

Q180367 – Pre-Submission Meeting

June 18th, 2018

Resilient Arthroplasty Device (RAD)

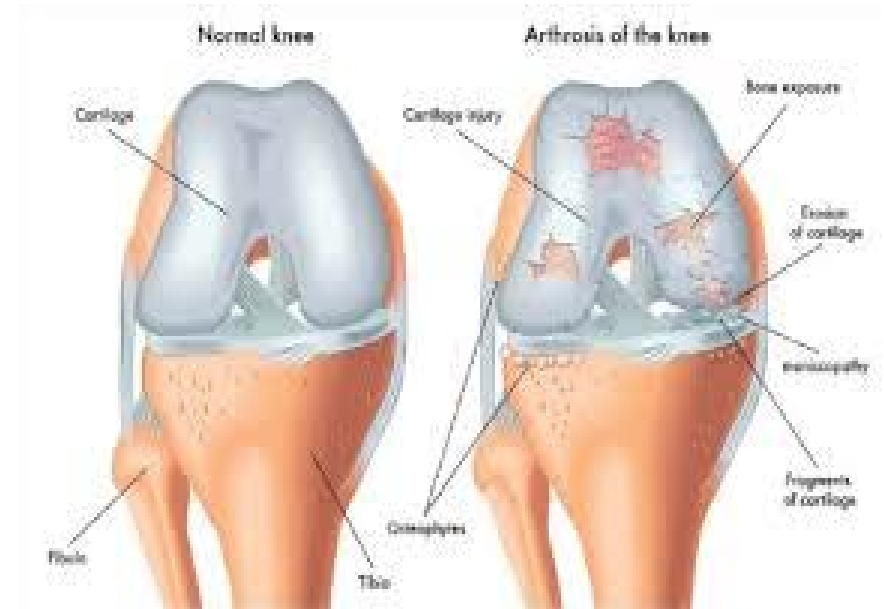
Agenda June 18th, 2018 FDA iOI EFS PMA Mtg

- Introductions and administrative information (5 minutes)
- Product-specific presentation (15 minutes)
 - Prototypes
 - Surgical procedure review
- Questions from FDA
- Discussion
- Answers to proposed sponsor questions
- Closing, summary of conclusions and action items to success

Team collaborators working toward better care

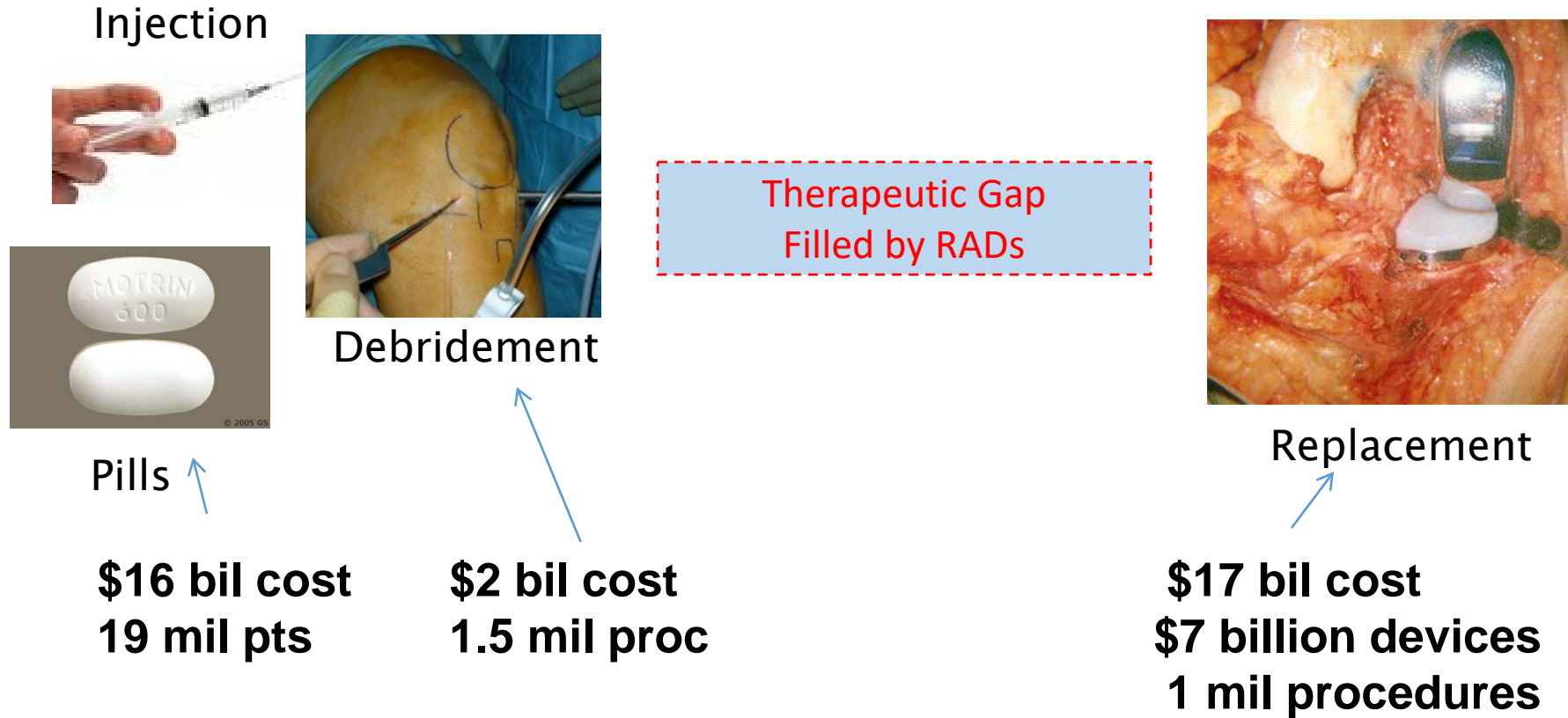
- FDA
- iOrthopedics Inc (iOI)
- DSM
- Empirical Testing Corp (ETC)
- Hogan Lovell Law Consultants
- Modified Polymer Components, Sunnyvale, Ca
- Flex Partners, Carlsbad, Ca
- Vijah Goel, PhD, Toronto, Oh
- Taylor Collaboration, San Francisco, Ca
- Surgeons from UCSF, Stanford, private

Knee Arthritis Problem



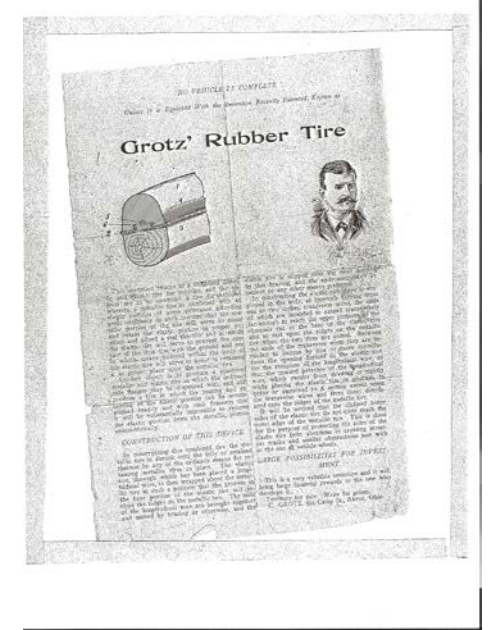
- No existing treatments to halt degenerative joint disease except Genzyme's Carticel stem cells, more recently Vericel's MACI *that earned FDA APPROVAL for distal femur; SAME Rx area as RAD*
- Joints breakdown with injury or disease causing pain and dysfunction
- Patients lose independence in ADL Quality of life suffers
- Current treatments are limited to palliative or ablative therapies

DJD Treatment : US data

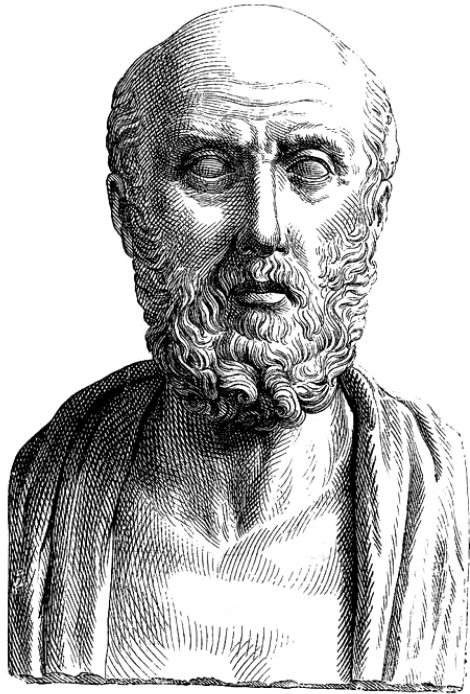


iOrthopedics Inc (iOI) transition TJR to RAD

- 1891 earliest Total Joint Replacement (TJR) attempt (for Tb)
- 1903 US technical advances
 - Rubber tires patented for cars; millions of cyclic loads (Christian Grotz)
 - DSM founded (30K employee, \$20B Royal Dutch Company => RADs)
- 1900s Interpositional arthroplasties trialed - fascia, mucosa
- 1925 glass interpositional arthroplasties failed; metal selected
- 1940 (first US THR); 1968 (first US TKA)ablative (sans PMA), ~ SAME NOW!
- 1950-2000 M on PE prostheses yield to M on M. 'Less wear' yet pathologic: synovitis, immunosuppression. Not physiologic care
- 21s century RAD restorative materials & design due for safe effective use



21 century interpretation of Art & Science



"First do no harm"

The Greek physician [Hippocrates](#) (460–370 BC), author of the oath.

危機 危机

In the Chinese language, the word "crisis" is composed of two characters, one danger and the other, opportunity.

After treating 25,000 patients through 100,000 injuries performing 10,000 surgeries including TJR of the shoulder, elbow, wrist, thumb, finger, hip, knee, ankle, plus 110 Carticels between 1996 & 2008 delaying TKA in 102/110, RADs appear preferable over ablative current techniques

Current State of Joint Replacements

- Restore neither proper joint spacing nor cartilage cushioning
- Ablate remnant tissues; disposing to garbage
- Implant hard metal/hard plastics, that may dislocate, and too often fail due to loosening or infection
- Major surgeries require 4-10” incisions for routine replacements



Figure 1

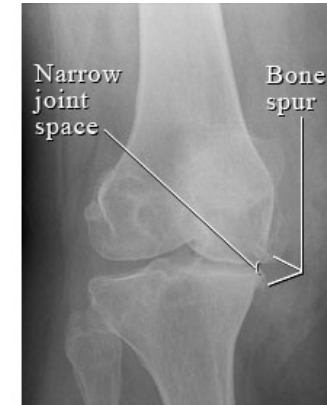
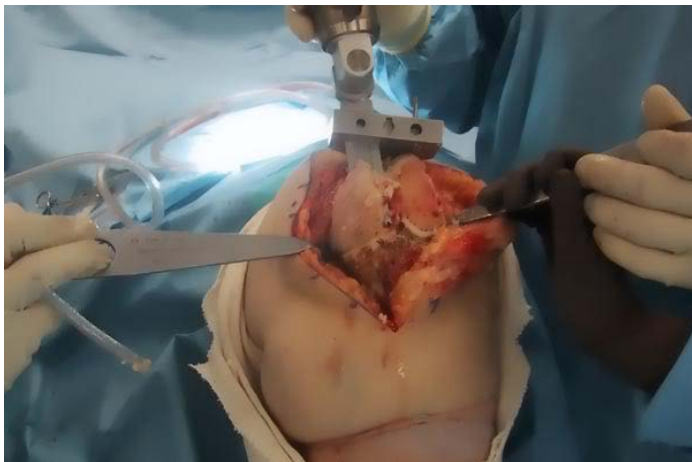


Figure 2



Total knee replacements cut joint open, remove arthritis plus normal remnant cartilage, ACL, destroying femur/tibial/patellar interfaces, removing natural joints for use of metal and PE. Joints CAN be Restored



Quote from patient with total knee replacement:

- **“TKR surgery WARNING** Tell your families that this is what they did to you during surgery:

1. They gave you various types of anesthetics and more or less knocked you out.
2. They sliced you open (my incisions are about 9" in length.).
3. They sawed off two bones, and they were not gentle about it.
4. They pounded, grappled, and fitted you with your implants
5. They glued, and screwed implants to your sawed-off leg bones
6. They closed you back up with sutures/staples/etc
7. They brought you out of the anesthetic
8. They made you walk on your BTKR or TKR within a day of surgery!

I had arthroscopic surgery years prior to my BTKR, and I was really amazed great I felt---I had it on Thursday and on Monday I was ready to return to school.
My BTKR recovery, though, was something else!

I went back to the classroom at eight weeks post-BTKR and that was too early”

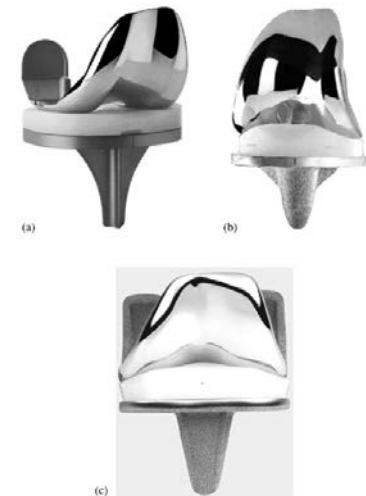


Fig. 1. Total knee replacement devices tested in knee simulator studies: (a) PFC Sigma; (b) PFC Sigma Rotating Platform; and (c) LCS Rotating Platform.

- ***RADs save joint remnant cartilage, ligaments in outpatient surgery; TKAs are still an option to patients***

Rationale for developing restorative RADs

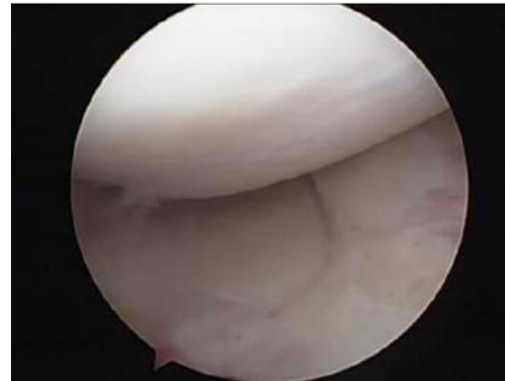
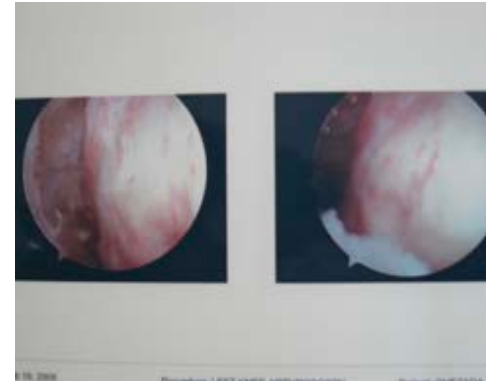
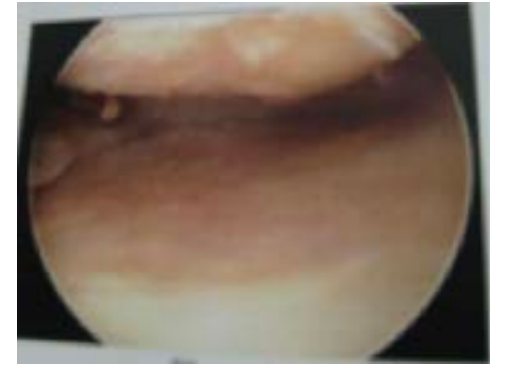
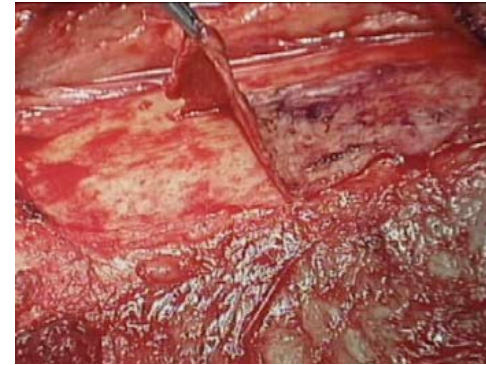
Bandages can provide extra cushioning for added comfort and protection from re-injury until the wound is completely healed so you can stay active while healing faster!



UNCOVERED



COVERED



Bionate safe, long use history, physiologic

Bionate in both appendicular and axial skeleton after decades of cyclic loads shows excellent safety results



Active Implant menisci 'fill the gap between MIS & TKA; mimics function natural meniscus'



Bryan Cervical Disc Replacement

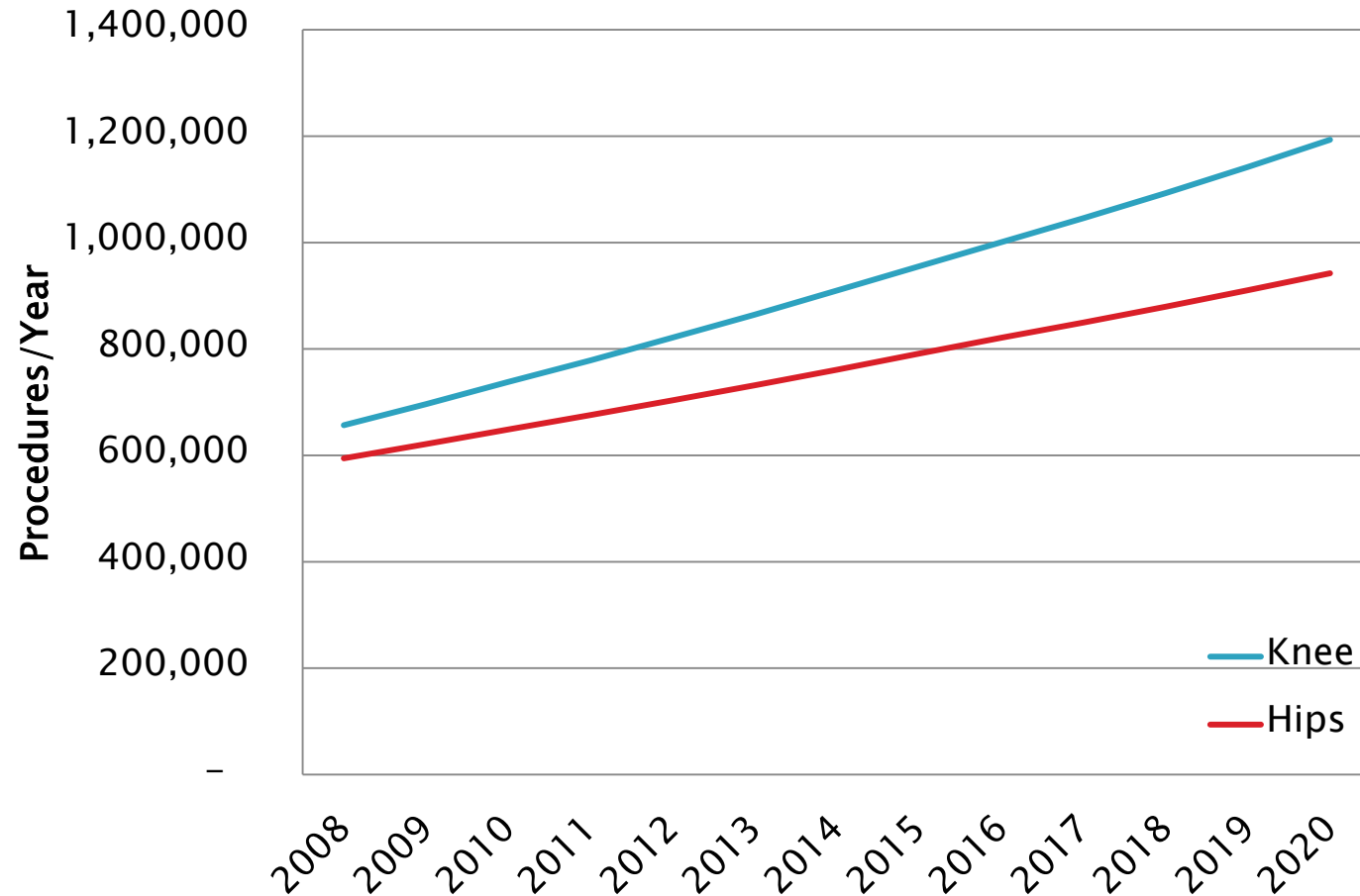
\$40 BILLION MEDICARE TKA COST 2017

800,000 PROCEDURES AT AVERAGE COST OF \$50,000. AVERAGE AGE 66



RAD TECHNOLOGY ESTIMATED TO REDUCE OVERALL COST BY 35%

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

Driving Market Trends Warrant FDA iOI RAD Allegiance

- Aging population
 - 18% growth in US population from 2010 to 2020
 - 65 and older age group will double in the U.S. from 2010 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

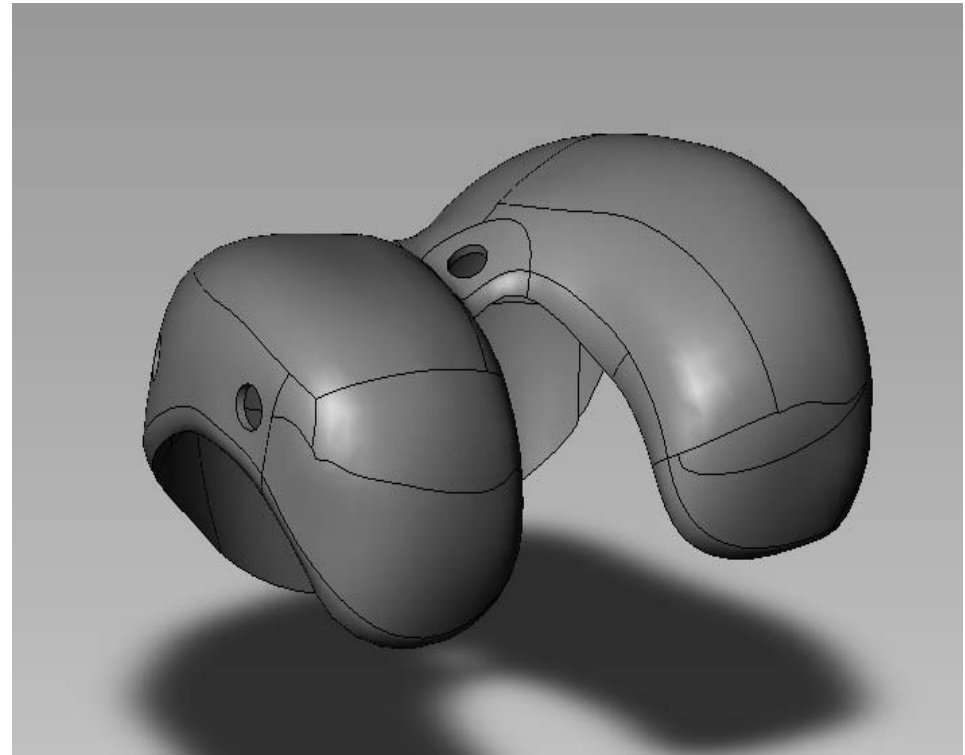
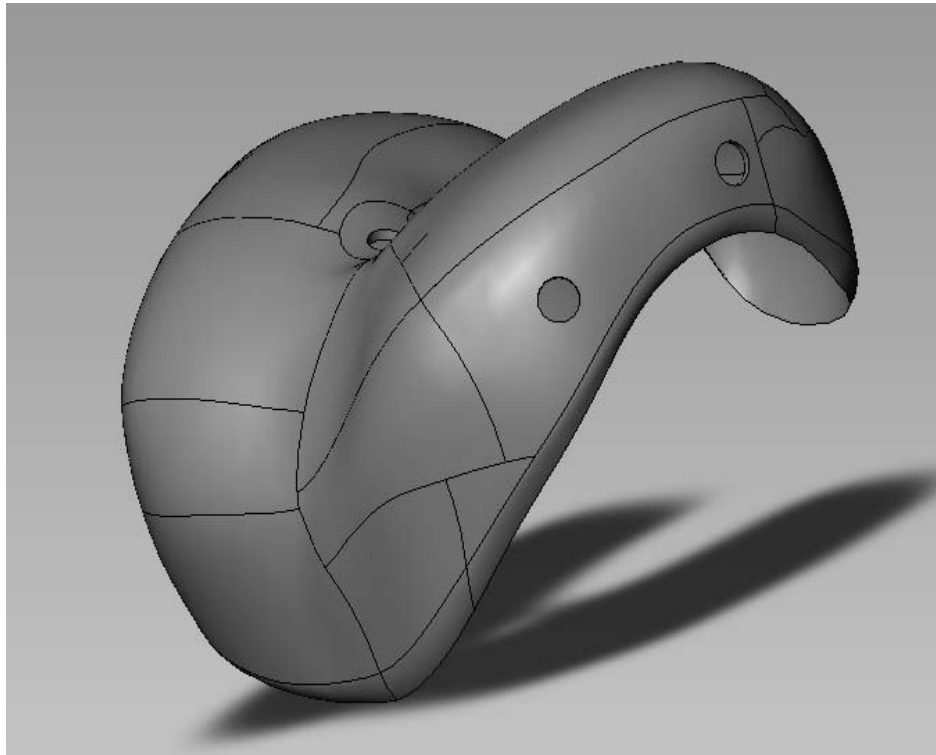
Resilient Arthroplasty Device (RAD); Goodness of Fit (compliant material)

DSM, ETC, iOI et al offer clarity regarding RAD design, fit, fixation, durability, safety and efficacy

Surgical Technique MIS/Arthroscopically facilitated/Parapatellar 2-3 cm wound plus scope loci

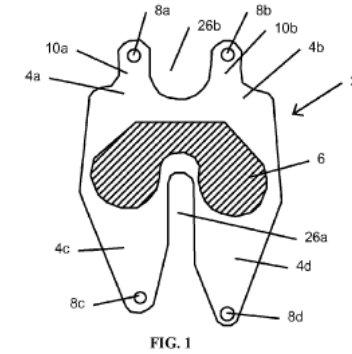
RADs **pad** joints, **cushion** limbs, **salvage** normal tissue; fill treatment gap: faster, better, cheaper

iOI gratefully acknowledges FDA concerns, respectfully requesting collaboration to serve patients

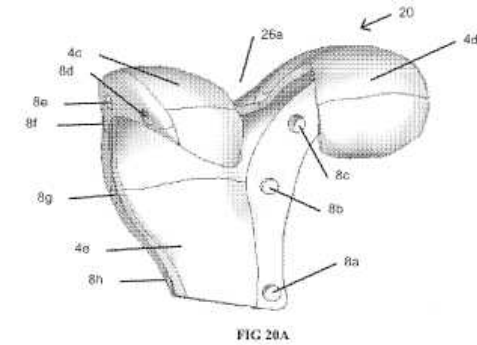
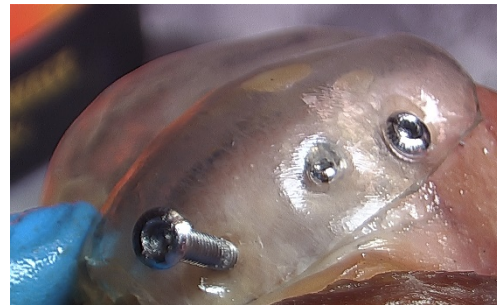


RAD evolving prototypes: Safe and Useful

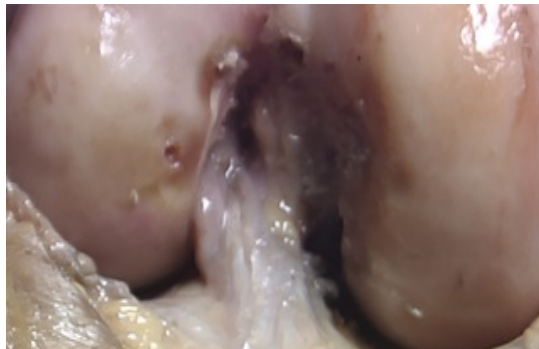
First RAD Bionate prototype from cadaver knee MRI, 3D print, mold followed 2D and 3D testing:



Fixed to cadaver femur with screws, aiming for bone in growth



After RAD prototype removal femoral hyaline cartilage protected and fixation worked after 150 test cycles

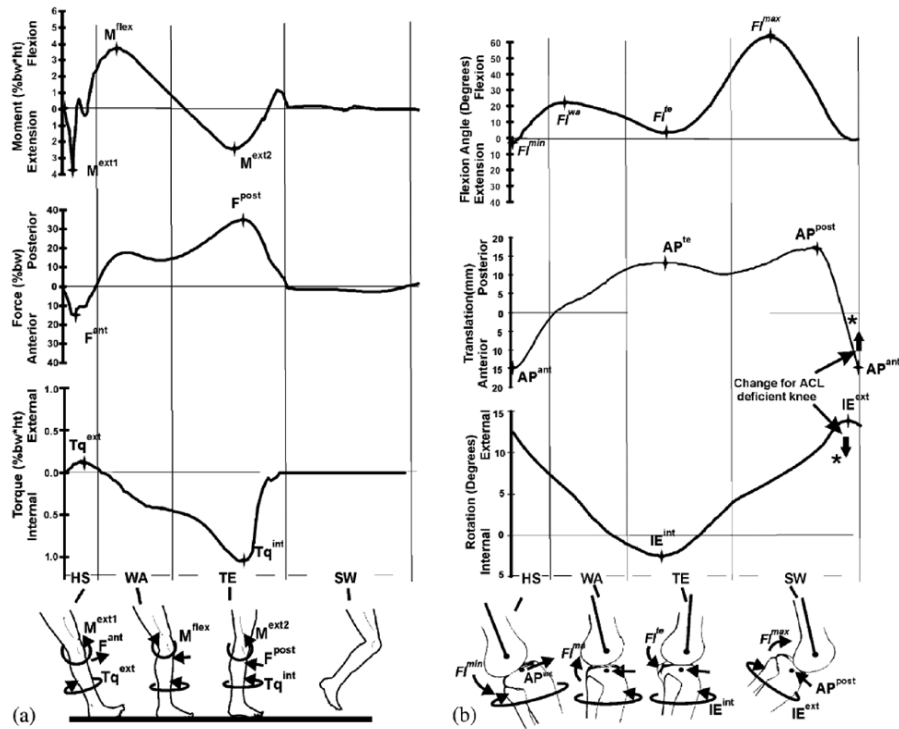


RAD seen arthroscopically preserving joint



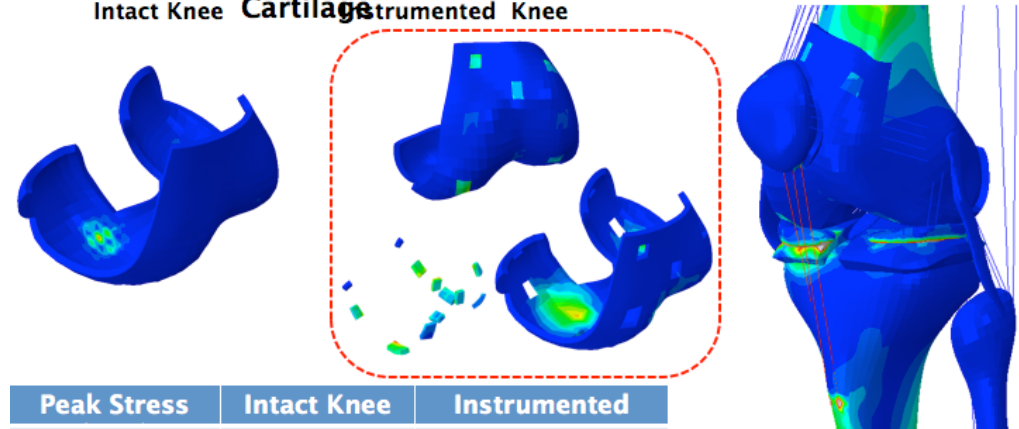
Preliminary RAD testing assures safety for human trials

iOI acknowledges the FDA advice toward more analysis; please work with us



Stress Distribution on the Model Components

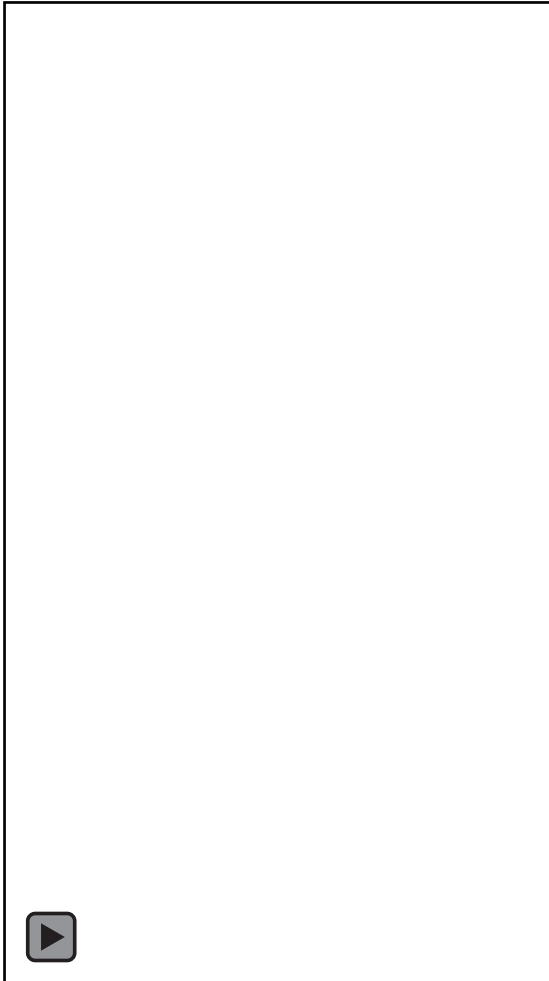
Stress on Femoral Cartilage



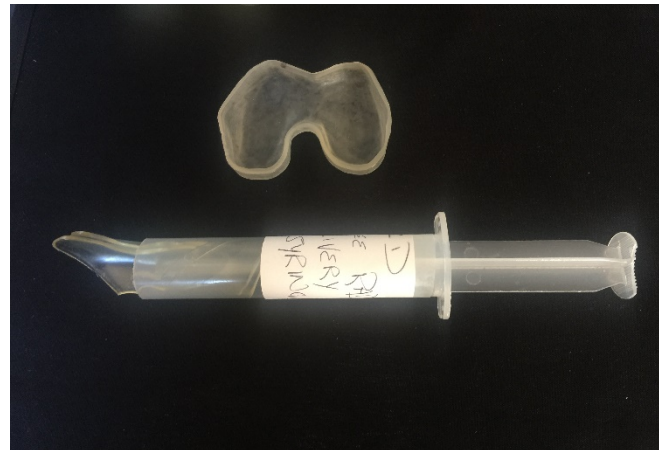
Peak Stress	Intact Knee	Instrumented
Femoral	3.46	2.73
Tibial Cartilage	2.83	2.41
Titanium Plaque	---	19.6

RAD load-motion testing, modified for human tissue

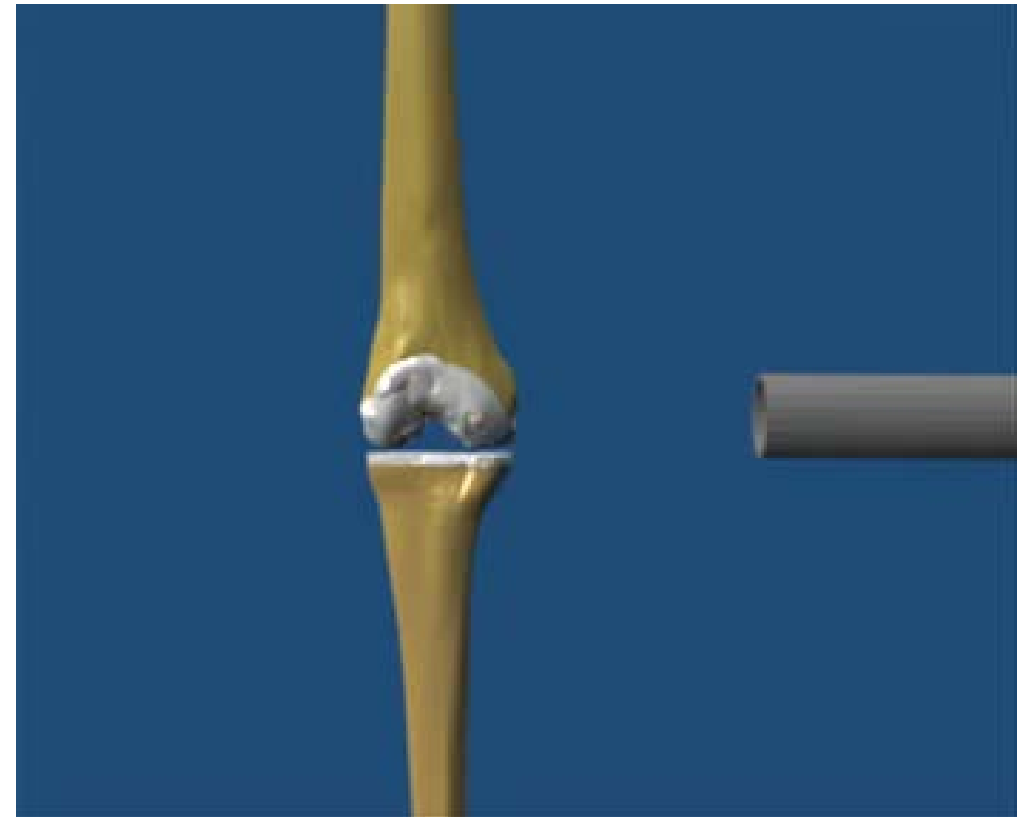
This knee motion tester
is that used for all TKAs



RAD physical folding toward
surgical delivery (FDA concern)



Computer video showing RAD MOS insertion
through conduit or open parapatellar incision



Comparative Analysis (Knee Arthritis Treatments)

	<u>Total Knee</u>	<u>RAD</u>
Surgical duration	2-4 Hrs	~ 1 Hr
Bone, cartilage, & ligament anatomy	Ablated; normal remnants excised inducing instability	Preserved as is knee stability
Revision surgery	Difficult	Easy
Duration of surgery	2-4 Hrs	= < 1 Hr
Bone & cartilage	Ablated	Preserved
Blood loss	1 unit (500 cc)	10 cc
Revision possible	Difficult	Simple
Anesthesia type	General or Spinal	Local, epidural
Infection risk	= < 5 %	= < 1 %
Function limitations after surgery	Major Cannot kneel or run	Minimal Can do normal activities

RAD versus TJR results in patients, community



	RADs	TJR
Joint Sparing	YES	NO
Procedure Cost	\$15K-\$20K	\$45K-\$50K
Recovery Time	2-3 Days	1-2 Mos.
Failure Rate	~20 Years + (?)	Avg 18 Years
Pain Reduction	80%-100%	50-75%
Components	1 Polymer PU	3 Metal/Plastic PE
Minimally Invasive Procedure	Yes	No



RAD Benefits

- ▶ RAD addresses arthritis physiologically
 - using robust safe soft pliable polymer in lieu of metal and hard PE
- ▶ Does No Harm -- whereas current technology destroys entire joint, discarding bone, cartilage and ligament preclusion healing
- ▶ Vastly more economical treatment, aims to reduce pain, improve ADL
- ▶ Outpatient Minimally Invasive Surgery expected to save time & money
- ▶ Faster recovery; immediate weight bearing; enables Right to Try
- ▶ Return to activities of daily living in days, not months

Conclusions: RADs are overdue

Patients Deserve Right to Try

- ▶ Polymer use will safely pad cartilage, cushion joints
- ▶ MIS outpatient technique fills needed gap; gives patients a choice
- ▶ Shared work between FDA and iOI will expand use, better care
- ▶ More patients will be served by physiologic wellness advances
- ▶ RADs offer faster, better, cheaper care benefiting patients, families, insurers (Medicare), employers, doctors, hospitals; win-win
- ▶ FDA EFS/IDE RAD implantation fulfills sensible compassionate need
- ▶ Agreed safe and reliable analyses will assure reasoned care



Please help us better Heal Mankind *Thank you*

