How Ideas for Positive Change in Medicine Evolve into Reality

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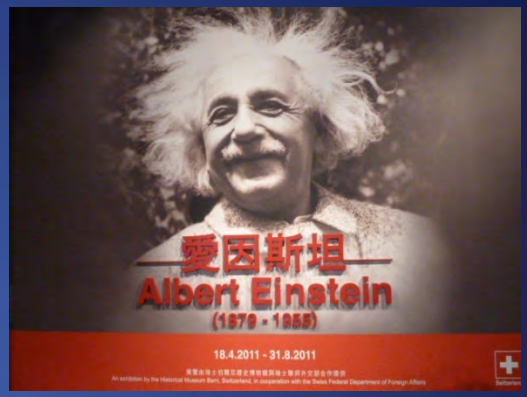
St. Louis, Missouri

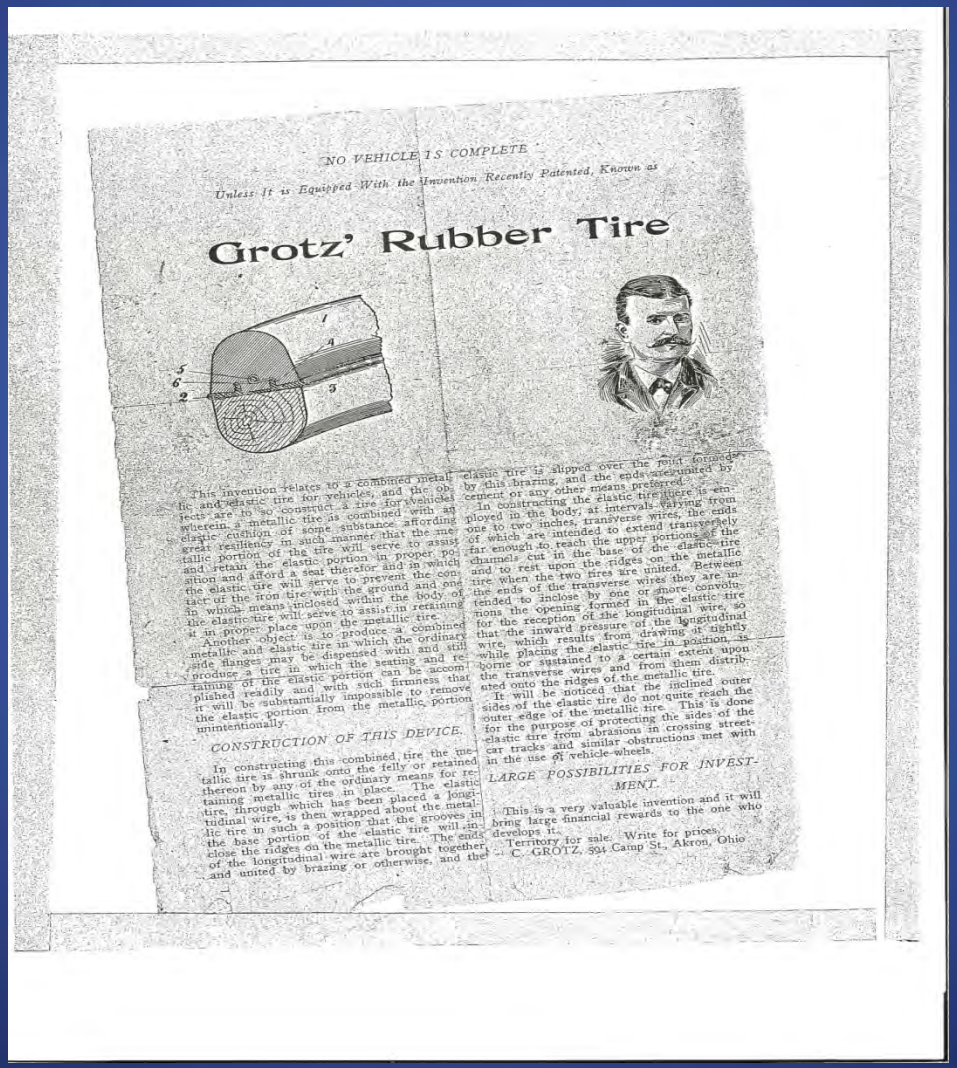
How Ideas Evolve into Reality

The Idea



- "AHA" moment
- Cognitive disinhibition
- Documentation is important
- Check FTO (Freedom to Operation) in IP space
- Start the patent process
  - Provisional
  - Enabling
- Plan for hard work and expenses

Christian Grotz 1903 Rubber Tire



NO VEHICLE IS COMPLETE

Unless It is Equipped With the Invention Recently Patented, Known as

Grotz' Rubber Tire

This invention relates to a combined metallic and elastic tire for vehicles, and the objects are to so construct a tire for vehicles wherein a metallic tire is combined with an elastic cushion of some substance affording great resiliency in such manner that the metallic portion of the tire will serve to assist and retain the elastic portion in proper position and afford a seat therefor and in which the elastic tire will serve to prevent the contact of the iron tire with the ground and one in which means inclosed within the body of the elastic tire will serve to assist in retaining it in proper place upon the metallic tire.

Another object is to produce a combined metallic and elastic tire in which the ordinary side flanges may be dispensed with and still produce a tire in which the seating and retaining of the elastic portion can be accomplished readily and with such firmness that it will be substantially impossible to remove the elastic portion from the metallic portion unintentionally.

CONSTRUCTION OF THIS DEVICE.

In constructing this combined tire the metallic tire is shrunk onto the felly or retained thereon by any of the ordinary means for retaining metallic tires in place. The elastic tire, through which has been placed a longitudinal wire, is then wrapped about the metallic tire in such a position that the grooves in the base portion of the elastic tire will inclose the ridges on the metallic tire. The ends of the longitudinal wire are brought together and united by brazing or otherwise, and the elastic tire is slipped over the joint formed by this brazing, and the ends are united by cement or any other means preferred.

In constructing the elastic tire there is employed in the body, at intervals varying from one to two inches, transverse wires, the ends of which are intended to extend transversely far enough to reach the upper portions of the channels cut in the base of the elastic tire and to rest upon the ridges on the metallic tire when the two tires are united. Between the ends of the transverse wires they are intended to inclose by one or more convolutions the opening formed in the elastic tire for the reception of the longitudinal wire, so that the inward pressure of the longitudinal wire, which results from drawing it tightly while placing the elastic tire in position, is borne or sustained to a certain extent upon the transverse wires and from them distributed onto the ridges of the metallic tire.

It will be noticed that the inclined outer sides of the elastic tire do not quite reach the outer edge of the metallic tire. This is done for the purpose of protecting the sides of the elastic tire from abrasions in crossing street-car tracks and similar obstructions met with in the use of vehicle-wheels.

LARGE POSSIBILITIES FOR INVESTMENT.

This is a very valuable invention and it will bring large financial rewards to the one who develops it.

Territory for sale. Write for prices.

C. GROTZ, 594 Camp St., Akron, Ohio

Patent Published; the Race is On

Selling the Idea

- Patent Agency must believe its unique after reviewing the world's patent history
- FDA (Food and Drug Administration) ideally will be persuaded the concept is standard
- "Substantial equivalence" earns 510k FDA clearance…the short regulatory course
- PMA (Premarket Approval) …long and expensive road to use clearance

Charlie Mayo:
“There’s No Fun Like Work”

FDA
510k/90 days/<$1M versus
PMA long road/5-10 years/?$50M

Carticel patent Example

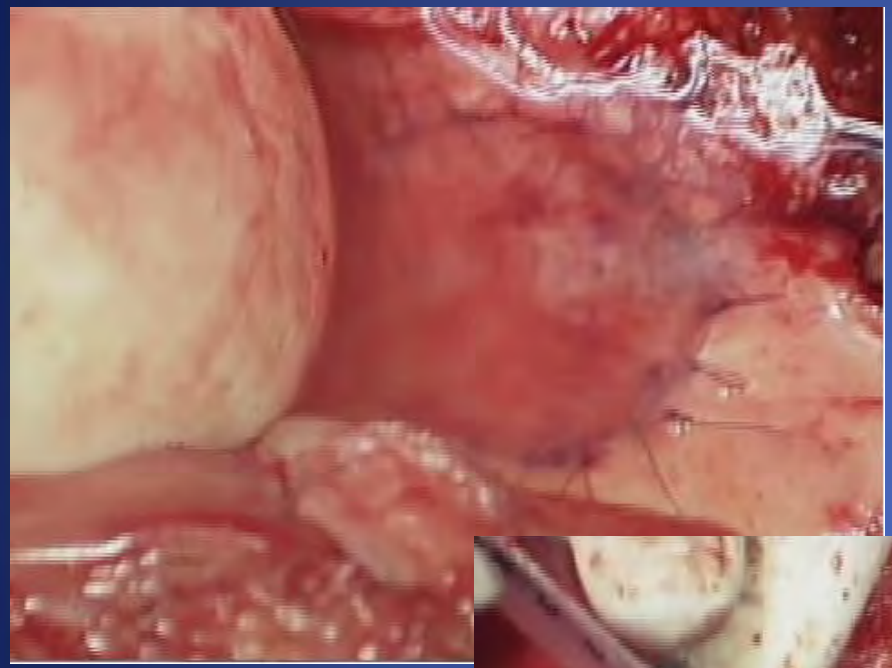
Carticel procedure -- transplantation

Patent requested by Genzyme Co.

Be Careful what you ask for

Understand the implications as they relate to later R&D

Chondrocyte Implantation



Conclusion

- Autologous chondrocyte implantation offers a viable alternative to joint replacement arthroplasties, for patients with substantial articular surface damage.

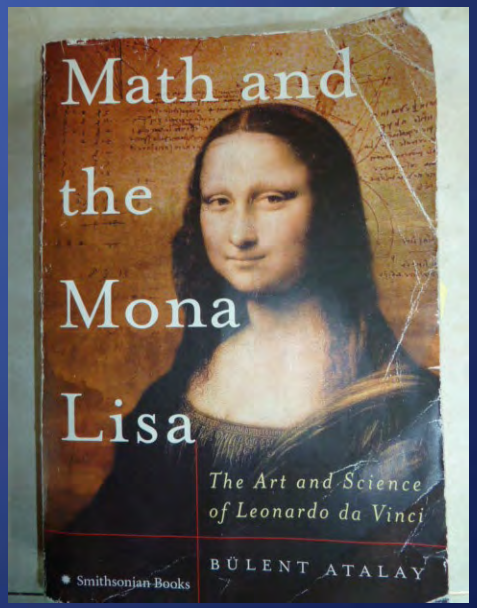
- Thank you

Medical Eponyms, Acronyms

- FTO Freedom to Operate
- FDA Food and Drug Administration
- IDE Investigation Device Exemption (FDA)
- IRB Institutional Review Board (hospital)

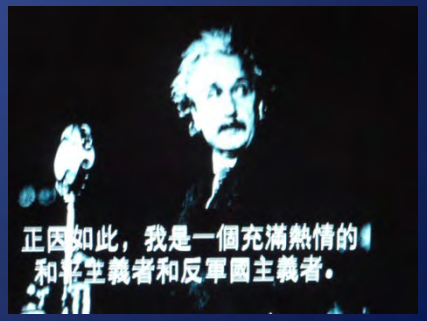
Definition of Medicine

The Art and Science of Healing



Terms in medical device industry

- Repair Fix what's broken; reattach to bone
- Reconstruction Replace damaged tissues
- Regeneration Restorative treatments
- Replacement Remove joint; implant parts
- Interpositional arthroplasty Joint sparing



The History of Medicine

- Prehistoric Medicine
- Antiquities Egypt, India, China, Greece
- Renaissance
- Modern times

Prehistoric Medicine

- Herbalism
- Tribal cultures
- Shamans
- Apothecaries

Antiquity Medicine

- Ancient **Egypt**
- Herodotus Public health system
- Papyrus 3000 BC
- Kahun Gynaecological Papyrus 1800 BC
- Houses of Life

Antiquity Medicine

- Ancient **India** Charakasamhita Rx feasible
- Susruta Medicine intent to cure the sick
- Text: Susrutasamhita defined surgery(s)
- Unani Medicine Alternative Body elements:
  - Fire
  - Water
  - Earth
  - Air

Antiquity Medicine

- Ancient **China**
- Traditional Chinese Medicine…empirical
- Taoist physicians… causative principles
  - Material
  - Mystical
  - Correlate with universe natural order
- Text: Huangdi neijing…first stethoscope
  - Two books Basic Questions;Divine Pivot

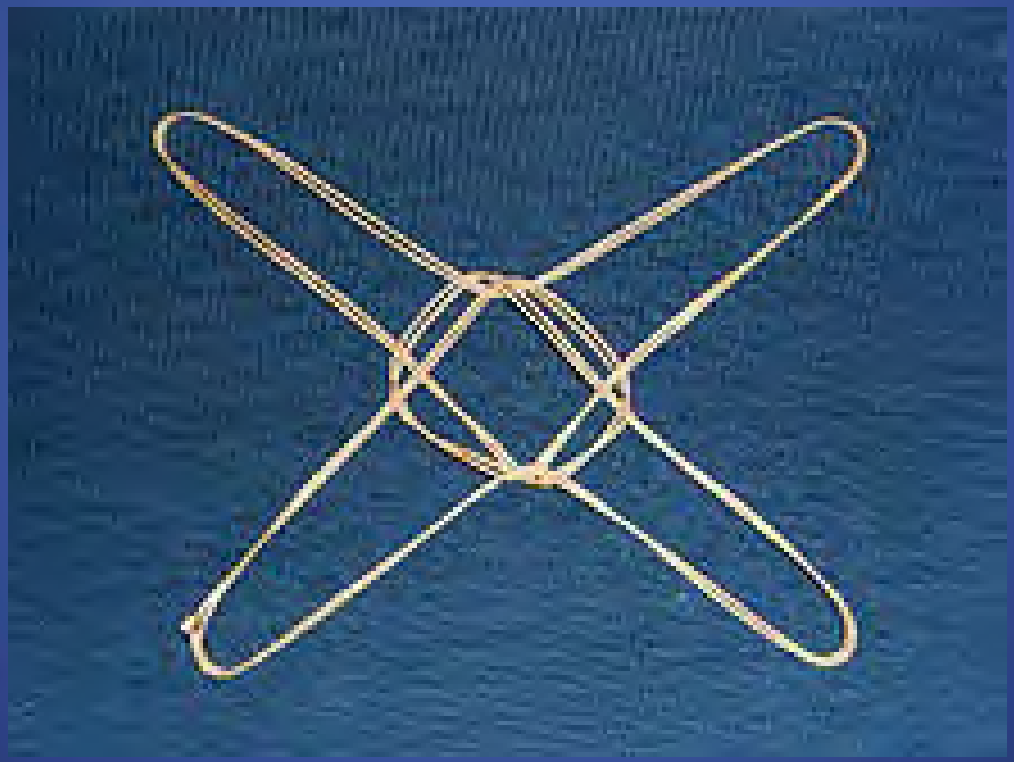
Antiquity Medicine

- Ancient **Greece, Rome**
- Hippocratic Corpus
- Cnidus 700BC First Greek Med School
- Focus Balance of Humours
- Temples dedicated to healer god Asclepius

Hippocratic Corpus

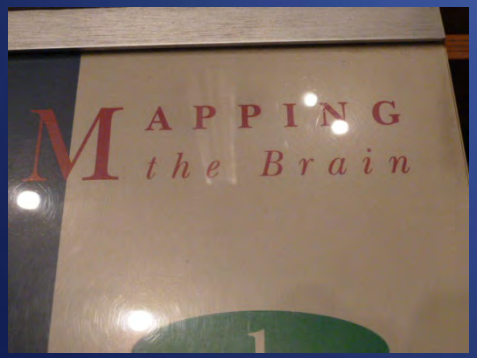
Askleipion of Kos (Hippocrates)

Sling for fractured Jaw Greek



First Intelligence Mapping

- Herophilus of Chalcedon Alexandria
- Distinguished arteries (pulse) from veins
- Mapped human vs animal brains
- First weight loss experiments; birds
- First discussion of body circulation systems



Christian Middle Ages

Anatomy Lesson

Rembrandt 1632

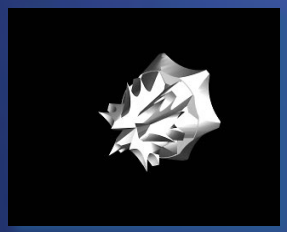
Christian Middle Ages

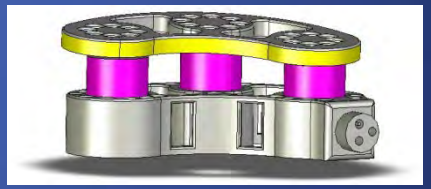
- Salernitanus Chirurgia; foundation manual
- Versalius Organ dissection anatomy
- Drugs limited Opium, quinine, toxic metals
- Leeuwenhoek 1676 Microscope Bacteria
- Semmelweis 1847 Hand washing pre delivery
- Lister 1865 Germ theory/antisepsis
- Darwin 1859 The Origin of Species
- Watson and Crick 1953 DNA

19th 20th Century medicine

- Louis Pasteur Linked bacteria with disease
- Claude Bernard (also) Pasteurization
- Robert Koch Nobel Prize 1905 Tb Cholera
- Florence Nightingale
- Elizabeth Blackwell (1821-1910)
- Henry Dakin Solution still in use
- War inventions X-ray, ECG, Pcn, Psych
- Evidence based medicine; exponential progress

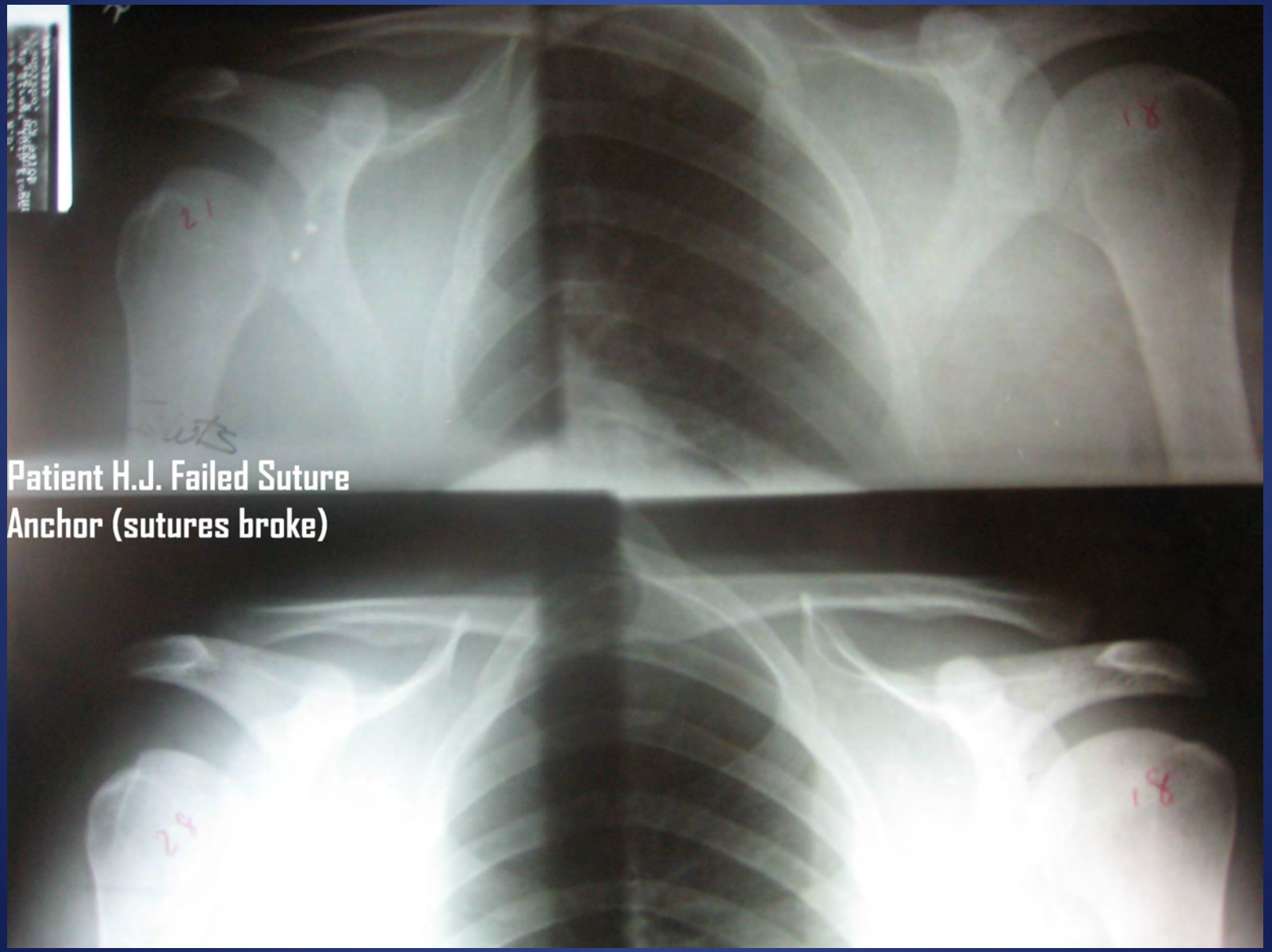
I S I





Innvotec Surgical Inc.

Suture Breakage



ISI Mission

The ISI mission is to deliver immediate stability in peripheral joints and in turn facilitate more rapid healing and return to full mobility patients facing joint repair and replacement

Market

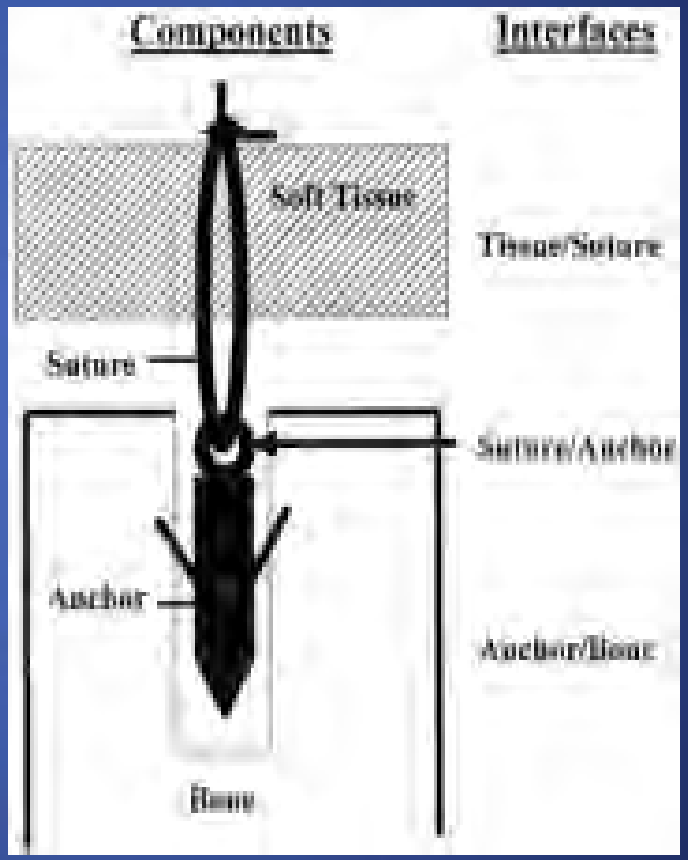
- $25-30 Billion orthopedic market
- 700,000 shoulder repair procedures annually
- 300,000 ACL reconstructions annually
- Small Joint use also being investigated

Product Areas

- Joint Repair/ Reconstruction (Soft Tissue Connectors)
- Joint Preservation Alternative (Joint Spacers

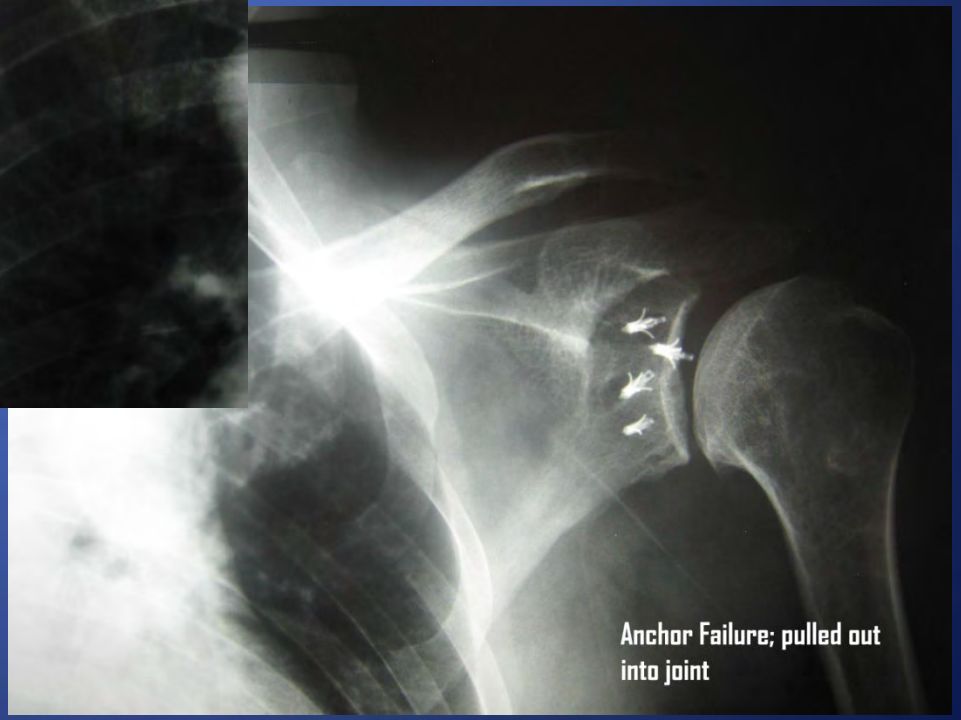
Weakness of Anchor Designs

- Anchor-suture interface commonly determines the weakest link in soft tissue to bone fixation
- Suture breaks at 30lbs or less of force
- Weeks of immobilization required to ensure healing of tissue to bone.



Rupp, S. et al. Fatigue Testing of Suture Anchors. American J Sports Med. 2002, 30: 239-247

Anchor Failures

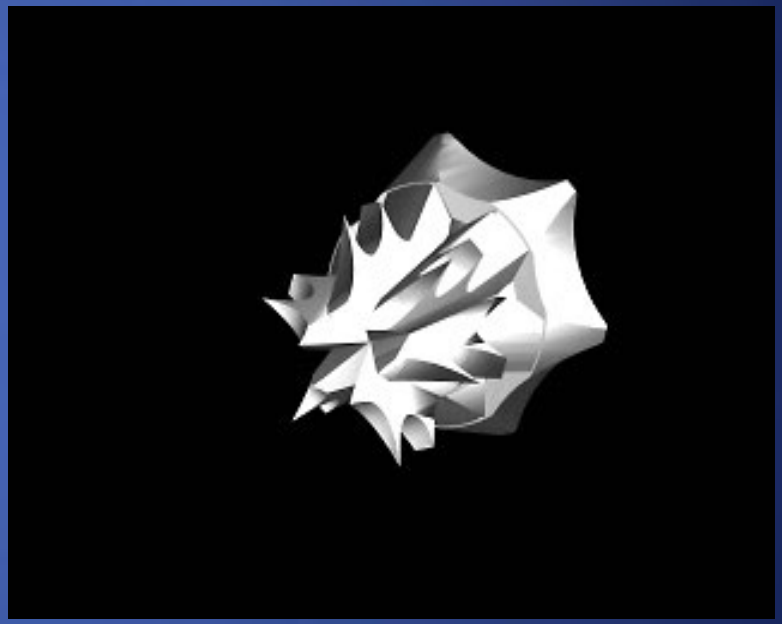


Stabilizer Invention Technology Description

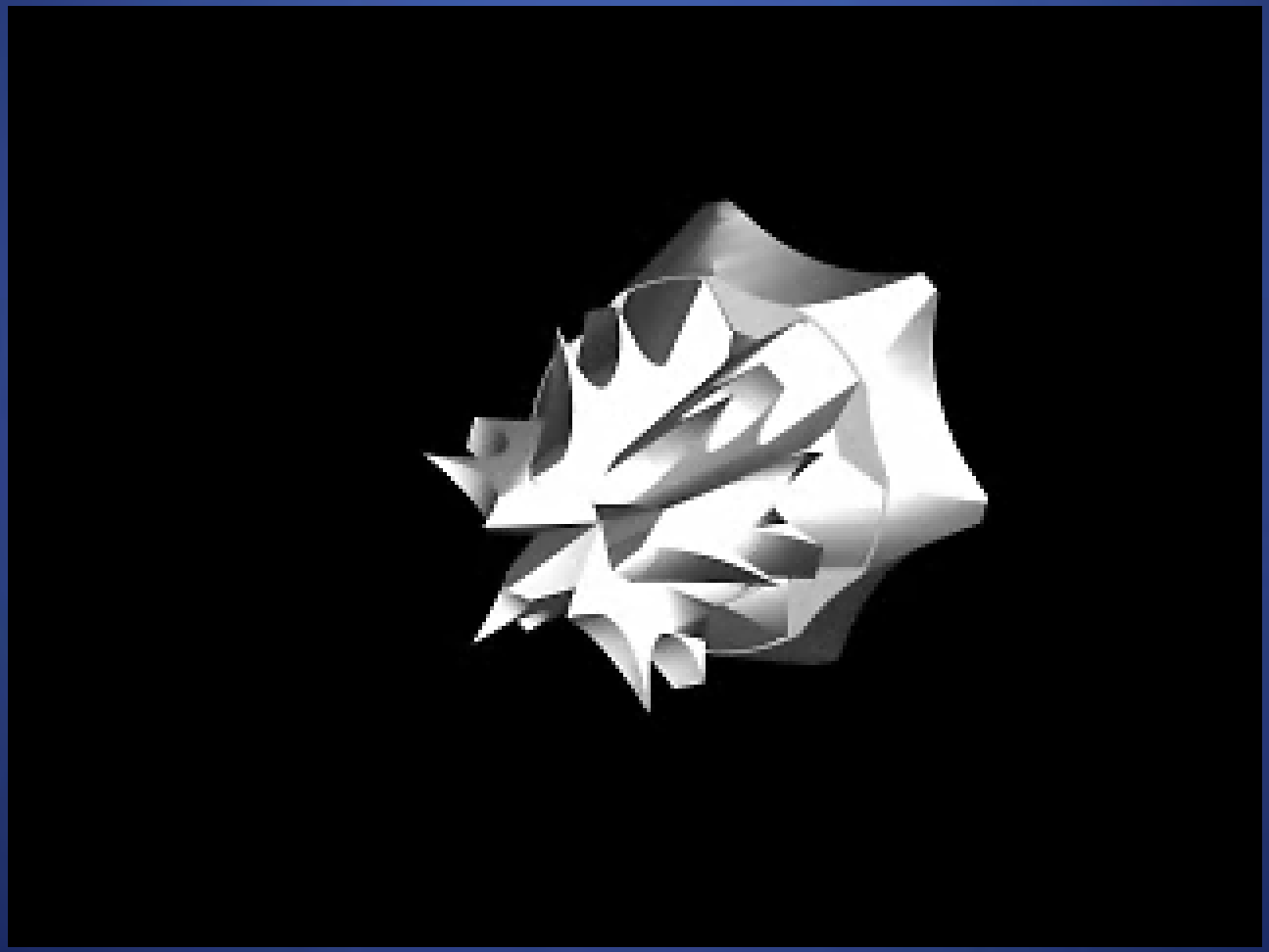
- 4 – 8 mm diameter washer-like device
  - Stainless steel or Titanium
- toothed bone anchor prongs
- Skewer and hold soft tissue
- Graft driven into pre-drilled bone tunnel
- Expansion of teeth with remarkable holding force:
  - **600 pounds (2669 Newtons)**

Stabilizer Delivers:

- Optimal healing, by better repair and reconstruction of injured joints
- Faster mobilization of repaired joints and the patient
- Less pain with improved function

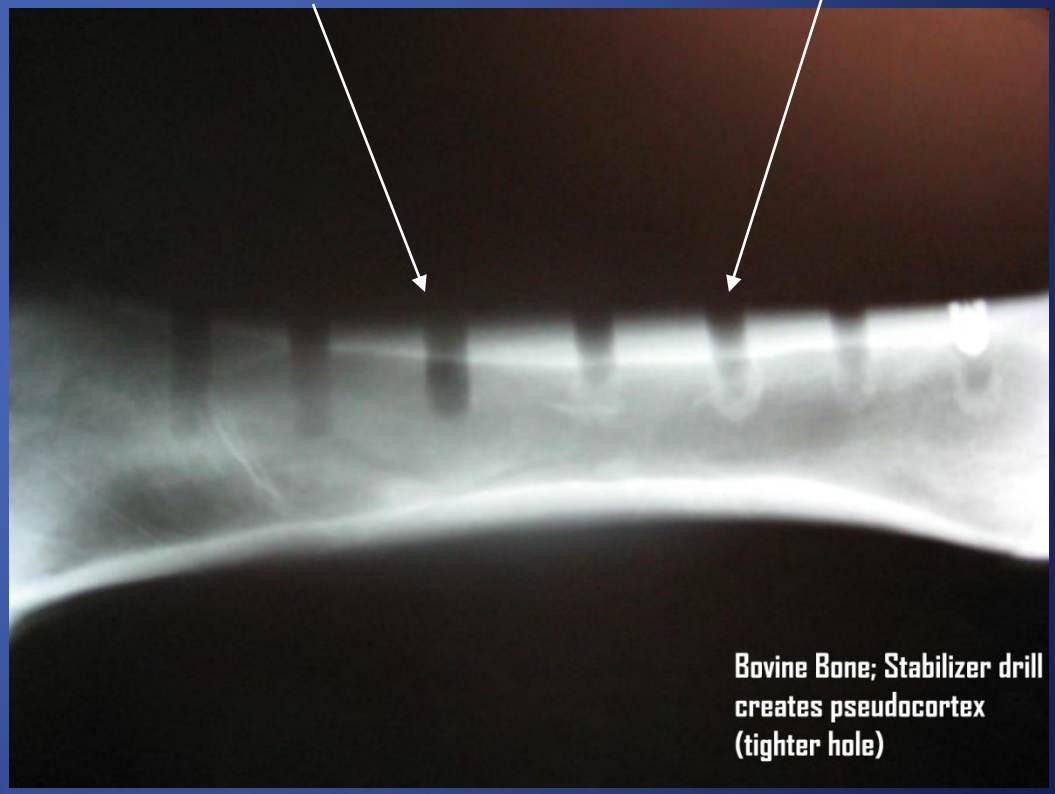


Stabilizer Expands



Stabilizer Drill Advantage

- Pilot tip enables “no slip” drilling
- Zero rake allows bone debris to be captured and deposited into bone hole, creating a tighter receptacle for Stablizer implant.



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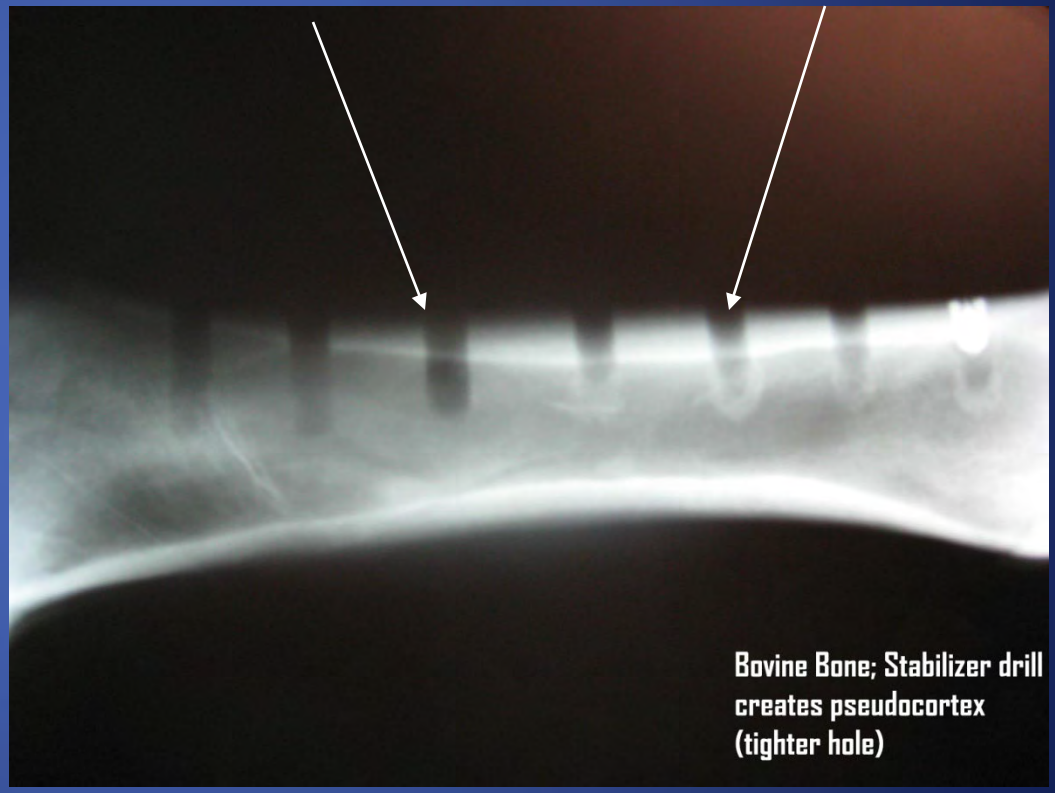
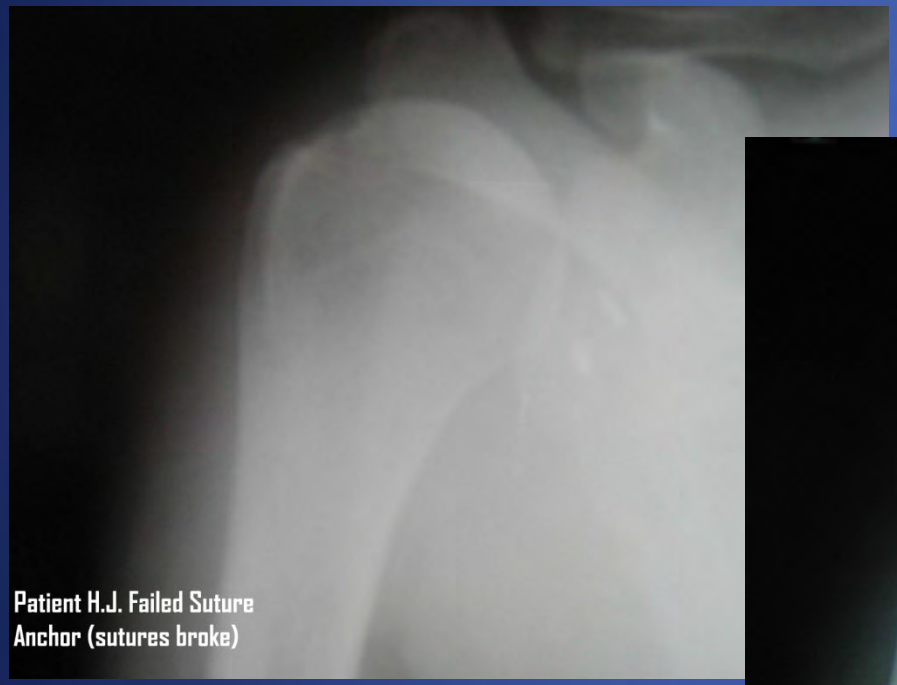
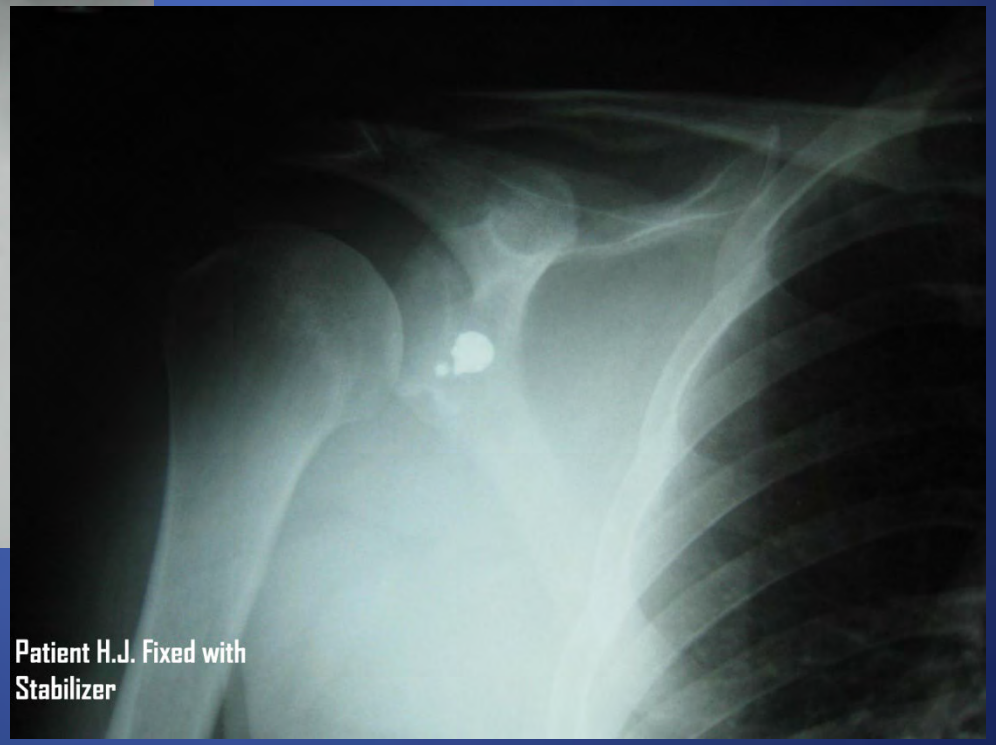


Stabilizer Repair



Patient H.J. Failed Suture Anchor (sutures broke)



Patient H.J. Fixed with Stabilizer

Comparison with Competing Technologies

Stabilizer	Suture Anchors/ Interference Screw
Stabilizer skewers the graft itself	Typical anchors rely on sutures
Stabilizer holds at 600 pounds	Mitek Anchor → 42 pounds Suture → 30 pounds
Stabilizer directs tissue around 360 degrees of bone hole	Interference screws hold 180 degrees
Immediate stabilization with little down time	Delayed healing; gradual rehab

Proposal

- **Capital - $3 million, follow-up $5 million at end of 2008 to drive market development**
- **1.5 - 2 year time frame**
- **Goal – Validate Stabilizer for clinical release. Transfer to manufacturing. Advance Joint Spacer designs and materials**
- **Initial Requirements**:
  - 2-3 Engineers, 1 technician
  - 1 administration.
  - Small lab space, appropriate equipment
  - Prototyping, testing, re-design
  - 30-40 patient pilot validation study for safety efficacy
  - 150 patient clinical trial to assess rapid rehabilitation
  - Design transfer to manufacturing with tooling

Failures as the Best Teachers

- Partnerships set up with wrong team
- Money contributed misused
- Personality issues hidden/negatives
- Bankrupt accounts led to loss of IP
- Family/friends suffered
- After downtime, partially recooped

Lessons Learned

- Know your partners; pick the right ones

- Retain as much equity as feasible
- Create contracts that return IP if problems
- Maintain primary goal to heal patients
- Be tenacious; Never never never give up
- Combine passion, opportunity, bravery

Collaboration growing between Scientists and Investors

- Inventions = 1/1000
- VC funding = 1/500
- Working together is mandatory between inventors, engineers, and investors
- The patient is most important
- Tenacity is King

Alfred Nobel

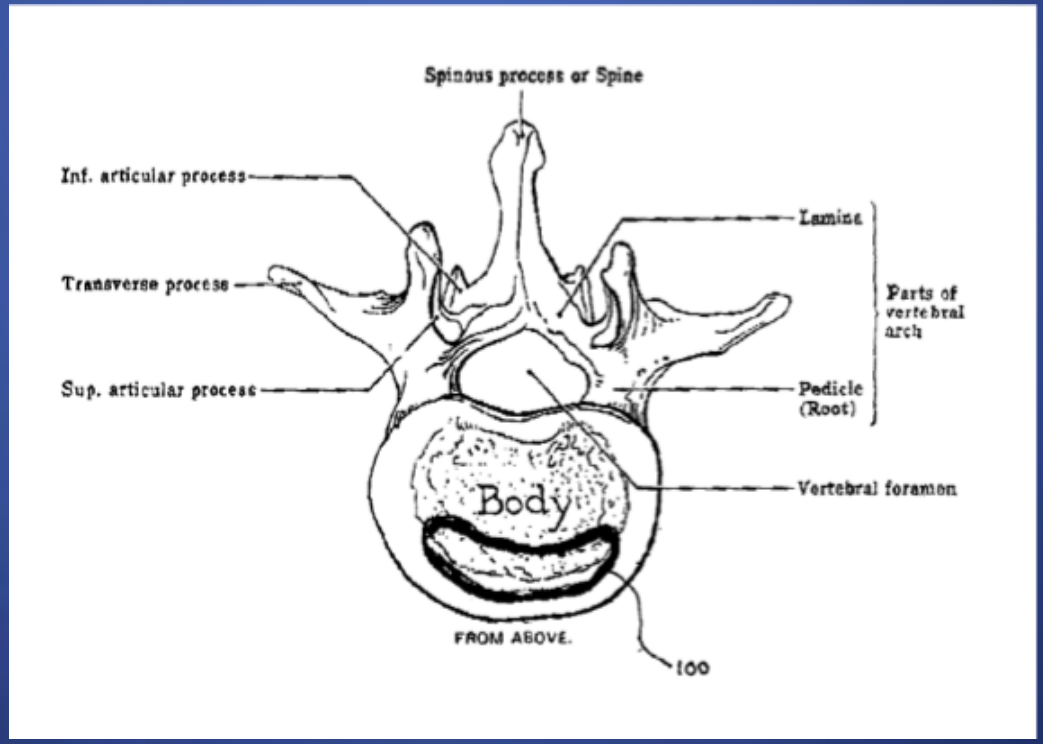
Selectively Expanding Spine Cage

SEC

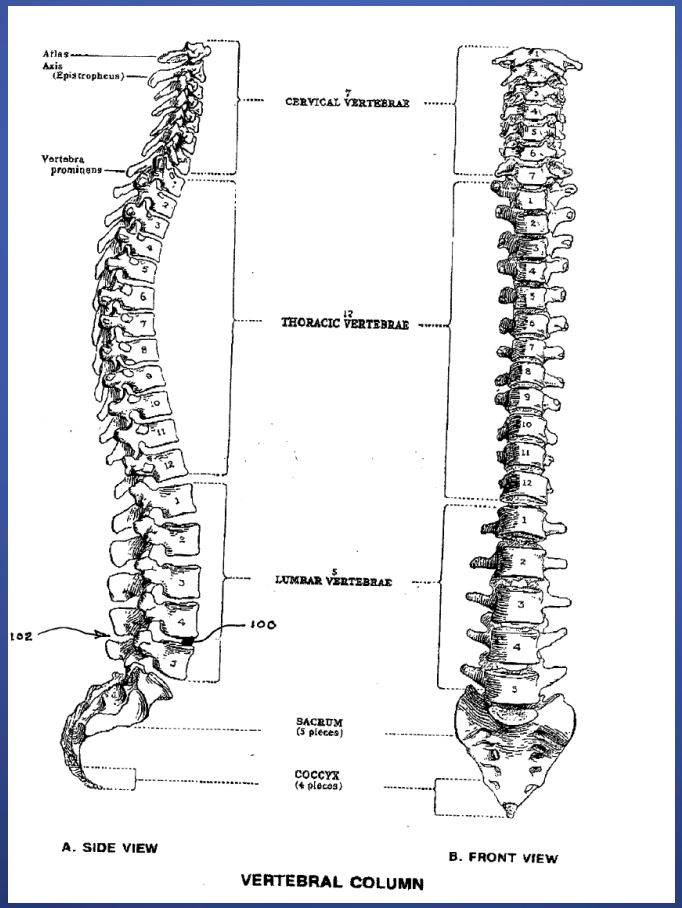
R. Thomas Grotz, M.D.

Invertebral endplate

- SEC enters posterolaterally, placed into anterior column



•Spine alignments
Natural curves maintained
Scoliotic curves corrected



Linearly Expanding Spine Cages

- Dual cages placed anteriorly
- Fill intervertebral disc space with trapezoidal expansion maintaining lordosis
- Enables immediate fusion effect, then healthy recovery

Linearly Expanding Spine Cage

- LEC (closed position)

- Existing cages
  - stationary
  - parallel

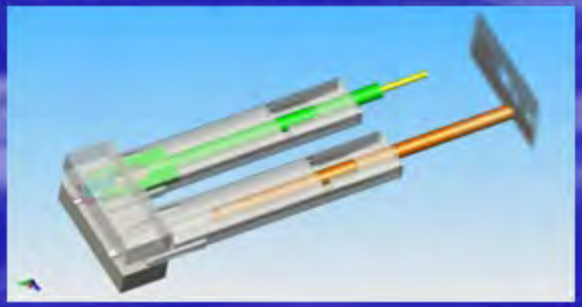
- LEC
  - expands (fixes)
  - trapezoidal

Linearly Expanding Cage

- LEC (open, expanded position)
- Enables early return to work or sports
- Decreases pain; increases function

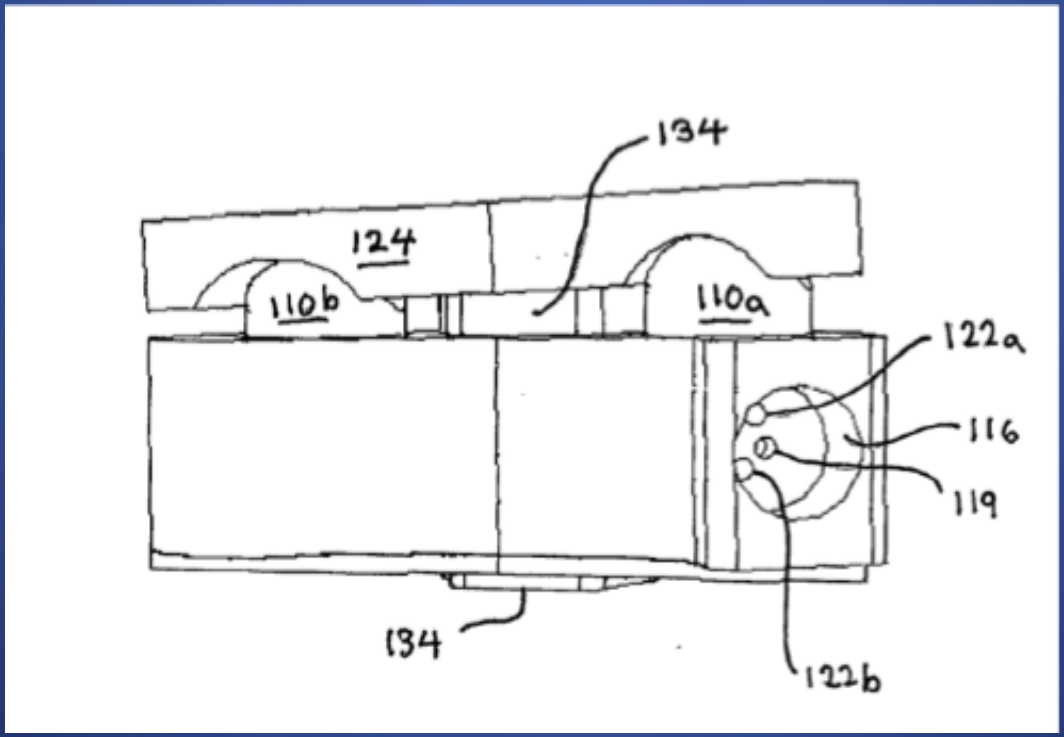
Precise insertional equipment

- Increases result accuracy
- Applicable to other cages
- Patents pending for implants, tooling, and method of surgery



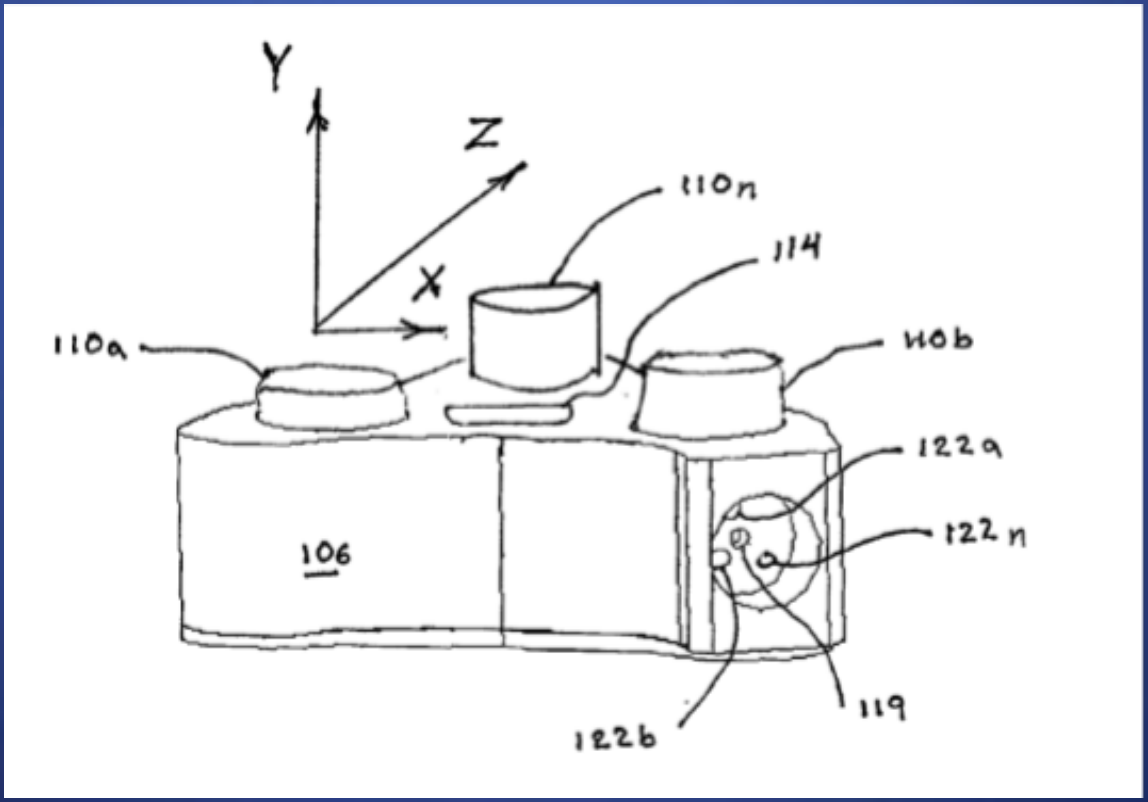
SEC patent drawing

- Superior Endplate elevating on right



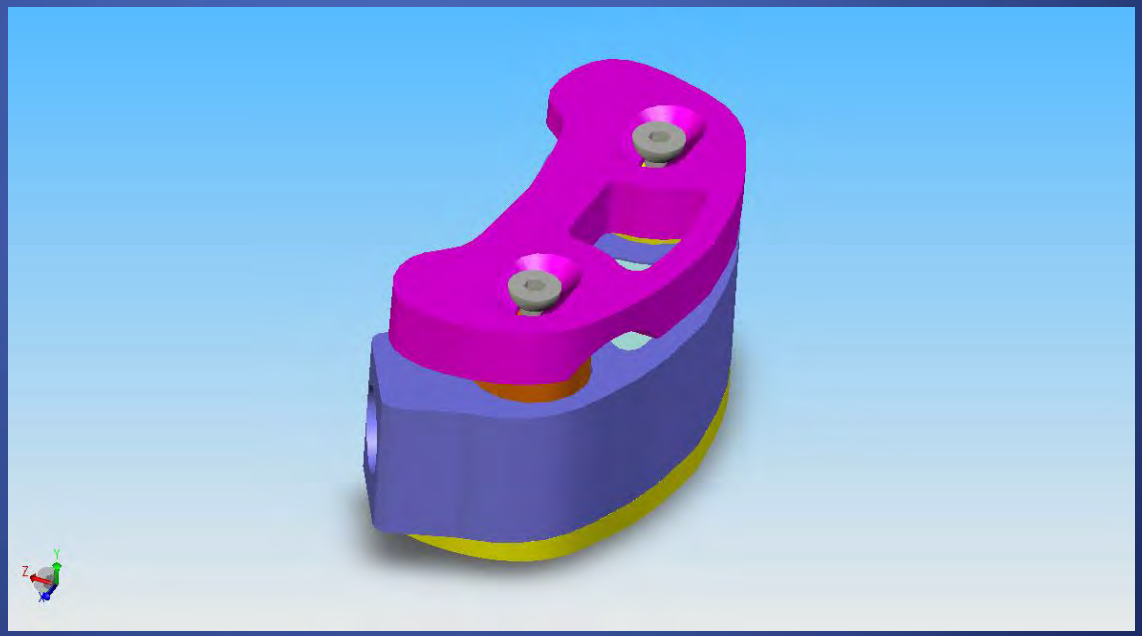
Patent drawing of pistons

- Three dimentional spine alignment control



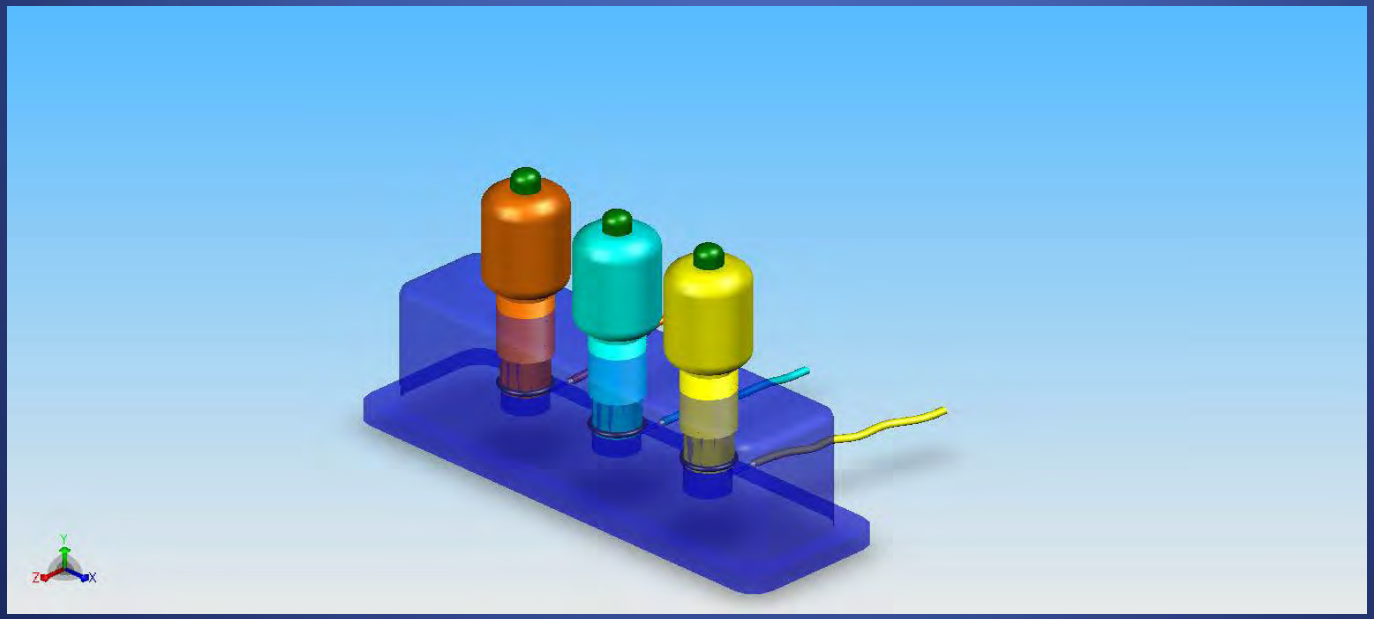
SEC Expanded state

- Pressuring expansion fixes spine during insertion



Master Cylinders

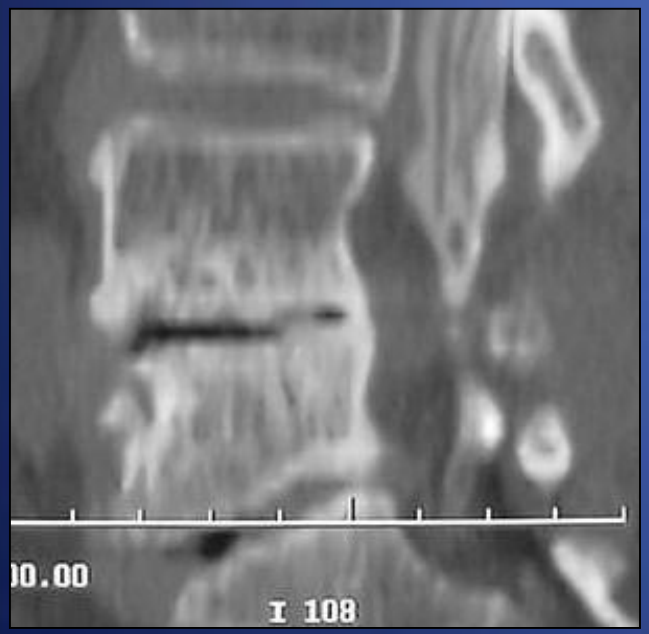
- Surgeon controls exact expansion force and spine angle changes



Selectively Expanding Cage

- AccuLif with CoAlign Innovations

SEC animation



Radiographic comparison of fixed cage vs. expandable cage in TLIF

Dennis Crandall*

Eric Huish^

Sigurd Berven#

Neel Anand@

Murali Kadaba+

Ryan McLemore^

**Sonoran Spine Center, Phoenix; #UCSF, San Francisco;@UCLA, Los Angeles; +CoAlign, inc.; ^Banner Orthopedic Residency Program, Phoenix*

Key Product Timelines to 510K

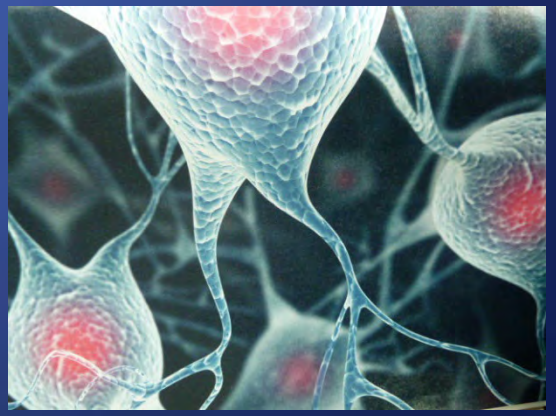
CoAlign™
INNOVATIONS

Study Conclusions

- An expandable TLIF cage increased anterior, mid, and posterior disc heights compared to the static control TLIF cage.
- The expandable cage increased average disc angle (segmental lordosis) compared to the control cage.
- Regional lordosis was unaffected by either cage.
- The ability to expand an interbody cage after insertion positively impacts segmental height and lordosis compared to static cages.

Invention Landmarks achieved

- Idea -- enter disc space, expand
- Patents filed – LEC earned; SEC pend
- FDA – first hydraulic 510k FDAs
- FIH – implanted in Capetown, USA
- Thought leader penetration
- Commercialization underway



RADJoint Orthopedics

RadJoint Orthopedics, LLC.

RJO develops products to halt degenerative joint disease focusing on cartilage protection and re-growth.

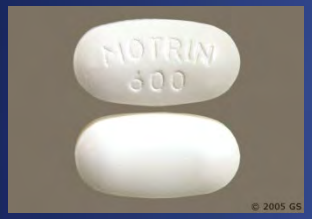
The Problem

- No existing treatments halt degenerative joint disease (exc. Carticel ~ $50,000)
  - Joints break down with use, injury or disease causing pain and dysfunction.
  - Current treatments are limited to palliative or ablative therapies.

DJD Treatment : US data

Injection

Debridement



Pills

Therapeutic Gap

Replacement

$16 bil cost
19 mil pts

$2 bil cost
1.5 mil proc

$17 bil cost
$7 billion devices
1 mil procedures

RadJoint Orthopedics, LLC.

Objectives:

1. Provide Resilient Arthroplasty Devices (RADs) to halt degenerative joint disease

2. Provide biologically active RADs to reverse arthritis, heal damaged joint surfaces

RJO's Solutions

- The Resilient Arthroplasty Device (RAD)

1. Polymeric inflatable implant ("interpositional arthroplasty")

2. RAD with bioactive substances: viscolubricants, chondrocytes.

RJO's Solutions

- The Resilient Arthroplasty Device (RAD)

  - Pads cartilage deficits, cushions joints and reverses arthritis (smooth, shock-absorbing, flexible, wear-resistant space between bones)

Comparative Analysis (Knee)

	Total Knee	RAD
Surgical procedure	Open	Arthroscopic
Incision size	4”-10”	2 incisions ≤ ½”
Surgical duration	2-4 Hrs	~ 1 Hr
Bone & cartilage	Ablated	Preserved
Revision possible	Difficult	Yes
Function limitations	Major	Minimal
Time back to work	6 wks	Few Days
Hospitalization	3-6 days	Outpatient

Regulatory Considerations

- US Strategy:
  - 510k with extensive bench testing data for substantial equivalence
  - PMA – for biologically active device
- OUS/EU Strategy:
  - CE mark with 25 pt study, 12 month follow-up.

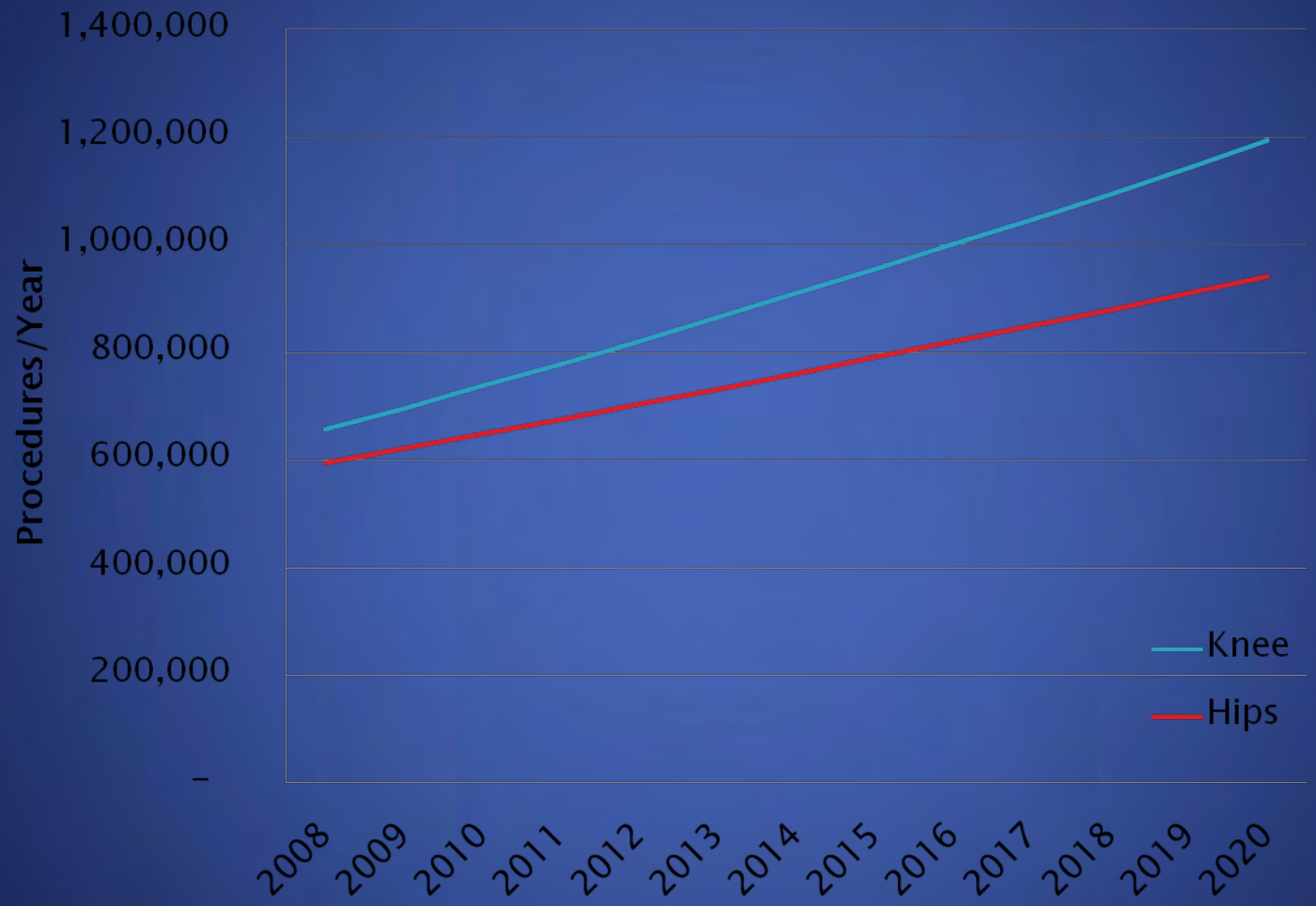
Intellectual Property Summary

- Five provisionals filed, one published (US and PCT)
- FTO is probable
- Hostetler (WSGR) is IP counsel

Driving Market Trends

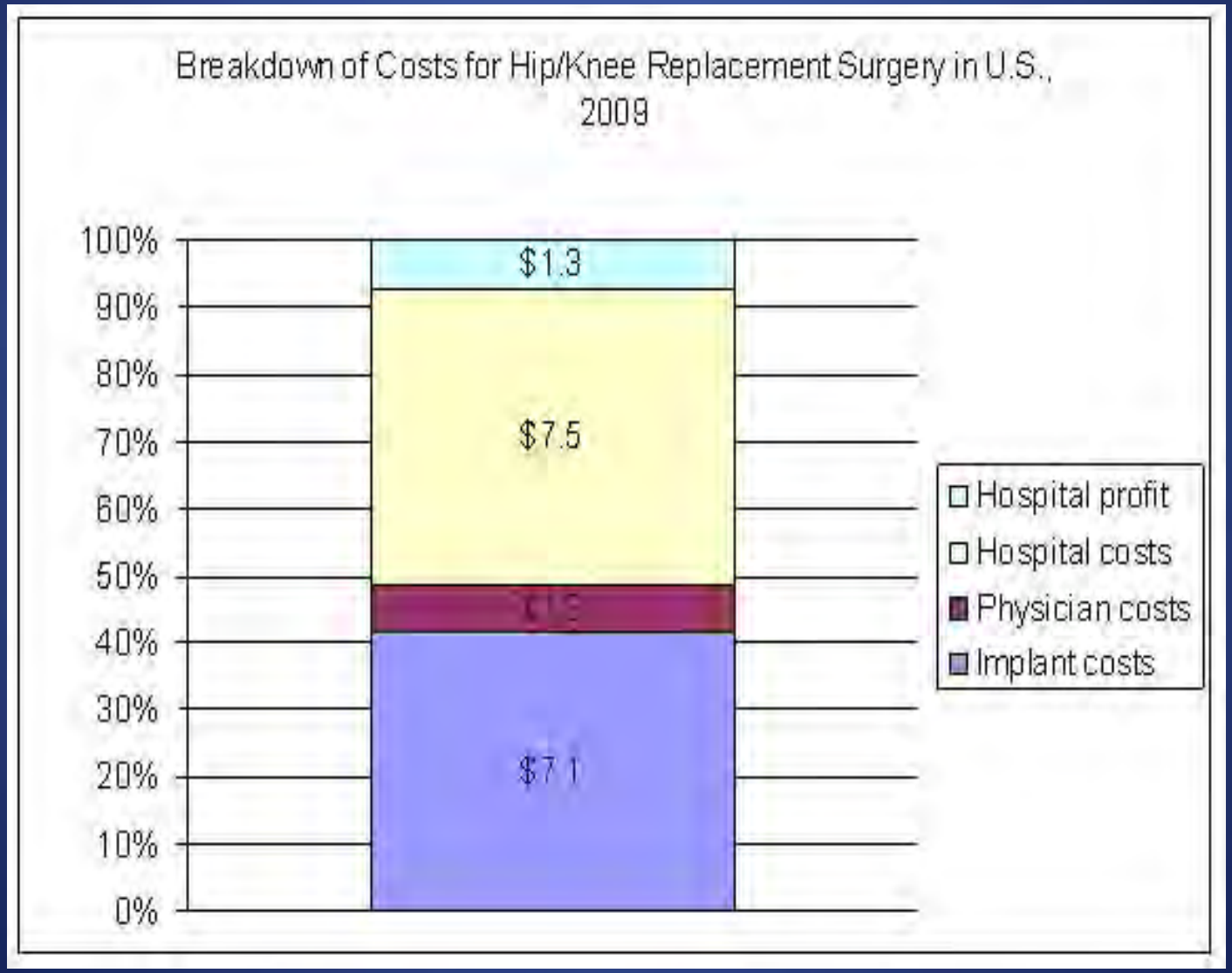
- Aging population
  - 18% growth in US population from 2000 to 2020
  - 65 and older age group will double in the U.S. from 2000 to 2030
- Increased longevity and activity expected
- Younger patients getting hip and knee implants
  - Increased 35% in the last decade (from 34% to 46% of surgeries)
  - Accounts for $6 billion of the hip and knee market
- Expanding market boundaries
  - Use in younger patients
  - Safer for older or ‘inoperable’ patients
  - More adaptable to emerging markets worldwide

US Knee and Hip Procedure Forecast



Stryker 2008-2009 Fact Book; various Wall Street analyst reports, including: JP Morgan, Thomas Weisel Partners and Credit Suisse

Implant = 40% of total cost (US)



New Interpositional Devices

- OrthoGlide® (ABS Corporation)

- UniSpacer® (Zimmer)
  - Re-operation rate: 5%-21%

- iForma™ (ConforMIS)
  - Requires custom manufacture
  - Bone resection

- NUSURFACE™ (Active Implants)
  - Prosthetic meniscus

Current State of Joint Replacements

- Restore neither proper joint spacing nor cartilage cushioning
- Ablate normal physiology
- Hard joint bearing surfaces, may dislocate, and eventually fail due to loosening or infection
- MIS require 4-8” incisions for knee replacement

Figure 1

Figure 2

Traditional Replacement vs. RAD

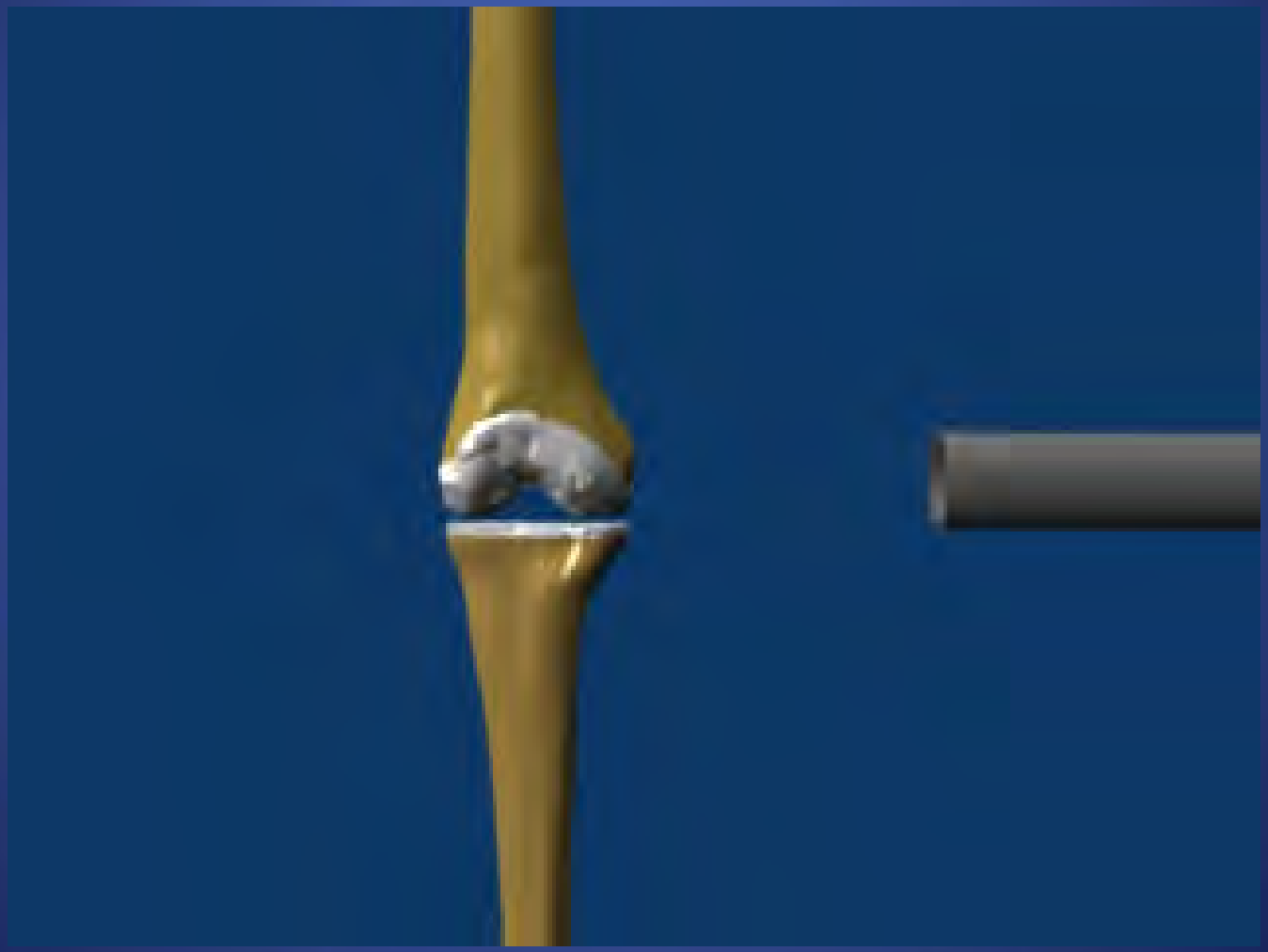
Traditional Replacement

- Major open surgical procedure with significant rehab
- Destroy joints, implanting plastic/metal
- Fail due to infection or loosening

RAD

- Arthroscopic out-patient procedure & faster recovery
- Preserves functioning tissue, renews joint space, reducing pain, restoring function

RAD = Resilient arthroplasty device



Materials Selection

- Two materials considered now:
  - Bionate: thermoplastic polycarbonate urethane
  - ChronoflexAR: thermoplastic polyurethane elastomer
  - Both materials have been tested for compliance with the demands of orthopedic applications

Future Solutions

- Beyond the knee
  - Hip
  - Shoulder
  - Ankle
- RAD variations
  - Drug-eluding RAD
  - Stem cell RAD

Ideas to Reality Course Summary

- Make sure your idea is a solution and unique
- Describe it accurately; create the patent/IP
- Decide how it will be safely used initially
  - FDA (USA) 510k short vs PMA long regulatory
  - OC (Other than US) early trials for data/profit
  - Do no harm; rather, improve existing care
- Earn FIH (first in human) milestones
- Fund/commercialize
- Remember: Passion/Opportunity/Bravery

Thank you