answer this question. Microfractures likely take place during orthodontic tooth movement although microfractures have not been studied in depth in orthodontics. If one agrees that the duration of orthodontic tooth movement and dentofacial orthopaedics is a function of the rate of tissue modeling/remodeling, then it follows that the speed of orthodontic treatment can be accelerated by ways that accelerate tissue modeling/remodeling. Are cyclic forces capable of accelerating orthodontic tooth movement and remodeling of craniofacial tissues? Converging data from several laboratories suggest so. All characteristics of mechanical forces, including their magnitude and duration, have been examined in experiments and clinical practice of orthodontic tooth movement and

craniofacial orthopaedics, with the sole exception of force frequency, until the past decade or so⁶. At present, ongoing clinical trials are in place to investigate the efficacy and safety of cyclic forces in the potential acceleration of orthodontic tooth movement. The outcome of these clinical trials, if positive, could represent a departure from a paradigm created by Edward Angle and his colleagues on the use of static forces in orthodontic tooth movement, a concept that has not been challenged for over a century of orthodontic practice.

2. Impact of stem cells and regenerative medicine on orthodontics

The field of orthodontics has experienced the impact of recent technologies including miniscrew implants, that act as immovable anchors for tooth movement^{17,18} and the induction of orthodontic tooth movement by multiple sets of active removable appliances¹⁹, which do not require brackets and wires that are the bread and butter of fixed appliances. Developments in the fields of stem cells, tissue engineering and regenerative medicine will undoubtedly impact on orthodontics. First, novel force delivery systems, including cyclic forces as discussed above, have the potential to modulate not only traditionally considered, orthodontically relevant cells, primarily bone cells, cartilage cells and fibroblastic cells, but also their progenitors known as stem cells. Stem cells are present in dental pulp, periodontal ligament and alveolar bone^{20,21}. Hyalinization is a documented example of cell differentiation into the 'wrong' lineage by conventionally applied, static forces, given the observation that non-cartilage cells in the periodontal ligament are transformed into chondrocytes in hyalinization, thus halting orthodontic tooth movement²². Whereas orthodontic textbooks describe hyalinization as an undesirable biological process in orthodontic tooth movement, the mechanisms of hyalinization are poorly understood. Do stem cells differentiate into cartilage cells or do osteoblasts, fibroblasts or endothelial cells transform into cartilage cells? Stem cells are usually quiescent but can self renew or be activated by factors such as mechanical forces to differentiate into multiple different cell types²³. Would it be possible to selectively differentiate stem cells into osteoclasts and osteoblasts by controlling their redistribution during orthodontic tooth movement? One must keep in mind that osteoclasts and osteoblasts derive from different stem/progenitor cell populations: osteoclasts from the hematopoietic/monocyte lineage whereas osteoblasts are from the mesenchymal lineage. Understanding the intricacies between stem cells and their differentiated lineages will help design more efficient and effective force systems with the potential to accelerate orthodontic tooth movements.

Cell based or protein based therapies are being developed or are now available for the regeneration of multiple dental, oral and craniofacial tissues, including the periodontal bone. A newly regenerated periodontal ligament will surely also impact on orthodontics. Experimental approaches are being explored towards the regeneration of cementum, dentin, dental pulp and even the entire tooth^{20,21}. What would be the impact of these regenerated tooth structures or entire teeth on orthodontic treatment as we know today? If it takes 1.5 to 2.5 years for orthodontic treatment, would there be motivation for the placement of dental implants in esthetically pleasing positions or one day to have whole teeth regenerated in esthetically pleasing positions? Would bioengineered cementum and/or dentine be a solution for root resorption? Even the decision of tooth extraction vs. non-extraction may be impacted by recent interest by the general public to have dental stem cells from their

extracted teeth ‘banked’ or cryopreserved²¹. Would a patient more likely be receptive to tooth extraction since extracted teeth are sources of their stem cells? For cleft lip or cleft palate, craniofacial anomalies or TMJ, what is the impact of bioengineered bone and soft tissue grafts that promise to become a standard practice in surgical approaches in relation to orthodontics^{24–27}?

3. Call to action for the orthodontic profession

Although time is needed for any of these new technologies to mature, it is predictable that postnatal or adult stem cells, the offspring of the very cells that generated dental, oral and craniofacial structures in prenatal development, can be manipulated to regenerate the same structures in the adult. When dental implants became a therapy, multiple dental specialties competed to engage in the delivery of dental implant treatments. When new technologies related to novel force systems, stem cells and regenerative medicine become therapies, it is conceivable that different fractions of dental or even non-dental specialties may attempt to engage as service providers. Therefore, how can the orthodontic profession prepare for new therapies that derive from innovation? I suggest the following:

- Engage in the generation of knowledge potentially leading to novel therapies by encouraging faculty, practitioners and residents to pursue innovative research;
- Professional organizations and foundations should allocate resources towards innovative research, as opposed to incremental addition of existing knowledge, in the field of orthodontics;
- Incorporate stem cell biology, tissue engineering and regenerative medicine in the postgraduate education curriculum so that the next generations of orthodontists are armed with the knowledge to deal with the impact of new technologies;
- Provide continuing education courses to current generations of practicing orthodontists so that they are prepared for disruptive technologies;
- Collaborate and partner with funding agencies such as the National Institutes of Health (NIH) via the National Institute of Dental and Craniofacial Research (NIDCR) on orthodontically related initiatives such as dental, oral and craniofacial regeneration, temporomandibular joint regeneration and tissue engineering for the healing of craniofacial anomalies;
- Raise funds for the generation of new technologies that orthodontic organizations may take at least partial ownership.

Those who wrote the history of orthodontics have every reason to be proud of previous innovations such as fixed appliances, functional appliances, pre-angulated brackets, adoption of novel metal alloys and arguably computer-generated active removable appliances. The current generation of orthodontists will be judged by history in their response to a pivotal point in the profession as novel force systems, stem cells, tissue engineering and regenerative medicine develop into disruptive technologies that impact on the field of orthodontics in a magnitude that is predictably far greater than new wires or brackets. The American Association of Endodontics has endorsed regenerative endodontics

as a future direction for the endodontic profession. Whereas only history will tell whether new technologies impact a profession positively or negatively, a lack of action appears to be the least desirable approach. This article represents a call to action for the orthodontic profession.

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