

# The OrthodontiCell Story...



- **RANKL is proven in over 3 decades of studies as the key protein involved with accelerated tooth movement.**
- OPG is proven in over 3 decade of studies as the key protein involved with teeth stabilization.
- RANKL needle injection studies demonstrated that the optimal increase was 46% to achieve safely 2/3rds reduction of teeth straightening time.
- RANKL and OPG needle injection therapies are not practical due to high costs and need for multiple painful and inflammation causing needle injections.
- **OrthodontiCell has patented precise bioelectric control of RANKL (46%) and OPG expressions.**
- **Acquirer of OrthodontiCell can anticipate 20+ years of 80% gross margins and market sales leadership with a superior product.**

# The 3 Most Common Patient Problems



## Duration

Straight teeth are worth the wait, but standard procedures take 18-to-24 months with patient burnout during the process.



## Unwanted Shifting

Wearing retainers continually to keep teeth straight is not convenient. Without consistent wear teeth will become crooked again.



## Discomfort

Many patients experience pain and discomfort for days after aligner changes or brace adjustments.

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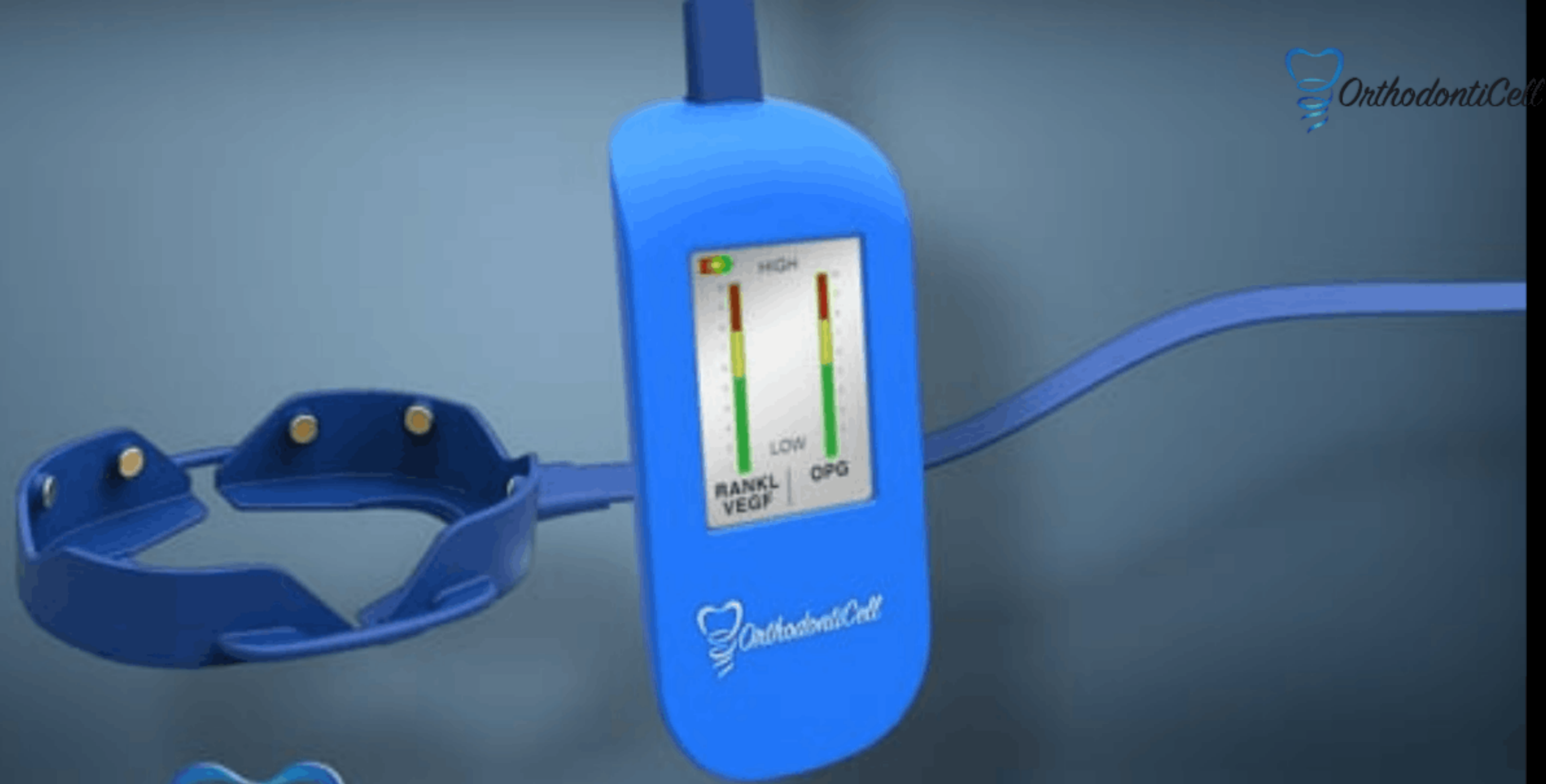
# How to Remain the Undisputed Leader in Aligner Therapy?

Partner with OrthodontiCell for faster and better outcomes with the **FIRST-EVER** technology that **straightens** and **stabilizes** teeth.



Bioelectric Accelerated Tooth Movement™ + Rapidly Enhanced Stabilization

John Marchetto DMD, Howard Leonhardt, Leslie Miller MD

 OrthodontiCell

# What is OrthodontiCell?



**A new and proven technology** that represents an important advancement in the orthodontic alignment market.

- 18-24 months goes to 6-9 months to straighten teeth.
- 70% decrease of discomfort.
- Freezes teeth straight with minimal use of retainers.
- Clinical trial data.





## Faster

treatment duration by 66%, meaning fewer office visits and fewer refinements in 2/3rds less time.



## Better

our technology's method of tooth movement (translation vs tipping) and because Orthodonticell is the **only technology** that improves stabilization with OPG.



## Discomfort

is decreased by 70%—as assessed by clinical trial patients.

## At Home

- ✓ Designed for home use under a practitioner's prescription.
- ✓ Simple protocol – 20 minutes, 2 times a week.
- ✓ Safe, ergonomic, and easy-to-use.
- ✓ Mouthpiece: advanced engineering allows for a simplified fit.





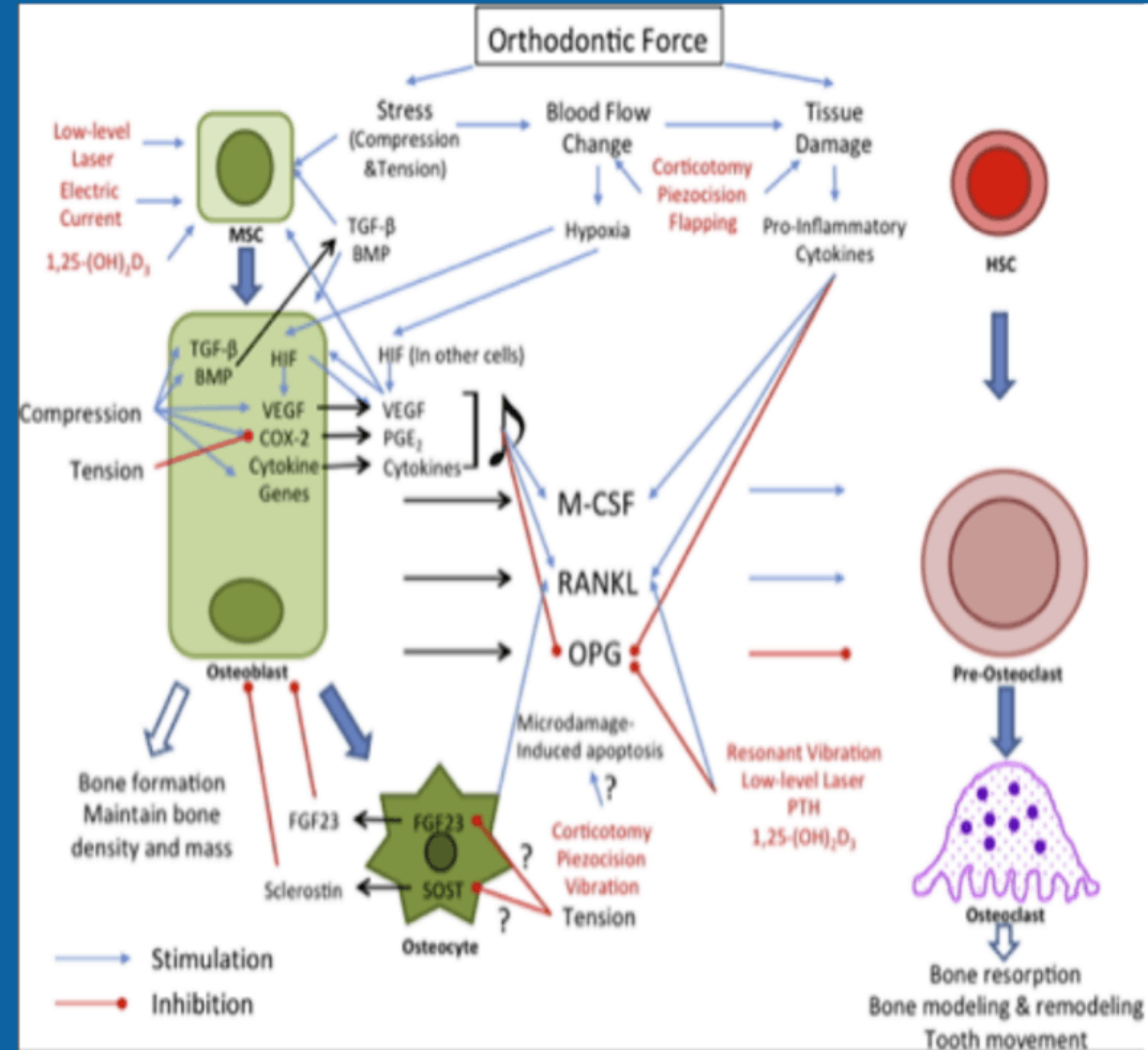


- Utilizes electrical stimulation to increase protein expression of **RANKL** and **OPG**.
  - **RANKL**-the underlying natural protein that governs tooth movement.
  - **OPG**-stabilizes teeth.

# The Science

## Precise Control of **RANKL** and other key proteins

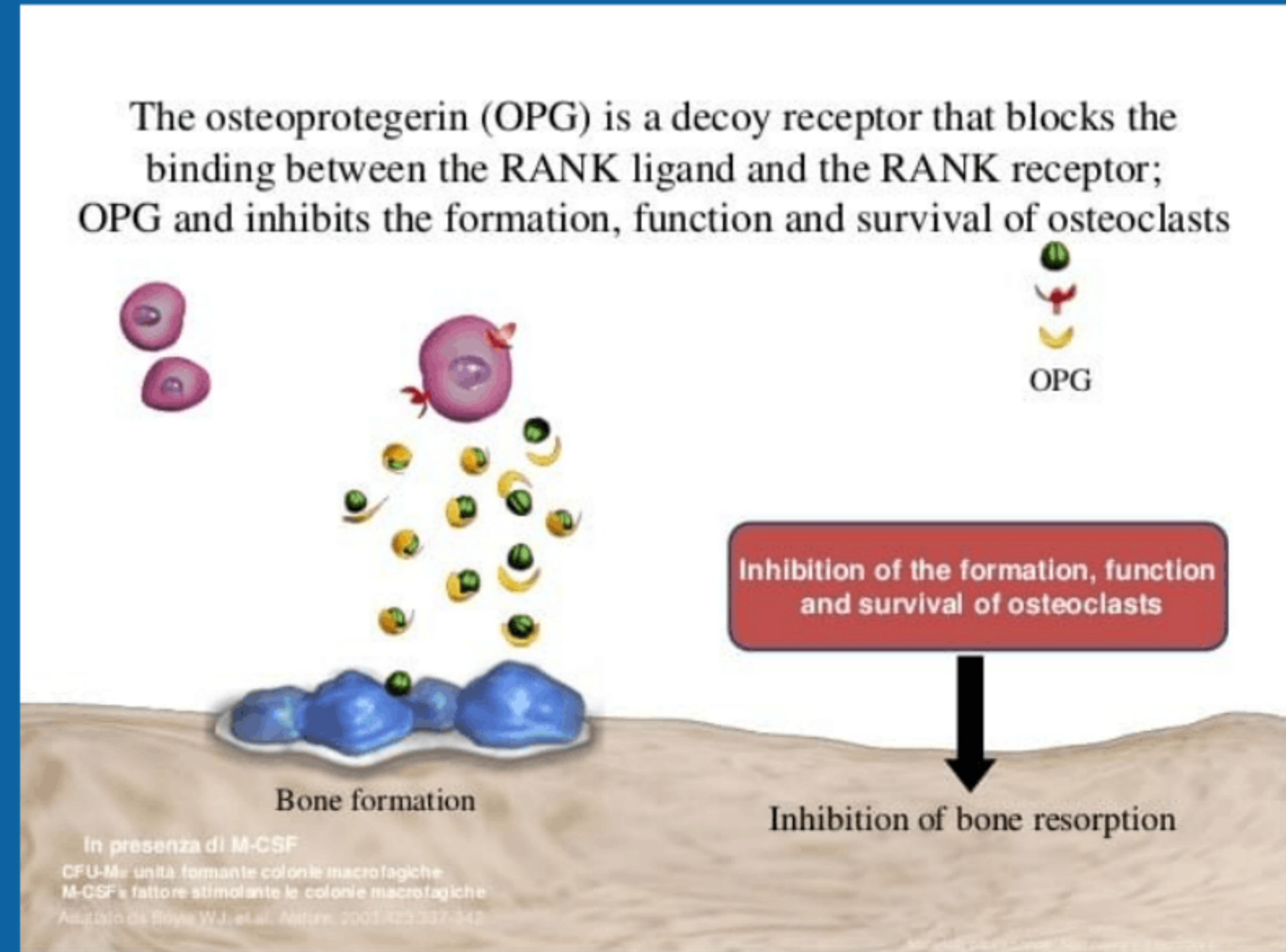
The OrthodontiCell bioelectric mouthpiece produces an up-regulation of RANKL, the key native upstream regulator for the molecular mechanism for accelerated tooth movement. OrthodontiCell controls the precise percentage increase at 44 to 46% for a safe and effective amount of RANKL. OrthodontiCell has built its' technology on a growing body of research, highlighting RANKL as the key protein involved with accelerated tooth movement.



# The Science

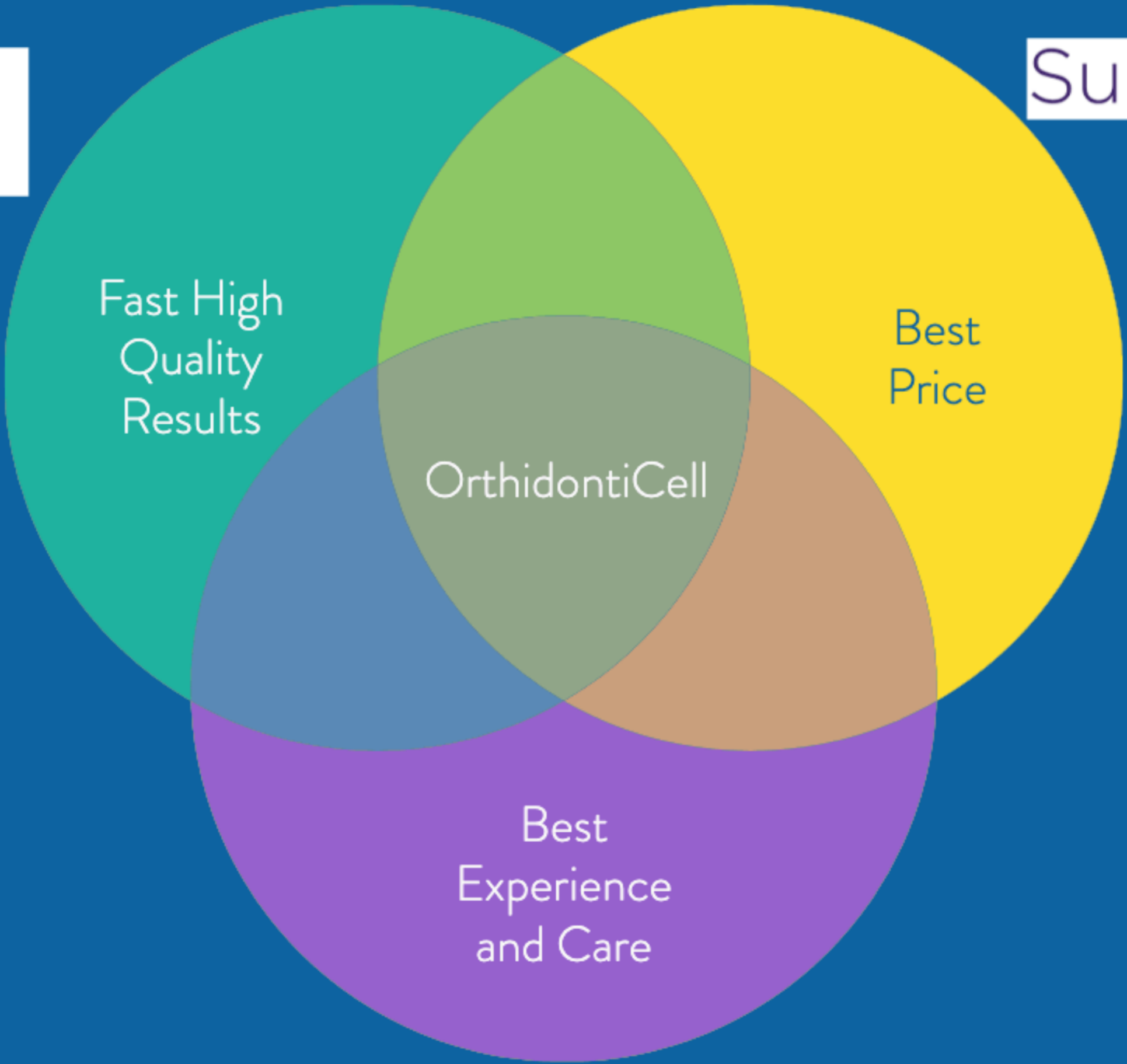
## Stabilization of Teeth **OPG**

The only patented bioelectric signaling sequence for up-regulating the release of OPG that promotes bone formation and stabilizes the final tooth positions with minimal use of long-term retainer wear.



	Near-infrared Light (OrthoPulse)	High Frequency Vibration (OrthoAccel)	Bioelectric Stimulation <b>OrthodontiCell</b>
FDA Approval	2015	2012	2020 (pending)
Energy Mechanism	Non-specific mitochondrial stimulation	Vibratory/mechanical stress	Timed up-regulation of RANKL and OPG
Stabilization	No	No	Yes
Speed	20-45%	20-30%	60%
Discomfort	Limited Reduction	Limited Reduction	Down 70%
Frequency of Treatment	Daily	Daily	Bi-weekly
Total Minutes of Treatment Per Week	70 minutes	140 minutes	40 minutes
End-user Price (price to patient)	\$950	\$800	\$450 (Stimulator and Mouthpiece)
Product Type	Single-use	Single-use	Sterilizable & re-useable stimulator, single-use mouthpiece

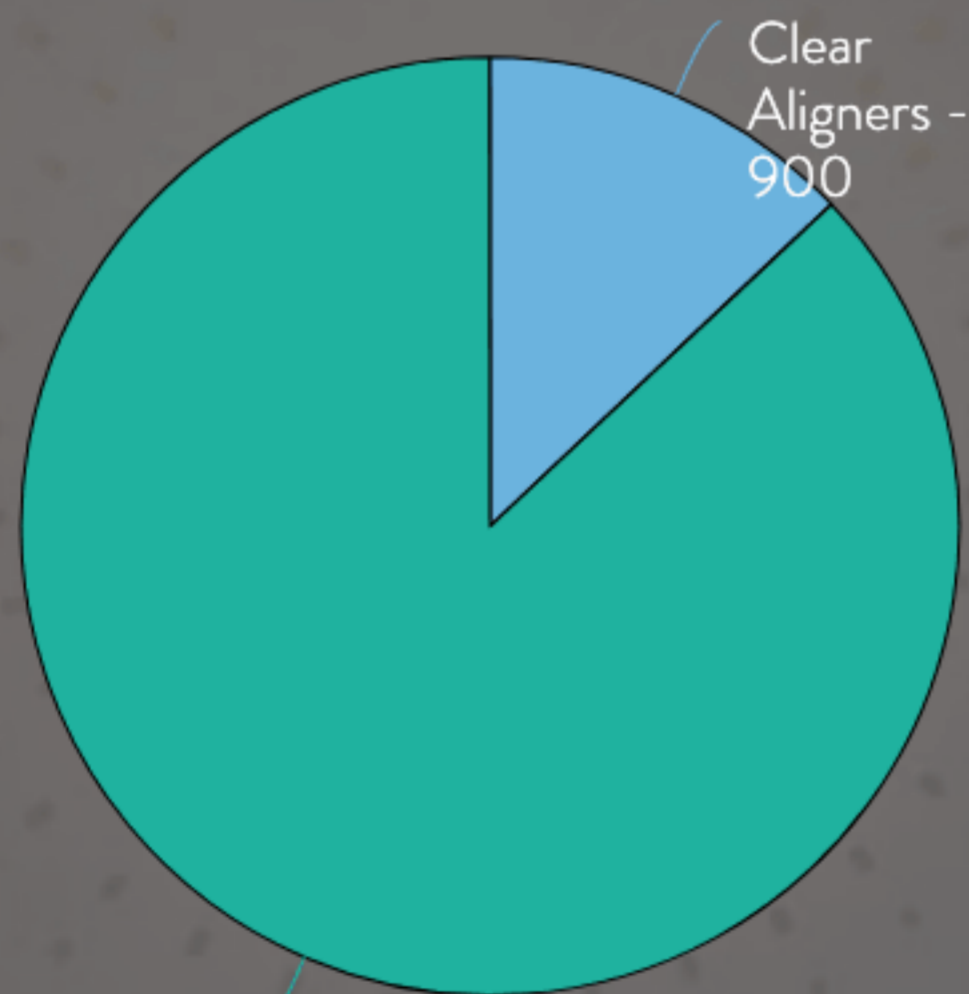
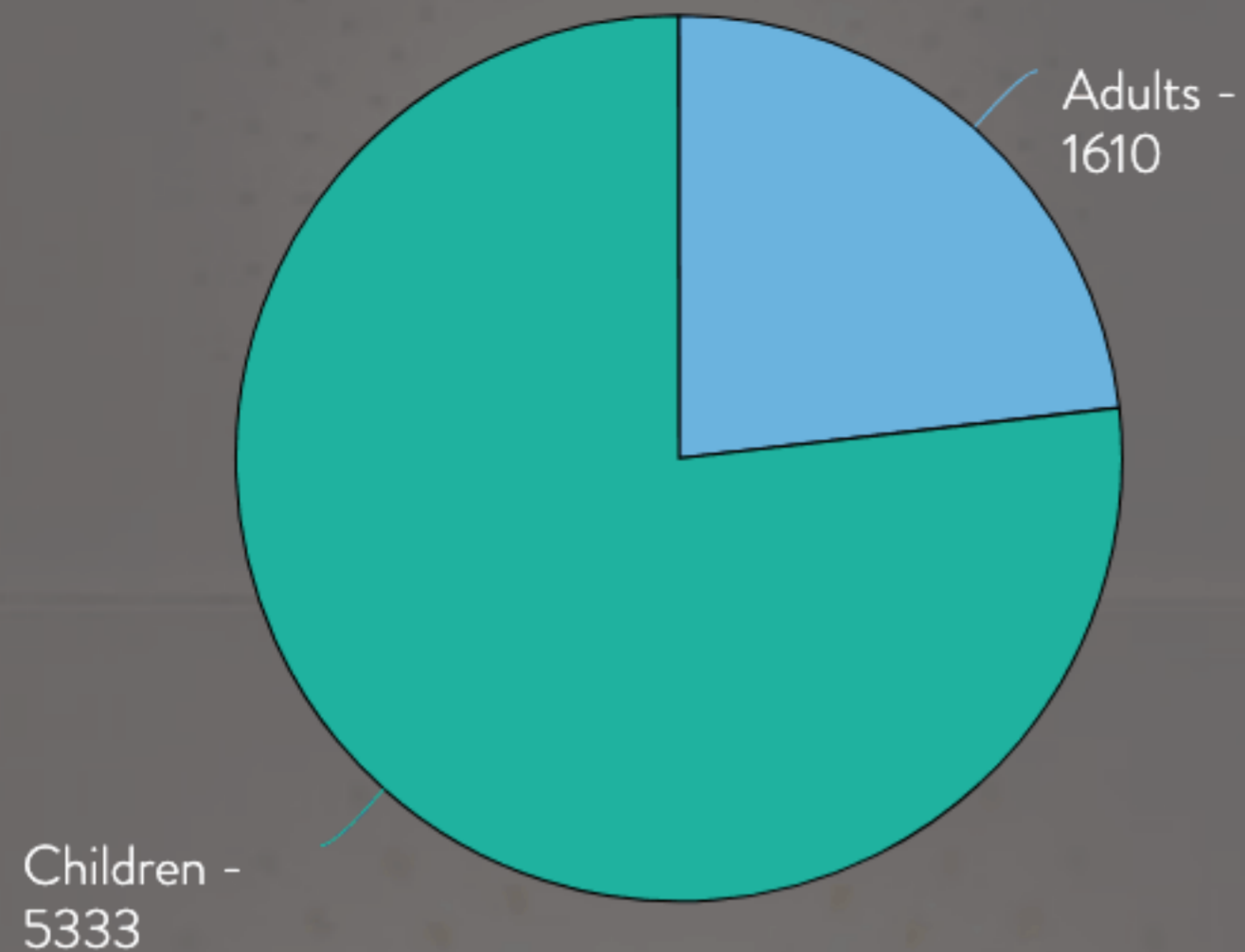
# SureSmile® Aligners



CANDID



# In Depth Look at Markets



## Target Markets

Vast majority of procedures:

- Children
- Traditional wires and braces
- Driven by Orthodontists

# Teeth Straightening Market Opportunity



**Align Technology's current valuation is \$10.8 billion**

**Smile Direct Club's current valuation is \$1.57 billion.**

- 1. Over 3 billion people worldwide with crooked teeth desire straight teeth!**
  2. 80% of U.S. children are under an orthodontist care.
  - 3. Standard braces and aligners take 18-24 months.**
  4. Braces and aligners cause pain and discomfort.
  5. Compliance with aligners and retainers drops dramatically after 6 months.
- OrthodontiCell can straighten 60% of teeth in 3 months and the other 40%\* in 6 months. After teeth are straight we have the only known technology to retain them straight with minimal use of retainers.**



**Market size** – aligners approximately \$4 billion annually worldwide.

**Continued shift** to clear aligners from wire braces – US market total of 6.7 million straightening procedures, 1.5 million aligners, roughly 22% penetration.

**Aligner Growth** – medium-to-high: U.S. around 15-20%; growth in the underpenetrated OUS market could be considerably faster, maybe 30-50%.

Economic Factors:

- Virtually **no pricing power** – many new competitors.
- Little or **no product differentiation** – essentially a “me-too” commodity.
- Companies and ADA **failed to control channels.**
- **No barriers to entry – nearly unlimited number of competitors.**
- **Bases of competition.**
- Price.
- Ease of use – impressions/scans.
- Aggressive marketing practices.
- Plastic molding capabilities (in-house or out-sourced).
- Scanning/impression process.



## A Smile is Eternal

57% of Americans would rather have a nice smile than clear skin.

87% would forego something for a year in order to have a nice smile for the rest of their life.

# The Biggest Market Opportunity

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3  
Billion

**People have crooked teeth  
but do not do anything  
about it - a large untapped  
market.**

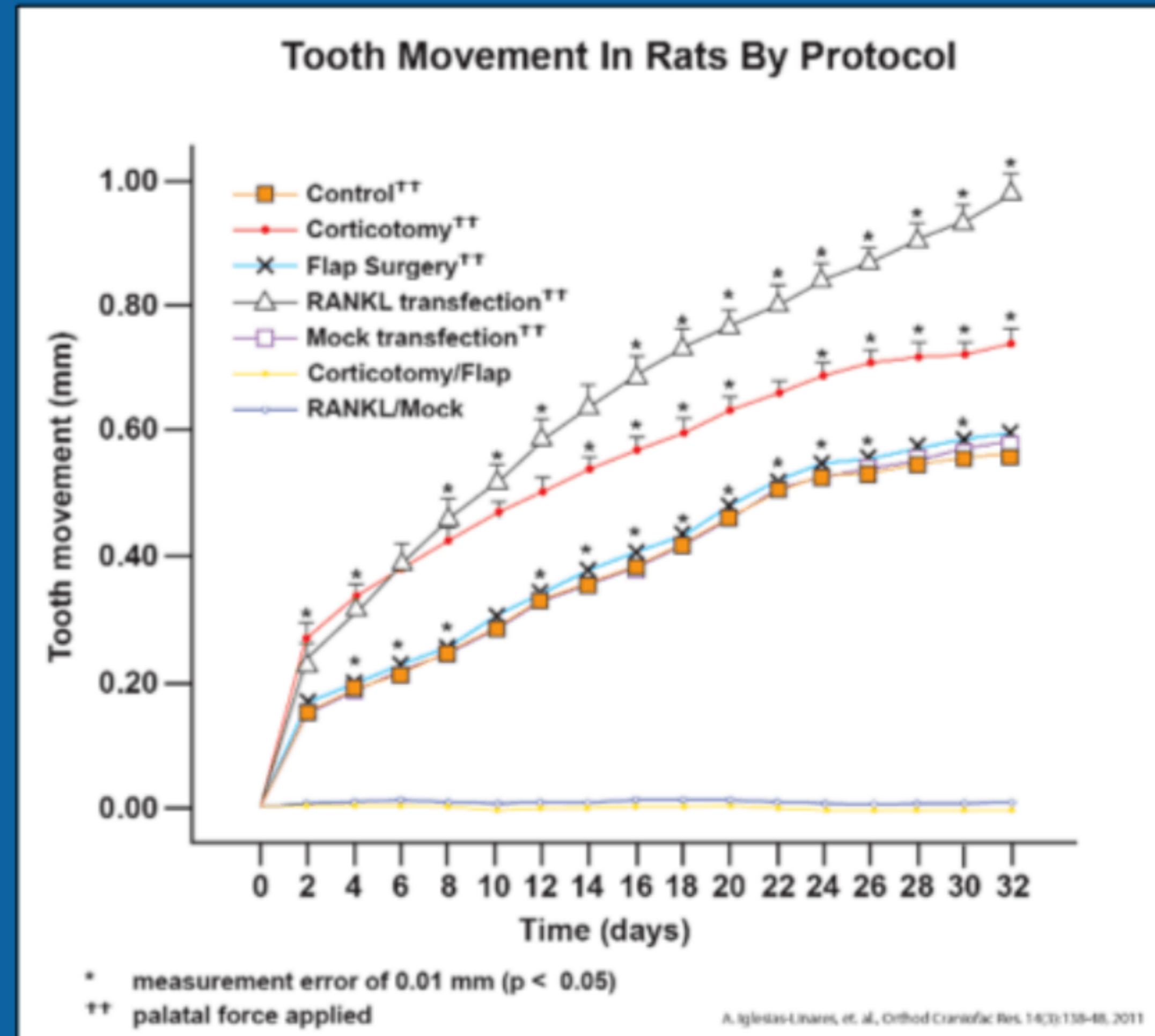
## Leading reasons people do not straighten their teeth

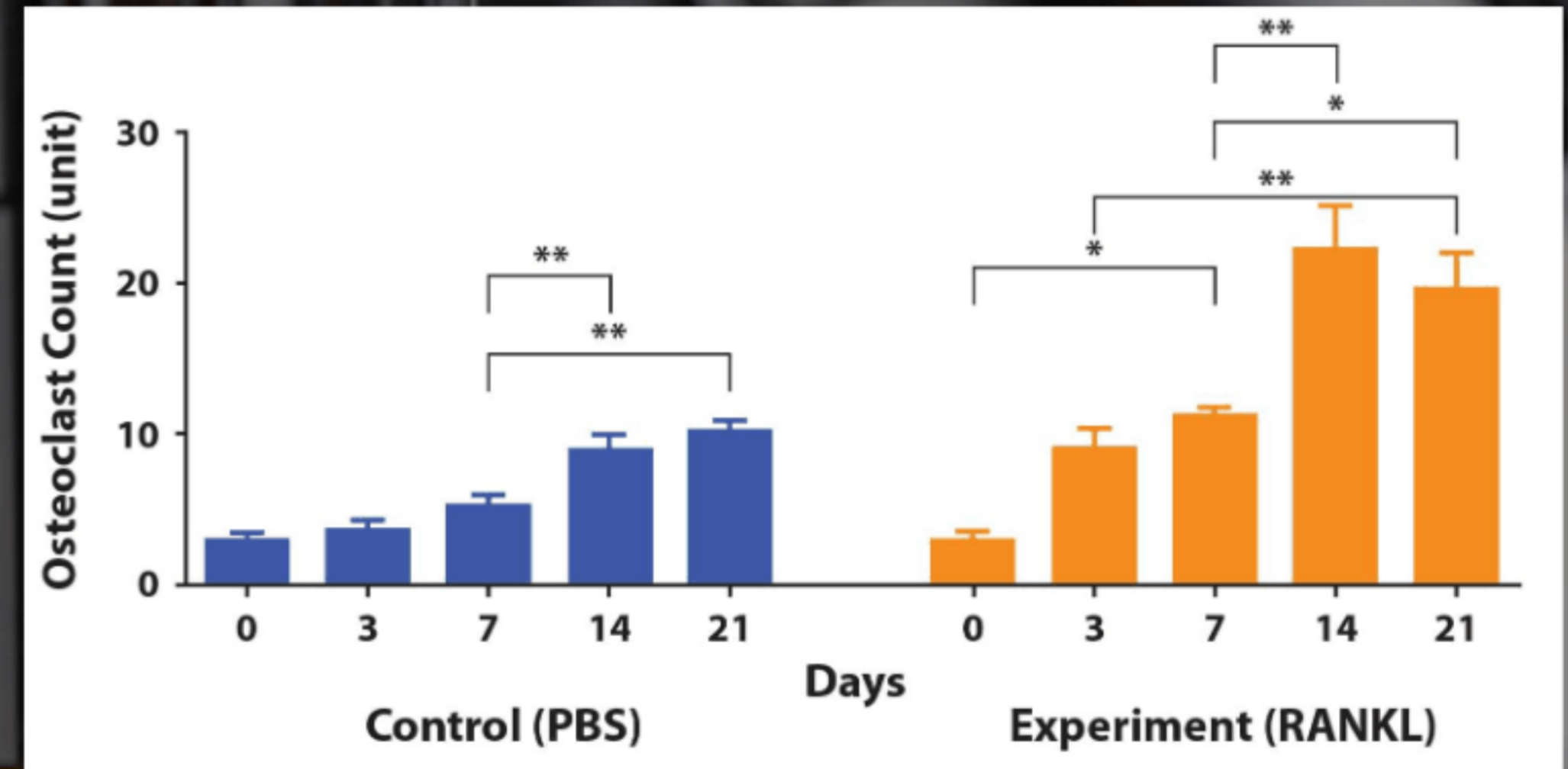
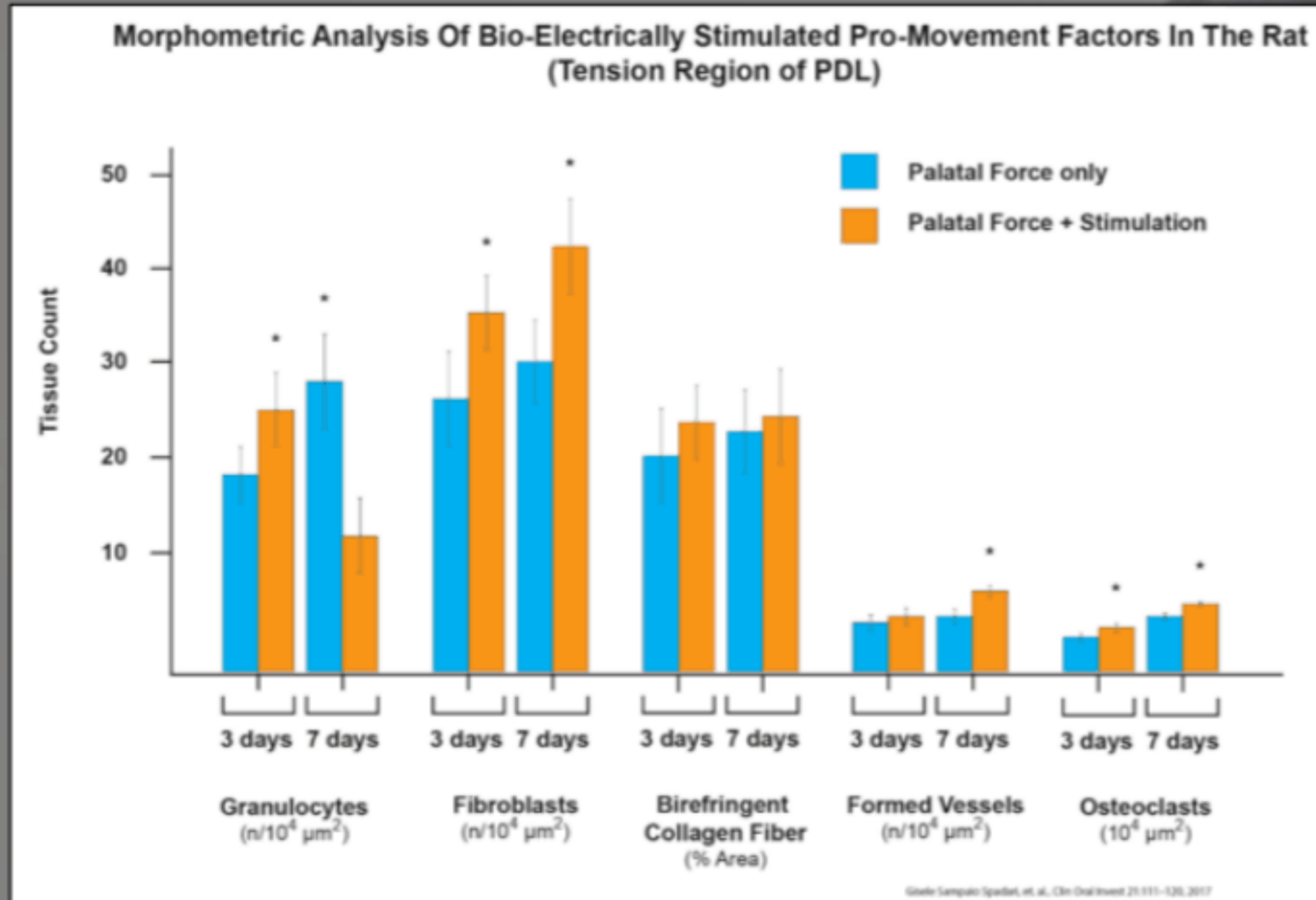
- Too busy to think about doing something.
- Cost too high.
- Fear of dentist and orthodontist.
- Anticipation of pain and discomfort.
- Others around them have crooked teeth so acceptable.
- Worried about time commitment involved.
- Think they are too old and it's too late.
- Parents did not take them in.
- Afraid of being laughed at with braces appearance.

# In Depth Look at The Data

# Multiple Pre-Clinical Studies Completed

Pre-clinical studies demonstrated the leading role of RANKL protein expression in accelerating tooth movement and OPG in stabilization.





OrthodontiCell's **mechanisms of action** are backed by solid scientific evidence from years of studies.

Orthod Craniofac Res. 2011 Aug;14(3):138-48. doi: 10.1111/j.1601-6343.2011.01519.x.

## The use of gene therapy vs. corticotomy surgery in accelerating orthodontic tooth movement.

### RESULTS:

In vitro experiments resulted in increased level of RANKL protein (46%,  $p,0.05$ ) and greater mineral resorption (39%  $<0.05$ ) compared to the controls. In vivo results showed increased RANKL immunorexpression for both corticotomy (twofold) and transfection groups (threefold) after 10 days. After 32 days, a similar result was achieved for the transfected group but not for the surgery group. These data correlate with the clinical effect of decelerating TM in the surgery group.

### CONCLUSIONS:

Selective gene therapy with RANKL has been experimentally tested as an alternative method to corticotomy surgery, showing higher effectiveness than surgical methods used for acceleratory purposes in orthodontics.



## RANKL Study Conclusions

- RANKL gene/protein delivery accelerates RANKL expression and thus tooth movement 300%
- Painful surgical one time corticotomy achieves 200% RANKL expression over baseline
- Gene/protein RANKL therapy is more sustainable than corticotomy for accelerating tooth movement
- RANKL expression will allow for rapid tooth movement within the proposed 6 month duration of final teeth alignment

**Orthod Craniofac Res.** 2009 May;12(2):113-9. doi: 10.1111/j.1601-6343.2009.01444.x. Yamaguchi M1.

**OBJECTIVES:** Orthodontic tooth movement is induced by mechanical stimuli and facilitated by remodeling of the periodontal ligament (PDL) and alveolar bone. A precondition for these remodeling activities, and ultimately for tooth displacement, is the occurrence of an inflammatory process.

**MATERIALS AND METHODS:** This review covers current knowledge regarding the role of the receptor activator of nuclear factor-kappa (RANK), receptor activator of nuclear factor-kappa ligand (RANKL), and osteoprotegerin (OPG) in periodontal tissue reactions, in response to orthodontic forces.

**RESULTS:** It has been found that concentrations of RANKL in GCF increased during orthodontic tooth movement, and the ratio of concentration of RANKL to that of OPG in the GCF was significantly higher than in control sites. In vivo studies have shown the presence of RANKL and RANK in periodontal tissues during experimental tooth movement of rat molars, and that PDL cells under mechanical stress may induce osteoclastogenesis through upregulation of RANKL expression during orthodontic tooth movement.

**CONCLUSIONS:** Considering the importance of RANK, RANKL, and OPG in physiologic osteoclast formation, it is reasonable to propose that the RANKL/RANK/OPG system plays an important role in orthodontic tooth movement.

Eur J Oral Sci. 2007 Apr;115(2):131-6 **Inhibition of tooth movement by osteoprotegerin vs. pamidronate under conditions of constant orthodontic force.**

**Abstract:** In orthodontic treatment, teeth can relapse after tooth movement without retention. The aim of this study was to evaluate the inhibition effects of local osteoprotegerin (OPG) gene transfer on orthodontic relapse. **METHODS:** 18 male Wistar rats were divided into 3 groups.

**RESULTS:** Relapse was significantly inhibited and the number of osteoclasts was reduced in the experimental group. On the other hand, bone mineral density and bone volume fraction of alveolar bone were significantly increased. Bone mineral density and bone volume fraction of the tibia showed no significant difference between the groups

**CONCLUSIONS:** Local OPG gene transfer to periodontal tissues could inhibit relapse after orthodontic tooth movement, through the inhibition of osteoclastogenesis.

Am J Orthod Dentofacial Orthop. 2012  
Jan;141(1):30-40. doi: 10.1016/j.ajodo.2011.06.035.

Local osteoprotegerin gene transfer inhibits relapse of  
orthodontic tooth movement.

#### **RESULTS:**

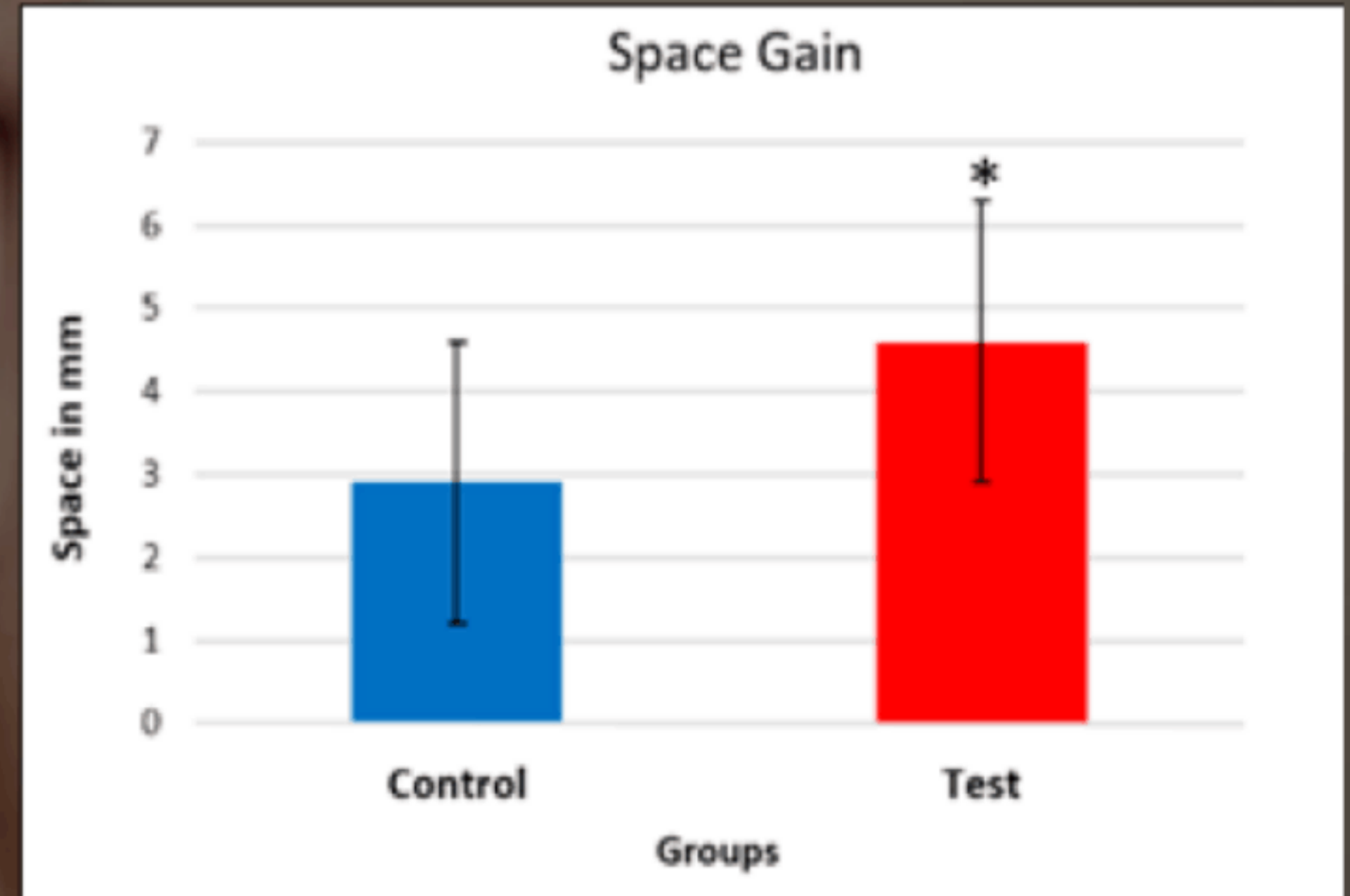
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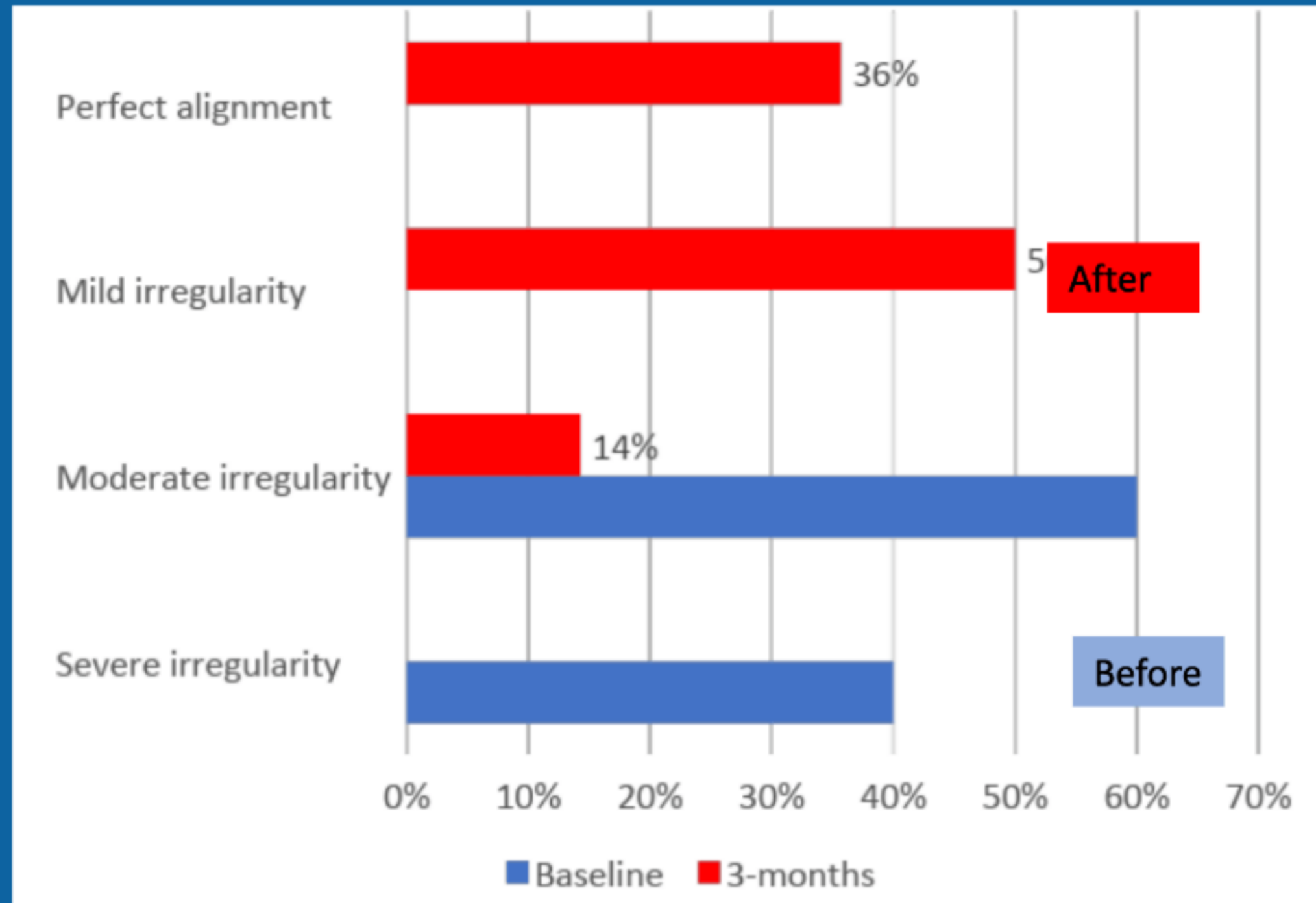
# The Solution Supported by Clinical Results

- **60% of OrthodontiCell treated patients had perfectly straight teeth in 3 months.**
- Patients with braces only had 14.3% with straight teeth at 3 months.
- The OrthodontiCell patients started with more severe mis-alignment and still achieved superior results.
- 70% reduction in pain and discomfort in OrthodontiCell patients.
- Strong improvement of pitch.

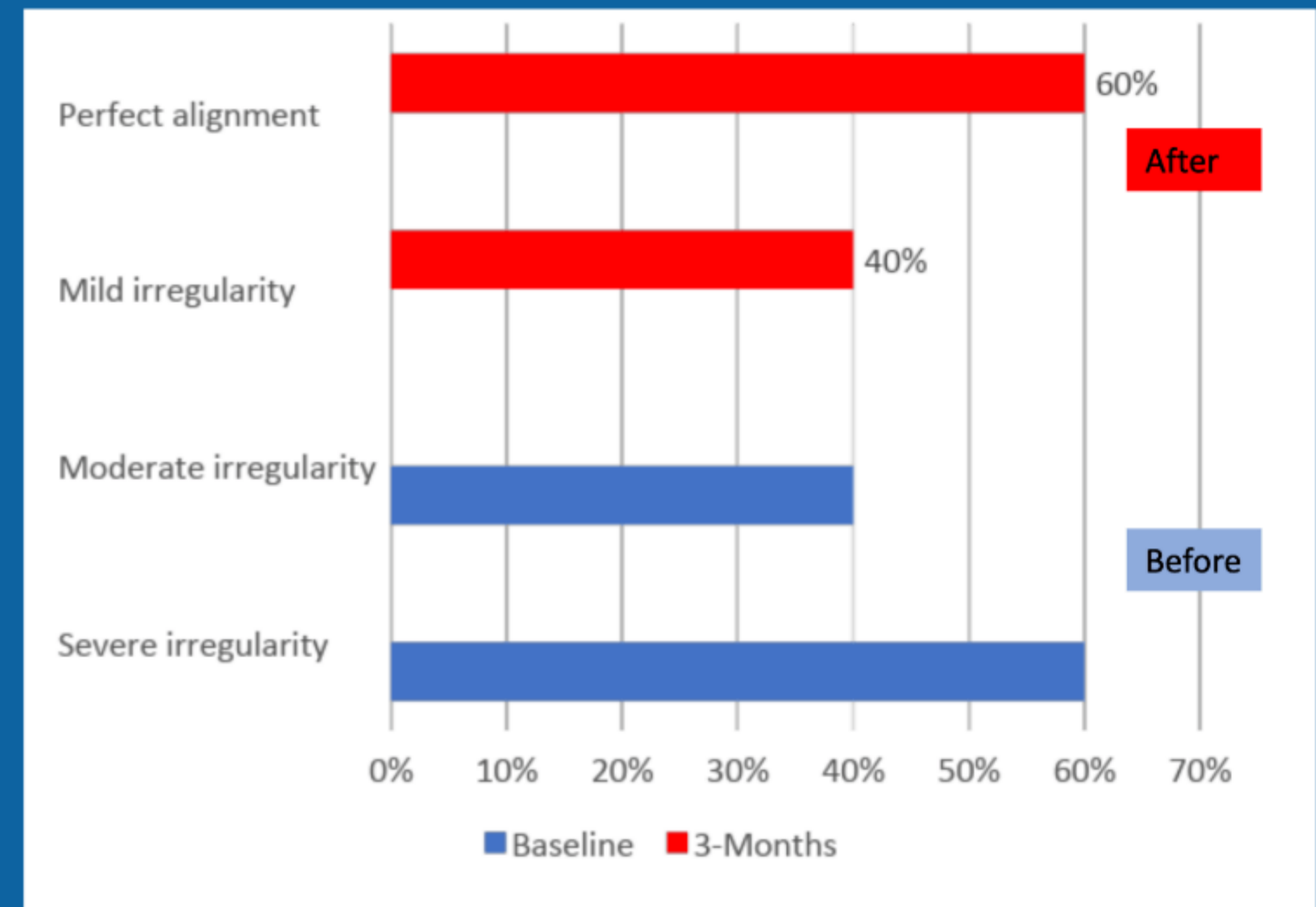


6 month data is pending as of Jan. 31, 2020. Only pilot data is available in small numbers data claims are not meant to be conclusive. Large scale clinical data is yet to come.

Control Group (n=14)

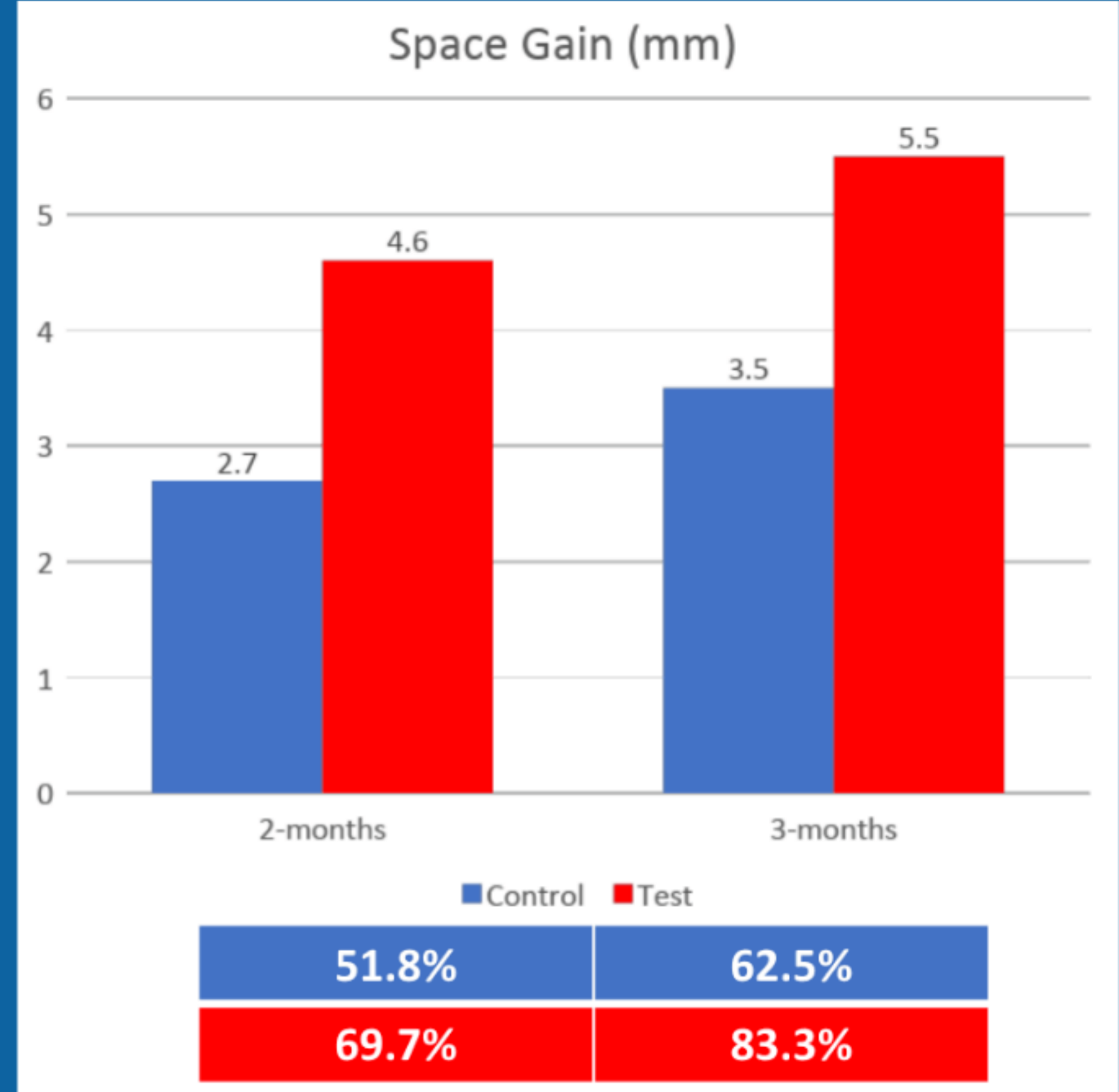
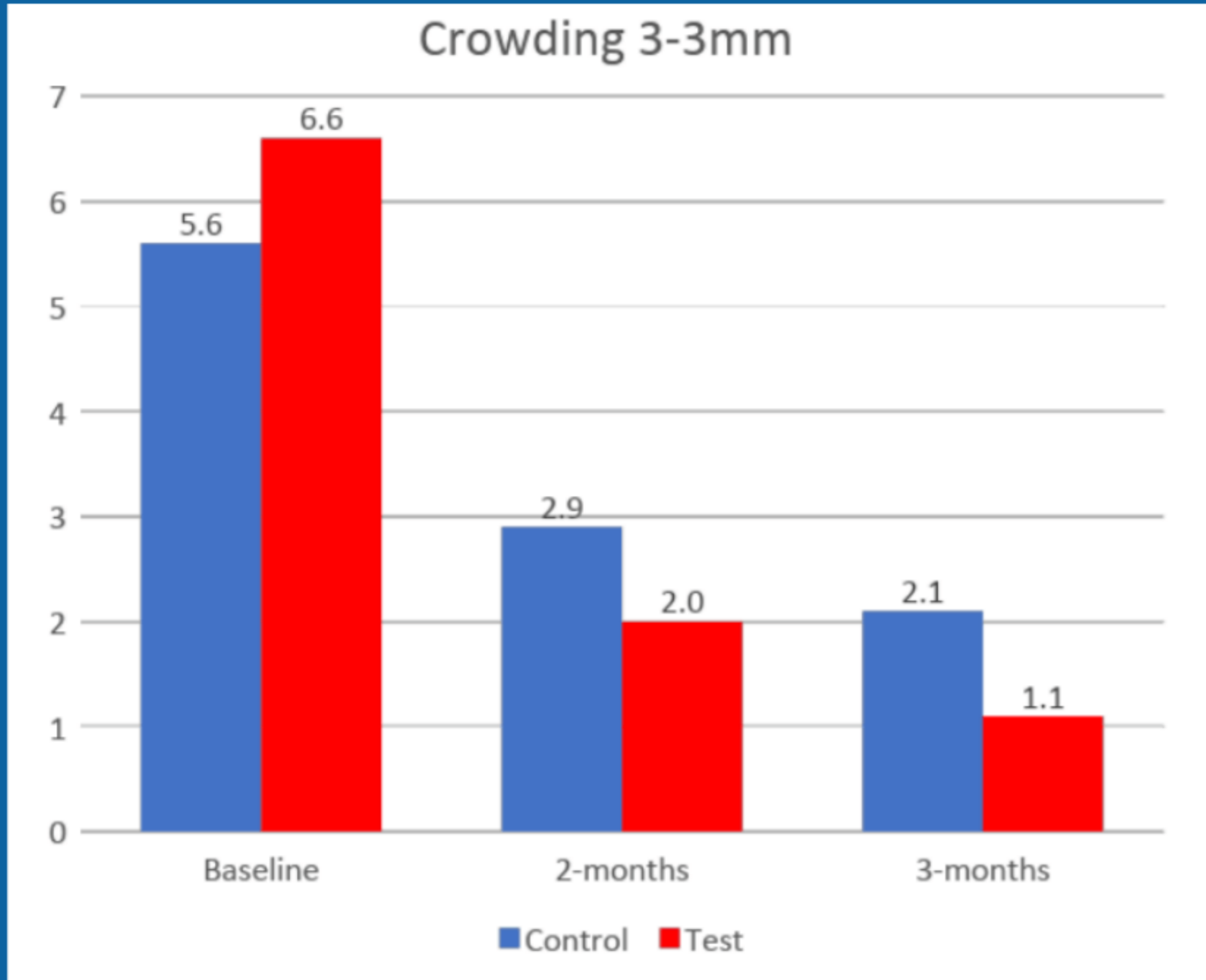


Test Group (n=15)



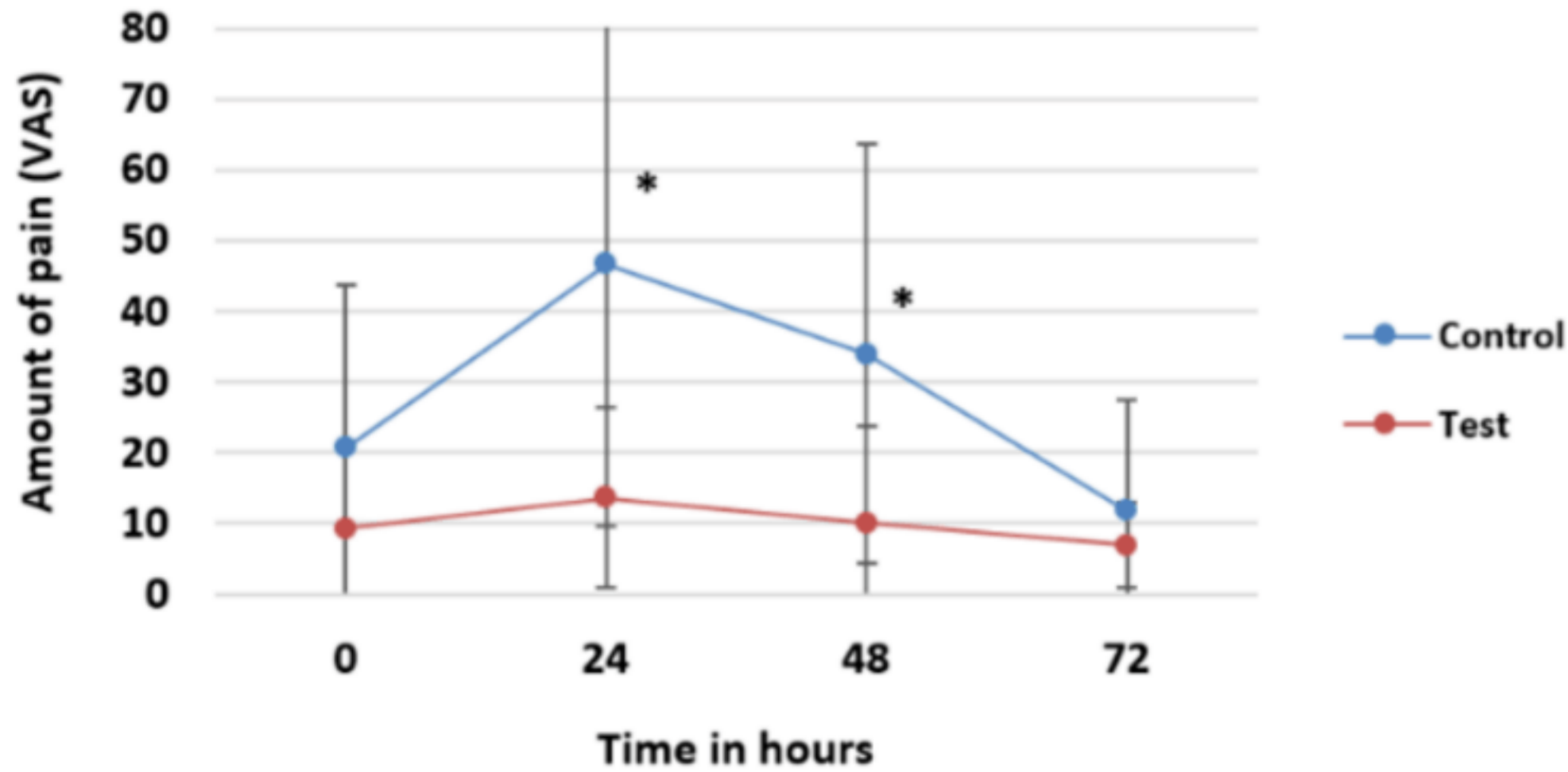
**Studies conducted on patients wearing braces. Test group had better outcomes (60% in test vs. 36% in control for perfect alignment) despite more severe irregularity at baseline.**

Both control group and test group had mouth pieces. Control group had no electrical stimulation.



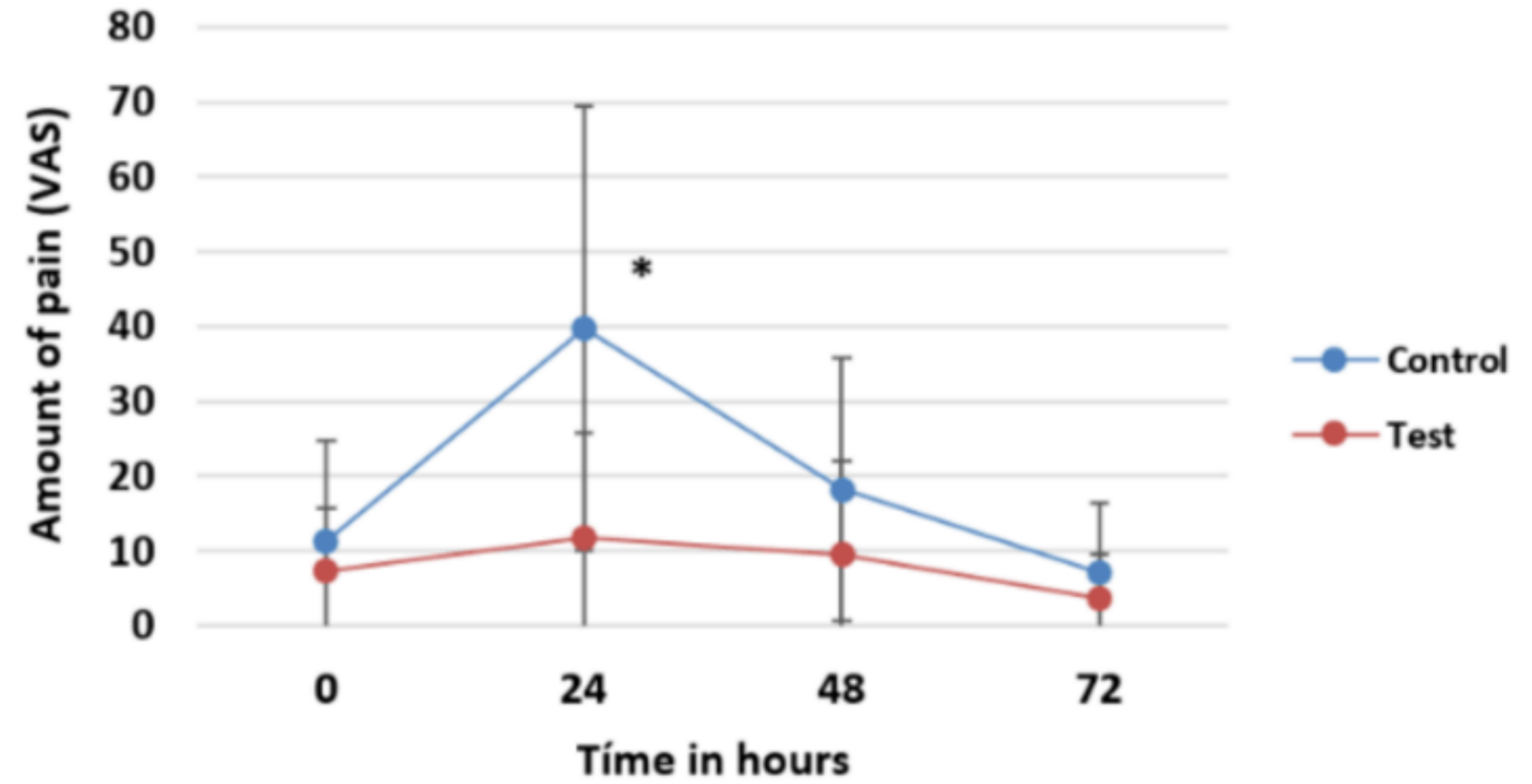
✓ Test group had less crowding and greater space gain at month two and three due to a difference in how the teeth moved (translated vs. tipped).

Pain after wire change (0014")



% reduction vs. control	70.8%	68.6%	41.5%
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Pain after wire change (0016")



% reduction vs. control	70.3%	47.5%	47.9%
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✓ Test group had less pain at 24, 48 and 72 hours following orthodontic adjustments.

Exception with 0.012" wire at 48 and 72 hours



# Clinical Study Completed

44 patients enrolled to date full followup on 29 so far as of Dec. 31, 2019

**Test Group**



**Control Group**



# Clinical Investigation Site Pilot Clinical Study



UNESP-Faculdade de Odontologia, San Jose de Campos, Brazil <http://www.fosjc.unesp.br/>



Leading Orthodontic University  
in Brazil



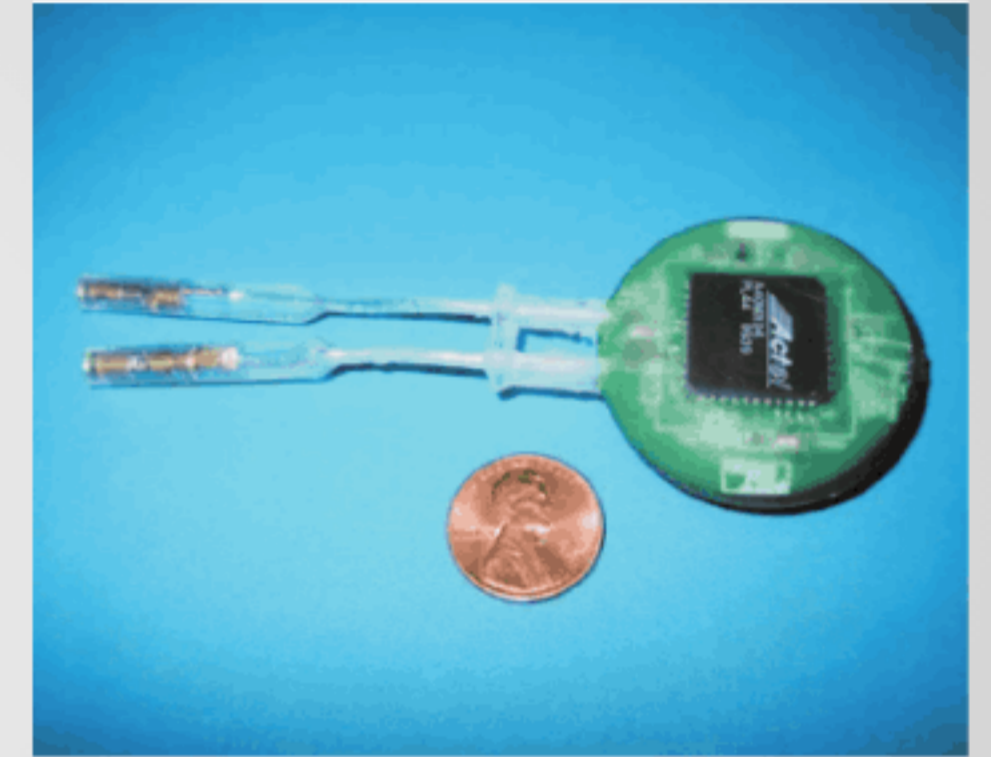
High Quality Patient Care



A teaching school.

# In Depth Look at The Device

# Pipeline of Stimulators in Development



**2019**

Benchtop stimulator  
- FDA 510K Market  
Cleared.

**2020**

At home use portable  
stimulator.

**2021**

LED graphics screen  
at home stimulator.

**2022**

Micro stimulator to  
load into mouthpiece.

# Solution in More Detail



Our bioelectric stimulator targets the release of key proteins to accelerate tooth movement ie; RANKL, SDF1, PDGF, VEGF - Pre-clinical and clinical studies demonstrate up to 2/3rds reduction in teeth straightening time.



Ours is the only product that offers post-treatment stabilization improvement via specific bioelectric signaling of controlled protein release to maintain the alignment corrections. This is accomplished in weeks rather than years.



Our mouth piece is comfortable and convenient and avoids the potential alternative of having repeated painful needle injections which is the only other way to get key proteins such as RANKL and OPG in effective therapeutic doses.

# In Depth Look at Patents



## Proprietary Technology / Expertise

- Specific protein expression controlled on demand.
- Comfortable mouth-piece.
- Accelerated tooth movement is controlled.
- Stabilization improvement is controlled.
- Eliminates prolonged treatment times.
- Superior pitch improvement.

# Pioneering Patents



We believe the strongest IP estate for tooth movement acceleration and stabilization

- U.S. 20200000709 **Combination of Bioelectric Stimulator and Plalet Rich Fibrin for Accelerated Healing and Regeneration** - Filed July 1, 2019
- U.S. 20190022389 **System and Method for Treating Inflammation** - Filed Sept. 20, 2018
- U.S. 20180064935 **Bioelectric Stimulator** - Filed Nov. 14th, 2017
- U.S. 20170274206 **Orthodontic Treatment - Bioelectric Controlled Expressions of RANKL and OPG** - Filed March 28th, 2017
- U.S. 8909346 **Frequency Specific Microcurrent for Treatment of Dental Indications** - Filed Feb. 17th, 2009
- U.S. 20170266371 **Bioelectric Stimulator, Pump and Composition** - Filed March 15, 2017
- U.S. 29/703,783 **Bioelectric Mouthpiece** - Pending Filed August 29th, 2019



# Pioneering Issued U.S. Patent Claims

1. Bioelectric **controlled release of RANKL** for **accelerated tooth movement**.
2. Bioelectric **controlled release of OPG for stabilization** - freezing teeth straight.

## United States

### Patent Application Publication

Leonhardt et al.

Pub. No.: **US 2017/0274206 A1**

Pub. Date: **Sep. 28, 2017**

#### ORTHODONTIC TREATMENT

Applicant: **CaIXStars Business Accelerator, Inc.**,  
Santa Monica, CA (US)

Inventors: **Howard J. Leonhardt**, Salt Lake City,  
UT (US); **Jorge Genovese**, Buenos  
Aires (AR); **John Joseph Marchetto**,  
Weston, FL (US)

#### U.S. Cl.

CPC ..... *A61N 1/326* (2013.01); *A61C 7/08*  
(2013.01); *A61N 1/0548* (2013.01)

# Founding Team

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Howard Leonhardt, Executive Chairman & CEO, 35 years experience, Inventor with 22 Issued U.S. Patents.



Dr. Johh Marchetto, President and Chief Scientific Officer, Orthodontist and inventor with 35 years experience, Tufts University



Dr. Leslie Miller, Chief Medical Officer, 241 publications, 81+ clinical trials, Co-Editor Leading Textbook on Regenerative Medicine

# Founding Team

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Dr. Brett Burton, VP R&D, Ph.D.  
Bioengineering U of Utah



Alex Richardson, VP Engineering  
& Product Development



Brian Hardy, Director of  
Marketing, 20+ Years Experience

## What Will it Cost, What Will it Sell For?

Factory Cost Bioelectric Mouthpiece and Aligners = \$450

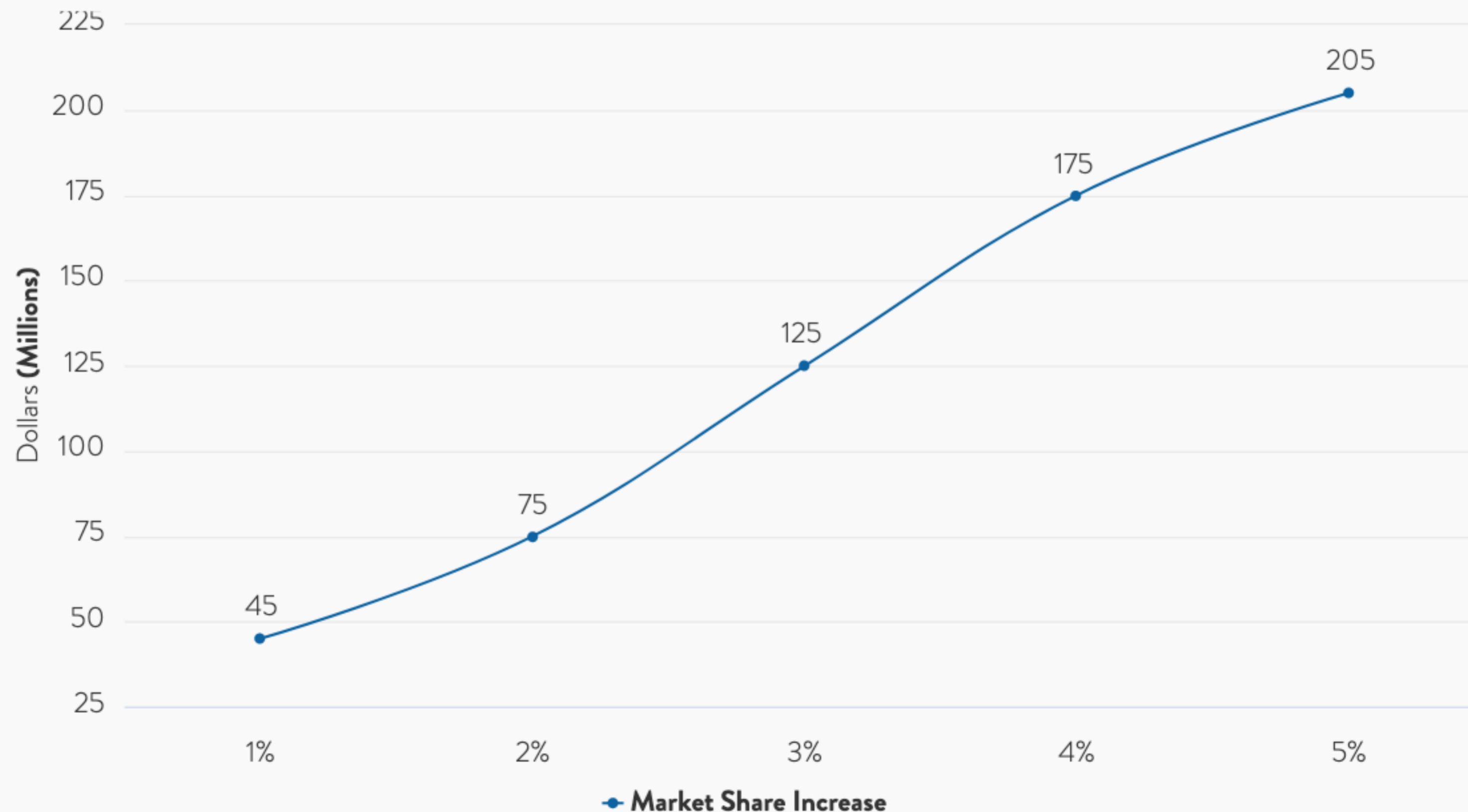
Retail Sell Price Bioelectric Mouthpiece and Aligners = \$4500

**Gross Margins = > 80%**

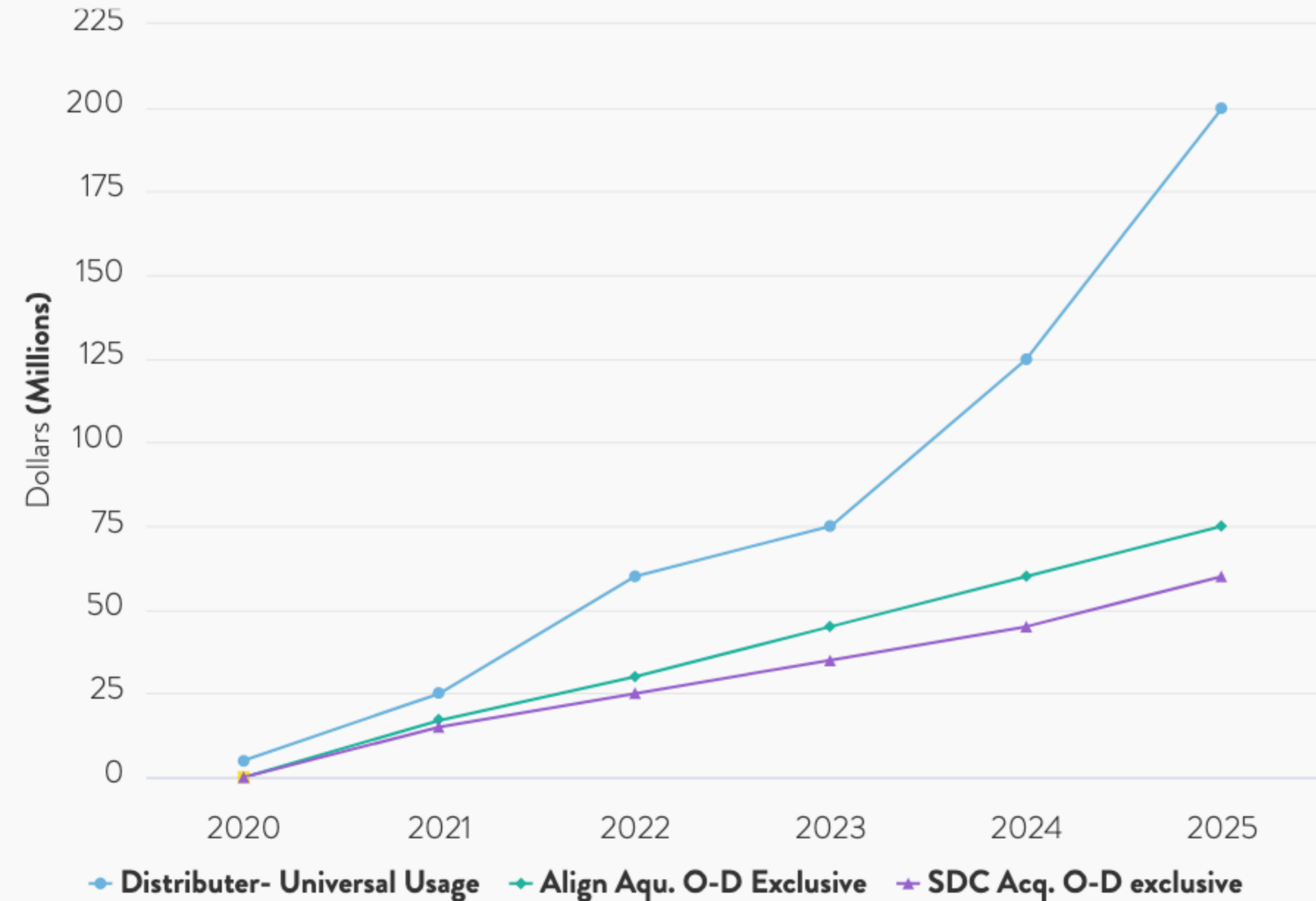
*\$4500 includes cost of aligners (much less aligners needed since finishing in 6 to 9 months instead of 18 to 48 months). Also, less discomfort and less risk of relapse. Aligners alone retail for \$4000. Only a \$500 premium for far more superior results.*

# Financial Information & Forecasts

# OrthodontiCell would bring about market share gains: Rough cut at what a market share increase in the aligner market is worth.



# OrthodontiCell Revenue Projections (U.S. Only)



- Dental distributor like Henry Schein would capture the large braces market, along with clear liners.
- Both Align Technologies and Smile Direct Club would sell mostly to their own customers.
- Align and SDC would drive higher adoption rates within their customers, but would likely miss the braces market.

# Business Strategy

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Complete pilot clinical studies then find strategic partner.

\$300 Million  
USD

Target down payment on Sell Price after Pilot Study Data  
- Milestone payments to \$2 billion over time

3%  
Royalties Sales

This bio-electric enhancement can revolutionize the way orthodontic treatment is delivered and completed!



## Milestones 2020



- **Complete aligner study.**
- **Complete stabilization study.**
- **Finish development of at home use portable unit.**
- **Present clinical data at major meetings.**
- **Get U.S. 510K full market clearance for specific indications of use.**

# Our Strategic Acquirer Becomes Undisputed Market Leader

Maintains gross margins of > 80% for next 20 years of patent life

- With OrthodontiCell TM for only the \$500 premium price retail customer gets much more value.
- Aligners alone sell retail for \$4000.
- Aligners + the OrthodontiCell Bioelectric Mouthpiece are expected to sell for \$4500 retail in combination, only \$500 more than the standard product.





## Benefits to Strategic Partner Acquirer

- **Opportunity to lead market in sales with a superior product.**
- **To be identified as the true science and technology leader in segment boosting stock price.**
- **FDA 510K market clearance ready. Revenues, sales, profits, ROI year one after acquisition.**
- **Ability to keep gross markings > 80% for next 20 years with patents and deep pipeline.**
- **Something immediate and new to sell to the previous 4,000,000+ existing clear aligner clients**