iKnee

PATIENT GUIDE

an introduction to the

Resilient

Arthroplasty

Device

the future of joint replacement.

PFD iOrthopedics

iOrthopedics PFD

the next logical step in the evolution of orthopedics is here!

The Resilient Arthroplasty Device

the future of joint replacement

Creating a new standard of care.

Metal knee replacements limit joint restoration, yet they unfortunately are the standard in our industry. In our mind, we're disrupting this $19.4B market that has used an approach of total joint replacement that is archaic (if not barbaric), when seeking joint salvage and restoration, using old technology for a millennium. New materials and design offer positive joint renewal.

In this guide, you'll learn about:

1. What is Osteoarthritis (OA)?
2. What is the current standard of care of medial compartment knee arthritis with respect to treatment efficacy, risk profile and economic burden?
3. What is a Total Knee Arthroplasty (TKA) and how does it work?
4. Is there a way to fill the therapeutic Gap between conservative therapy and TKA?
5. What is the Resilient Arthroplasty Device (RAD) technology and its first product application; the iKnee?

Contents

Welcome to PFD/iOI

at a glance

PFD/iOI was founded in 2017 to forward the development of advanced implantable orthopedic devices.

The technology was invented by Dr. Robert Thomas Grotz, a top orthopedic surgeon with over five decades of experience.

PFD/iOI has secured more than two dozen patents both in the US and internationally for its unique technology IP.

Our mission is to introduce a 21st century novel disruptive approach to fill the therapeutic gap between pills and ablative total joint replacements of joints with restorative, emergent, patient specific joint salvage technology.

PFD/iOrthopedics, Inc. (PFD/iOI) is the developer of advanced implantable orthopedic devices designed to bring renewed function to patients suffering from a variety of orthopedic issues.

PFD/iOI was founded in 2017 to begin the process of bringing to market the innovative discoveries in orthopedic device technologies that Dr. Robert Thomas Grotz, MD, one of San Francisco's top orthopedic surgeons, had been developing over the past 30 years.

PFD/iOI has secured 25 patents both in the US and internationally covering several of these innovations. With this strong IP portfolio, PFD/iOI stands to secure positions toward exponential regulatory requirement validations in bringing our products to market. Specific work on the Resilient Arthroplasty Device (RAD) technology and iKnee Resurfacing, which is the first product candidate using the RAD technology, began in 2009 when Dr. Grotz became frustrated with the failures and the incomplete recoveries of referred patients with complications from Total Knee Arthroplasty (TKA) procedures.

Prosthetic loosening, infection, limited relief of pain and restricted Activities of Daily Living (ADL) did not appear ideal recovery options

The iKnee with RAD Technology is positioned to provide an alternative treatment for patients with chronic debilitating knee pain whose only current option is a Total Knee Arthroplasty.

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from disease or injury. Dr. Grotz knew there had to be a better method and so he began work on a method that would use less invasive designs created with advanced materials to restore function, while at the same time mitigating the long list of side-effects and failure rates that were associated with TKAs. He applied for the first patent on the RAD technology before 2010, and fortified those claims with additional patents, prototypes, and extensive tests thereafter. Currently, PFD/iOI holds 16 patents on our RAD/iKnee technology which fully covers the unique differentiators that make the RAD/iKnee innovation a potential market disruptor in the orthopedic knee replacement sector.

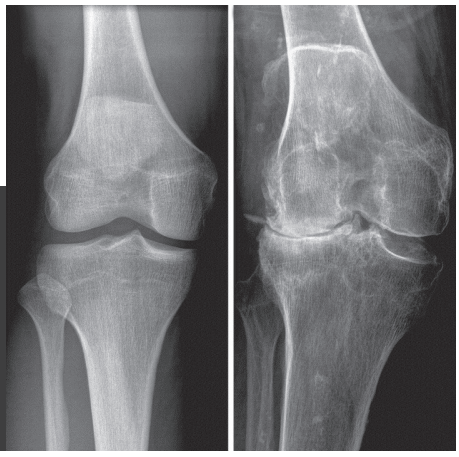
Understanding Osteoarthritis

Osteoarthritis (OA) is the most common form of arthritis. Some people call it degenerative joint disease or "wear and tear" arthritis. It occurs most frequently in the hands, hips and knees. With OA, the cartilage within a joint begins to breaks down and the underlying bone interfaces change.

Osteoarthritis occurs when the protective cartilage that cushions bones wears down over time causing debilitating pain and loss of motion.

Joints are composed of interfacing moving bone ends covered with white shiny hyaline articular cartilage that glides upon opposing surfaces, lubricated by synovial fluid, stabilized by connecting ligaments. The 'outside' container is the joint capsule with a velvety synovial lining for lubrication; once inflamed it becomes thickened, producing noxious enzymes.

When skin, muscle and bone gets injured, a blood supply mobilizes oxygen and nutrients toward healing. When articular cartilage breaks down, since there is no blood supply, it cannot spontaneously heal. Rough cartilage wears down to bone, aggravated by swollen synovial tissues and enzymes. Neither standard conservative care nor total joint replacement sufficient restore cartilage function.



The x-rays to the right show the difference between a normal knee (on the left) and one which has developed severe OA. As can be seen, the knee with the OA has lost most of its protective cartilage resulting in bone-on-bone contact which can cause severe pain.

OSTEOARTHRITIS RISK FACTORS

- Currently there are no existing treatments to halt degenerative joint disease except autologous chondrocyte implantation (ACI) using stem cells.
- OA causes joints to breakdown resulting in pain and dysfunction.
- The breakdown of cartilage can result in loose tissue material developing in the joint (chondrolysis).
- Untreated, OA can cause Bone death (osteo-necrosis).
- Overtime a joint may lose its normal shape due to grinding and small bone growths, called osteophytes or bone spurs, may grow on the edges of the joint.
- Bone or cartilage can also break off and float inside the joint space causing more damage.
- Stress fractures (hairline crack in the bone) can develop in response to repeated injury or stress.
- Bleeding and infection can occur inside the joint.
- Deterioration or rupture of the tendons and liga-ments around the joint can result in a loss of stability.
- Patients lose independence in their "Activities Of Daily Life" which compromises their overall "Quality of Life".
- Current treatments are limited to palliative conser-vative therapies or ablative Total Knee Arthroplasty.
- Maintaining overall musculoskeletal function is diffi-cult which can cause issues in other areas of the body.

The current standard of care of medial compartment knee arthritis with respect to treatment efficacy, risk profile and economic burden, remains very conservative in its approach. These conservative therapeutic options possess few, if any, characteristics of an ideal treatment. They do not provide significant pain alleviation, improve knee function, or correct compartmental knee loading aberrations.

Uncompensated mechanical loading, which is excessive force put on a weight-bearing or load-bearing joint during activity, is a primary culprit in the development and progression of OA in the knee. Joints are made up of opposing bones, stabilized by tendons and ligaments, that depend on smooth gliding surfaces for painless effective movements. When cartilage joint surfaces break down, they can't heal, which results in pain and loss of use.

At PFD/iOI, we believe that the therapeutic perspective of conservative treatment needs to shift away from pharmacological treatments, which have no influence on joint loading, provide a minimal potential to alter joint function while substantively increasing associated risks and financial costs, towards a minimally invasive load absorbing therapeutic intervention; like the iKnee.

The iKnee is a minimally invasive safe and effective medical device specifically engineered for symptomatic relief of medial knee OA. The iKnee works by limiting joint contact forces and has the potential to reduce the clinical and economic knee OA burden.

The knee is the most commonly affected joint and knee OA represents the leading cause of disability in the adult population. More than 1 in 3 Americans over 60 years of age have radiographic evidence of knee OA and 1 in 8 have symptomatic knee OA. With the continued aging of the population and the alarming obesity epidemic, the prevalence of OA is expected to increase by 40% by 2025.

OA is also responsible for a substantial economic burden, accounting for $128 billion per year in direct and indirect costs in the United States alone. Overall, the clinical and economic burden of OA is anticipated to increase and will remain a major medical problem for decades to come.

A wide variety of treatment options are available to the patient with knee OA, categorized as non-pharmacological, pharmacological and surgical.

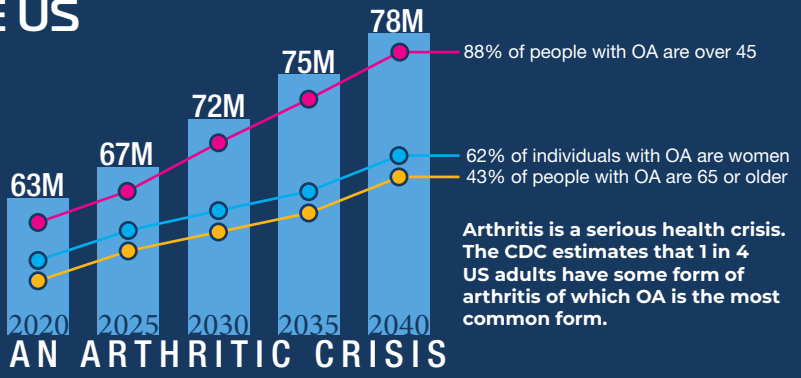
Commonly used non-pharmacological treatments include weight loss, lateral wedge insoles, bracing and physical therapy.

Pharmacological treatments include analgesics, non-steroidal anti-inflammatory drugs (NSAIDS), opioids, hyaluronic acid or corticosteroid injections and various drugs purported as disease-modifying osteoarthritis drugs (DMOADs).

Surgical options include arthroscopic debridement, synovectomy, chondroplasty,

THE GROWING COST OF OA IN THE US

$128B
ANNUAL DIRECT & INDIRECT COST OF OA IN THE US.



32.5M
ADULTS HAVE BEEN DIAGNOSED WITH DEBILITATING OA IN THE US.

- OA limits ability to manage other conditions such as hypertension and diabetes.
- A third of patients with OA have five or more chronic conditions.
- Reduced physical activity + co-morbidity conditions + adverse effects of treatments and medications increase the risk of heart disease by 50% and causes a 55% increase in mortality.

800,000
KNEE REPLACEMENTS (TKAs) ARE PERFORMED EACH YEAR IN THE US.

ABSENTEEISM COST DUE TO OA IS MORE THAN **$10B** ANNUALLY

"If only there were an iKnee."

osteochondral drilling, high tibial osteotomy, patella femoral realignment and unicompartmental or total knee arthroplasty.

Despite the fact that all of the 12 existing guidelines for knee OA management dictate that optimal management of OA requires a combination of non-pharmacological and pharmacological modalities, these conservative therapies have major limitations. Perhaps the most notable shortcoming of non-pharmacological and pharmacological treatment is a failure to successfully correct the underlying pathology, namely abnormal joint loading resulting in continued disease progression.

The Typical Knee Osteoarthritis Conservative Care Regimen

Conservative options for knee OA treatment can be classified as orthotic joint unloading therapies, analgesics, anti-inflammatories, opioids, DMOADs and hyaluronic acid injections.

In general, joint unloading therapies such as weight loss, lateral wedge insoles and bracing, are the preferred first-line treatments for symptomatic knee OA. If symptom improvement is not realized after an extended period, generally 3 to 6 months of use, add-on therapy utilizing analgesics such as acetaminophen is recommended. Topical NSAIDs and capsaicin, Lidoderm and Voltaren gel are also recommended as alternatives to oral analgesics or in combination with them.

The Standard Path of Care for Knee OA

The typical standard of care under today's conservative approach to treating OA in the knee, follow a very typical order or "try and escalate".

1. *joint unloading therapies*

Designed to modify the patients body to better balance or compensate for the "load" being put on the knee joint.

This includes:

- Diet modification
- Muscle and Joint Bracing
- Corrective Insoles



2. *add-on analgesics*

The next level is to add pharmaceutical-based treatment to ease inflammation and pain.

This includes:

- Analgesics
- Topical non-steroidal anti-inflammatory drugs(NSAIDs)


2. *escalated pain and inflammation therapy*

The final level in conservative care is to escalate the pharma-based therapy to treat the pain and inflammation.

This includes:

- Opiates
- Disease-modifying osteoarthritis drugs (DMOADs)
- Intra-articular injections


"If only there were an iKnee."

If acetaminophen does not provide sufficient analgesia, oral NSAIDs at their lowest effective dose are recommended, with the caution that long-term use should be avoided whenever possible because of their association with gastrointestinal side effects. In patients with elevated gastrointestinal risk, COX-2 inhibitors or nonselective NSAIDs in combination with a proton pump inhibitor are recommended, though these may produce cardiovascular adverse sequelae. If acetaminophen, nonselective NSAIDs and COX-2 inhibitors all prove insufficient (or intolerable), DMAODs such as glucosamine sulfate, chondroitin sulfate or diacerein may be attempted.

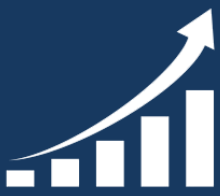
Opioids, with or without acetaminophen, may be used if other oral analgesics fail, although stronger opioids are discouraged except when very severe pain is present due to concerns of dependency and complications.

Intra-articular injections of hyaluronic acid are considered if oral medications fail to provide symptomatic relief.

The prevalence of analgesic use in symptomatic knee OA patients is staggering. Over 650,000 patients in the US chronically consume NSAIDS and over 350,000 have a chronic opioid prescription. Additionally almost three out of four knee OA patients, representing three million patients, have used analgesics in the last month.

EXPANDING THE VIEW
a global perspective

Though OA of the knee has it predominance in the US, its impact across the globe is substantial and is the cause of economic and health burdens.



525M
CASES OF OA.
THIS HAS MORE THAN DOUBLED IN THE LAST THREE DECADE

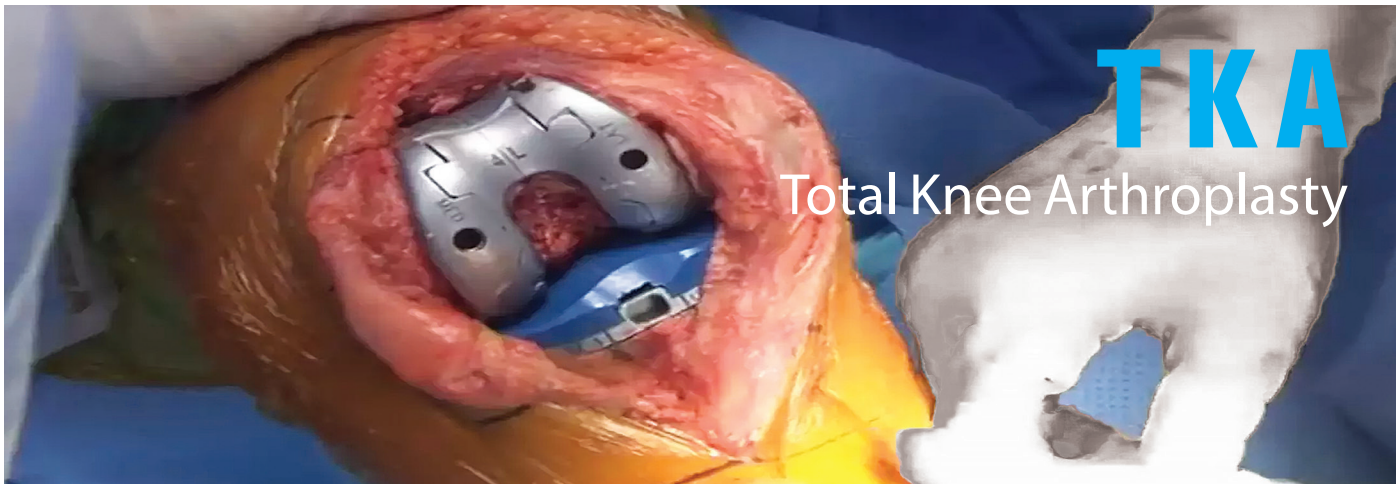
$321B
IS SPENT IN THE TOP FIVE INDUSTRIALIZED COUNTRIES FOR OA.

OBESITY
IS CITED AS ONE OF THE MOST PREVALENT GROWING RISK FACTORS IN OA

LONGER LIFESPANS, SMOKING and LACK OF EDUCATION HAVE ALSO BEEN CITED AS GROWING CONTRIBUTORS.

WOMEN RULE
IN BEING MORE PRONE TO DEVELOPING OA ACROSS IN ALL AGE SPECTRUMS

"If only there were an iKnee."



PFD/iOI was created to develop viable options for patients facing invasive major orthopedic surgery treatments as their only option for relief. Total Knee Arthroplasty, or TKA, is one of the most invasive and disruptive options for patients with chronic knee joint issues.

TKA is a surgical procedure in which parts of the knee joint are replaced with artificial (prosthetic) parts. A normal knee functions as a hinge joint between the upper leg bone (femur) and the lower leg bones (tibia and fibula).

TKA's require the removal of significant portions of the patient's distal femur, tibia and patella as well as remnant normal cartilage and normal anterior cruciate ligaments, to make room for a prosthetic device. The cost is enormous and the chances of complications as infection, loosening, mobility compromise, and even death are risks.

Total Knee Arthroplasty requires the joint to be cut open in order to remove the arthritis plus all normal interfacing bones, remaining cartilage and stabilizing ligaments. As a result the femoral, tibial and patella interfaces are destroyed, and the natural joints are ablated to insert the metal and hard polyethylene prosthetics.

TKA has become one of the leading operations for senior citizens, both in cost and frequency. When a patient has a disabling knee condition limiting mobility and quality of life there is only one medical option; TKA. The operation is a significant procedure and but is not without significant risk.

First, TKAs are considered a major surgery so complications associated with this type of procedure need to be considered. This includes anesthesia-related risks, allergic

and other medication reactions, potential impact during surgery from other co-morbidity medical conditions such as cardiac issues, liver or kidney dysfunction and others.

Secondly are the postoperative issues associated with TKA. This can include restricted movement, clicking and popping of the prosthetic, loosening of the prosthetic from its embedded bone, post-operative infections, which can be serious, even fatal, and rejection of the implant leading to secondary surgeries.

Finally, TKAs are very invasive and recovery and rehabilitation from the surgery can be a long and arduous path requiring anywhere form six month to over a year to reach the optimal joint restoration possible, which in the end, may not be full range of movement or full load capacity handling. Because of this, TKA patients have to live with a restricted Quality of Life.

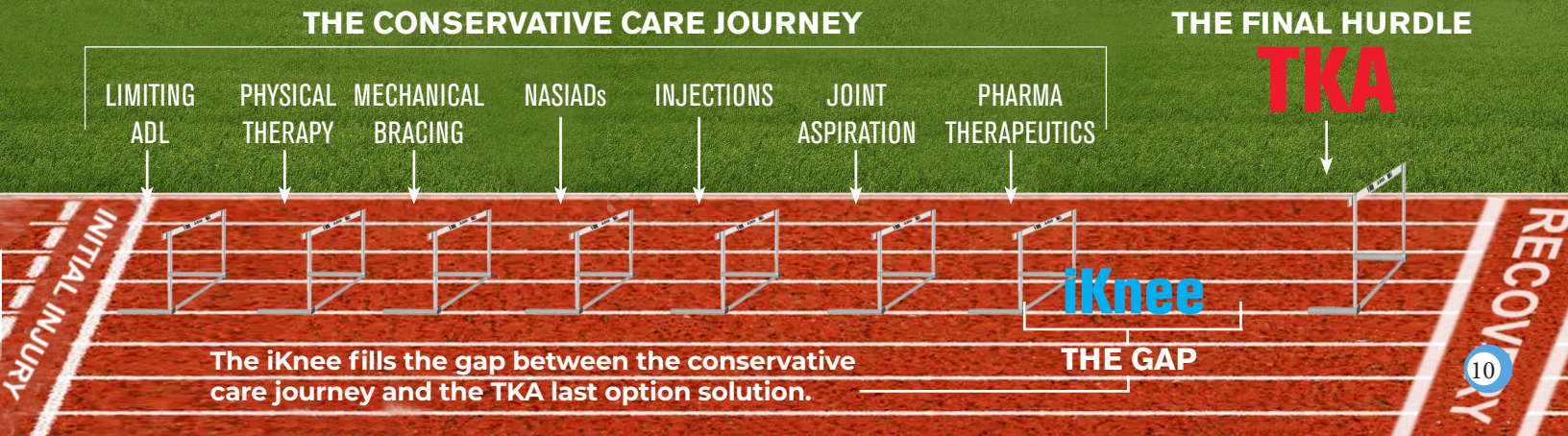
A recent longitudinal study that followed 1500 patients for close to six years after the initial TKA surgery found that almost 23% of the surgeries had failed to the point where a second TKA was required. The study found that infection was the cause of 38.5% of the failures with aseptic loosening accounting for 21% and instability of the prosthetic for 14%. Of those patients who had a revision TKA performed, the study showed that failure jumped to 33% of those patients with 67.2% of the failures due to repeat infections[1].

With the iKnee, PFD/iOI hopes to provide an outpatient, arthroscopic-based surgery that requires no removal of bone or tissue to provide temporary comfort and an effective alternative to TKA.

1 https://www.aaos.org/aaosnow/2020/aaos-now-special-edition/research/557_knee/#:~:text=Overall%2C%2022.8%20percent%20of%20TKAs,percent%3B%20P%20%3D%200.19).

THE GAP

The path to restoration from debilitating knee OA can be a long and difficult race with many hurdles to cross. Each hurdle is an attempt to bring relief and repair to the patient, but when it fails, there is always another hurdle to jump until in the end a patient may face having to take a big leap to reach a cure by undergoing a TKA. With the iKnee, PFD/iOI hopes to fill the gap between the conservative care hurdles and the intrusive and problematic TKA surgery with a technology that provides immediate pain relief, restoration of movement and a potentially long-term solution to patients suffering from knee OA.




the iKnee
SOLUTION

PFD/iOI is introducing a disruptive technology that brings a novel personalized, patient-driven, restorative, joint salvage outpatient approach for those suffering from chronic knee OA and who are facing TKA as a last alternative. The iKnee is an effective solution to fill the gap between the costly, inefficient and non-therapeutic conservative care approaches and the invasive metal joint replacements that limit care options to deal with knee pain and reduce daily activities and quality of life for patients suffering from osteoarthritis.

This additional interventional option may potentially eliminate or at least delay the much more dramatic and life-altering surgical replacement of joints with a simple outpatient procedure.

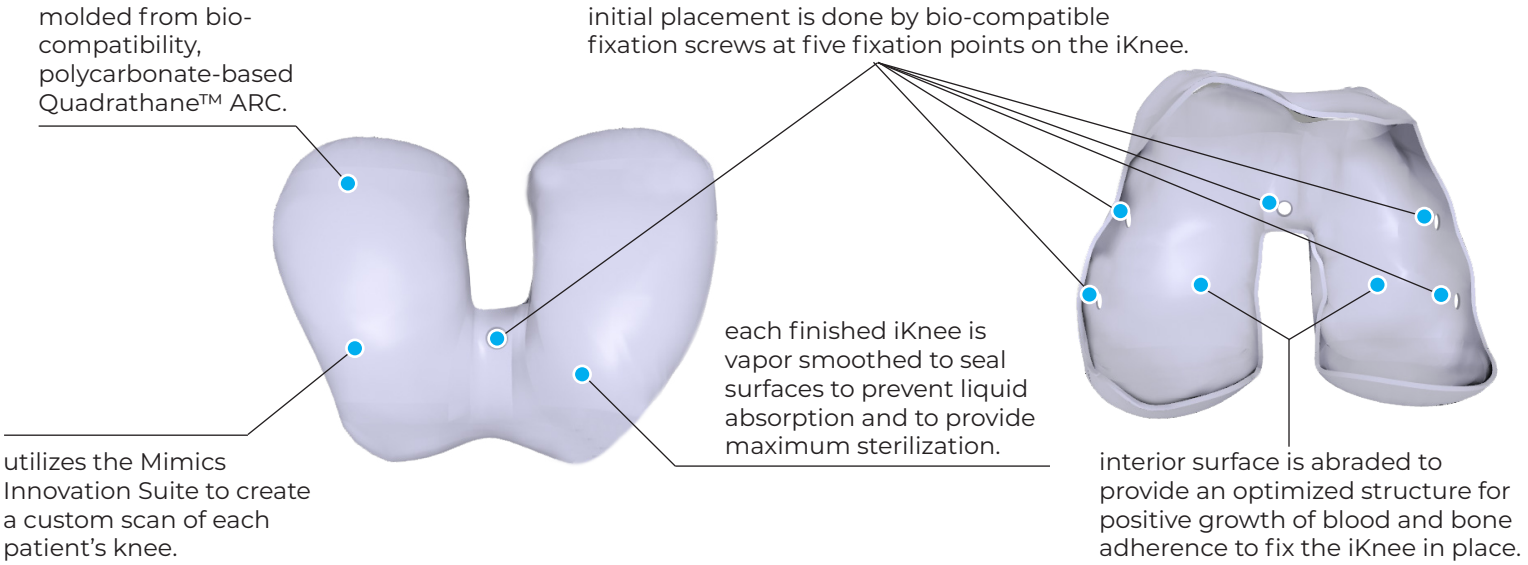
The RAD/iKnee solution bridges the gap between non-invasive and totally invasive ablative, barbaric and antiquated surgery.

Since 21st century art and science now offer materials and designs sparing joints, keeping proprioception, maintaining ligamentous stability, protecting damaged cartilage while renewing surface hyaline, informed patients want the right to try modern measures.

We use CT, MRI and X-Ray imaging technologies to 3D print a patient specific custom replica of the outer distal femoral surface of their knee; the iKnee. The iKnee bio-compatible polymeric implant application aims to protect, pad and restore cartilage over dominant surfaces of damaged joints, paired with other restorative technologies.

the iKnee difference

The iKnee delivers a promising approach to providing joint movement restoration and an immediate decrease in pain levels for those whose chronic knee OA has not responded to traditional conservative treatments and are now facing TKA as their only viable alternative. The RAD technology employed in the iKnee offers several unique differentiators that make it an attractive alternative to TKA.



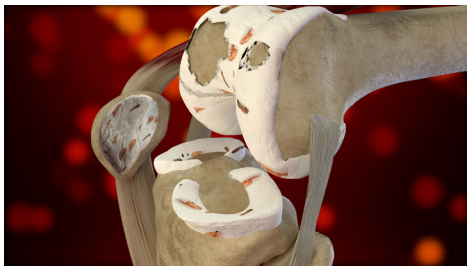
The iKnee will change the pain profile in restoring, cushioning and regenerating natural cartilage.

- No more metal
- No irreversible destruction of tissue
- Protective restorative bio-compatible polymeric implant
- Minimally invasive
- Preserves remnant cartilage and ACL ligament
- Offers joint salvage with regeneration potential
- iKnee's are arthroscopically facilitated
- Potential stem cell adjuncts to regrow natural hyaline cartilage joint surfaces.

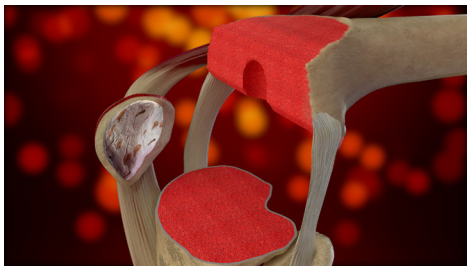
Resilient Arthroplasty Device – The RAD/iKnee

The patented RAD technology and the iKnee, the first product candidate for the RAD technology, provides orthopedic surgeons a potentially superior option in bringing restored health to their patients suffering from severe damage to the knee joint. By creating an arthroscopically implantable device that does not require the wide open joint resection in a patient, with the removal of large sections of bone, and the implantation of heavy hardware made from metals and hard polyethylene prosthetics, the RAD/iKnee allows a patient to be literally back on their feet in less time, at a lower cost and with less chance of complications as those of TKA's.

the TKA



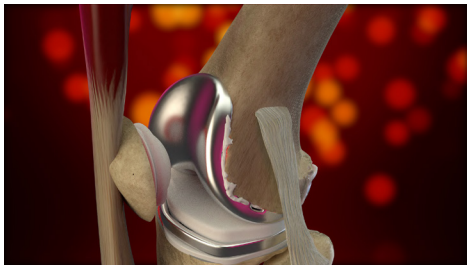
Major surgery requiring large incision into the length of the knee joint.



A section of the distal femur, the top of the tibia and the surface of the patella are all removed.

Metal prosthetic hardware is cemented and screwed into the femur and the tibia.

Plastic cushions are placed on the tibia's prosthetic bed and the patella surface.



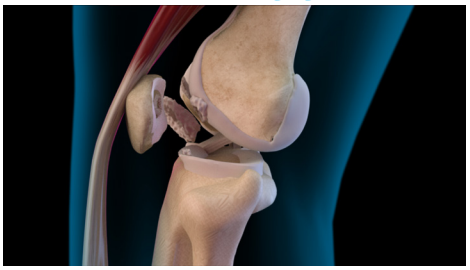
Joints and kneecap are moved back into place and the incision is closed in order for the long recovery to begin.

The RAD/iKnee implantable medical device, for knee OA patients, whether afflicted with osteoarthritis, rheumatoid, gout or injuries from acute or cumulative trauma, will reasonably expect comfort from the iKnee's robust compliant customized polymer femoral caps that interface both with the tibia and the patella.

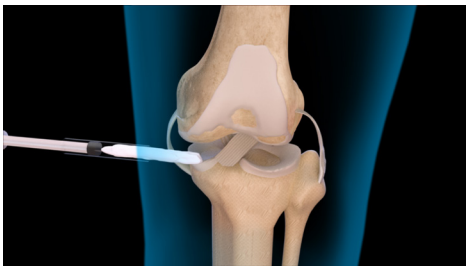
The padding, cushioning and protecting of the damaged joint surfaces of the knee, should induce – beyond the temporary comfort per se, protection from any ongoing cartilage degradative processes. The iKnee can also support restored cartilage; whether fibrocartilage from abrasion chondroplasties or "picking" or hyaline cartilage induced by cloned autologous cells (ala Carticel/MACI/Vericel). This seems the best chance to preserve and renew damaged joints.

In other words, instead of cutting away and removing significant portions of the patient's bone and cartilage, the device will cover

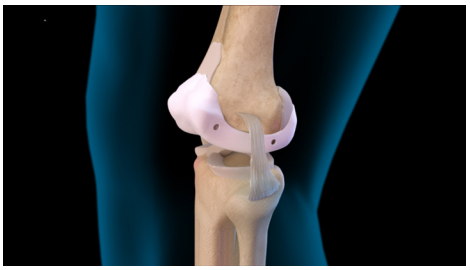
the iKnee



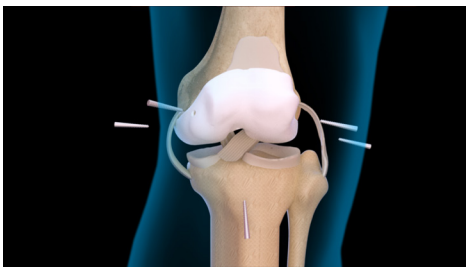
A small arthroscopic incision is made and any osteophytes are removed.



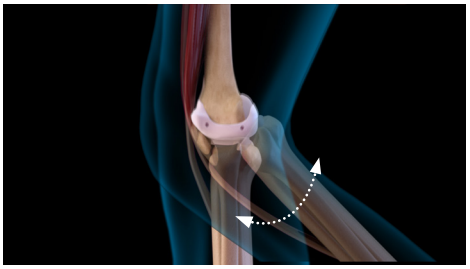
The compressed, custom-made iKnee is injected into the joint space.



The iKnee is unfolded and is fitted over the patient's distal femur.



Fixation screws are used to hold the iKnee in place while natural apposition begins



A range-of-motion test is done and the patient is sent home that day.

"Thank God there is an iKnee."

and protect the damaged surfaces, in effect, sparing the joint from resection.

Outpatient procedures culminating in the placement of a custom polymer resurfacing femoral arthroplasty device will save time, money, rehabilitation, lost employment, downtime in sports or warfare, while reducing pain, improving function in activities of daily living, aiming maximally to resume normal life.

The RAD/iKnee implantable medical device uses a special, FDA approved, material called Quadrathane as the polyurethanes used safely for decades. It is stronger than Kevlar and will retain its form and shape under extreme pressures and shear forces. The RAD/iKnee caps the bottom of the femur and attaches to the bone for immediate relief and function.

Immediate fixation is achieved by first the elastic deformation fit; analogous to a sock on a foot and secondarily, by the use of biodegradable, low profile screws. Post implant, the RAD/iKnee is secured by femoral apposition which is set in play by bone ingrowth between the patient's femoral recipient site loci – which is prepared during the implant procedure, and the iKnee under-surface that matches the patient's distal femur.

The RAD/iKnee resurfacing can deliver and protect healing adjuncts, as bio-active substances: viscolubricants and chondrocytes. (Stem Cells). The RAD/iKnee device is 3-D printed to exactly match each patient's unique bone structure by radiologic imaging, then using Materialise Mimics software to create a "Digital Twin" to "electronically sculpt the arthritic knee" so as to resemble a more normal joint surface. That computerized surgeon-created STL file data is directed into the Arburg 3D Freeformer 300-3X printer for an ideal "Goodness Of Fit" joint cap.

Upon device production, its external surface is smoothed to resemble an ice cube sliding across a glass desk, or more scientifically to resemble the hyaline natural cartilage articular joint surface coefficient of friction.

Toxicity testing and appropriate sterilization prepare for speedy surgical implantation with no substantive bone loss or prolonged tourniquet times to add concern.

The RAD/iKnee Resurfacing can endure all the variable joint forces and cyclic loads associated with normal activity and even heavy athletic motion while reducing pain and improving function after injury or disease.

The knee is not a standard hinge joint mechanism, but rather "screw-home' described

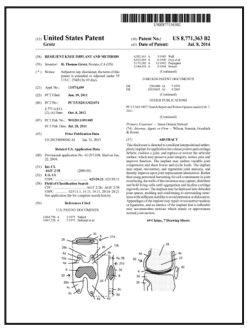
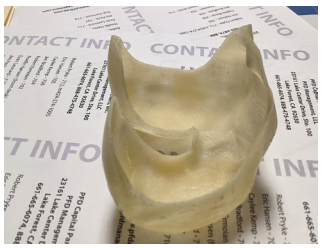
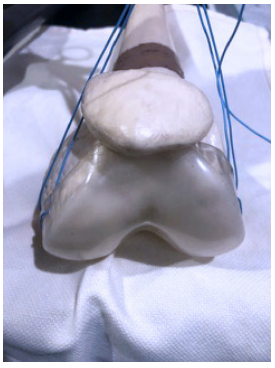
as "Andriacci's 6 axes of motion". These are taken into consideration with iKnee testing and manufacturing.

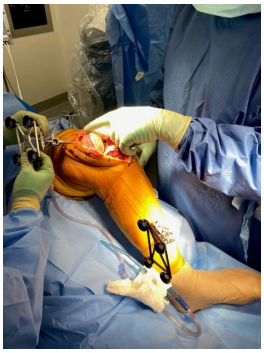
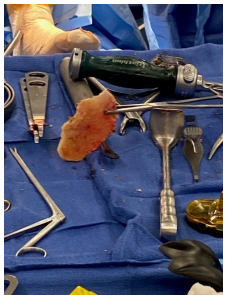
the iKNEE Benefits

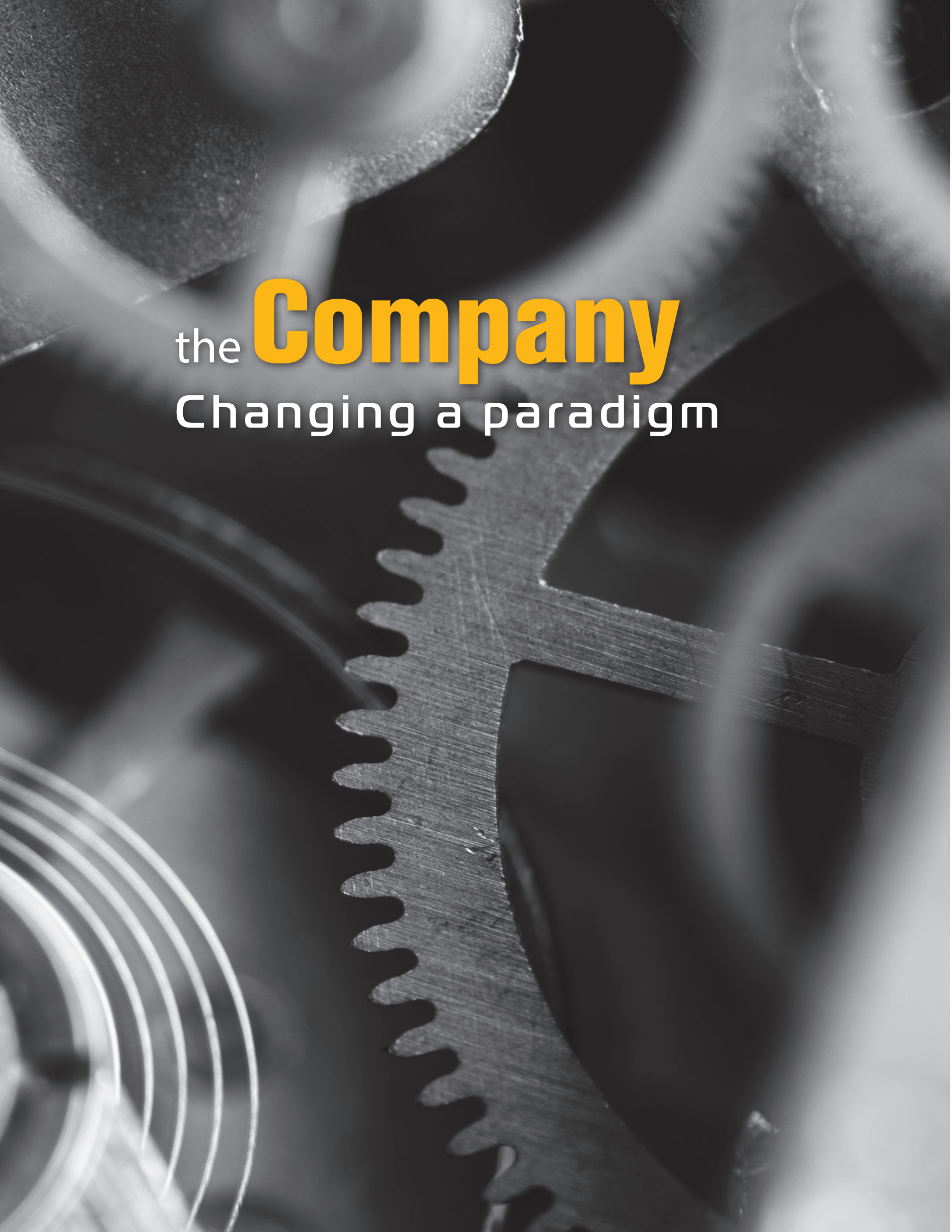
The iKnee Implant provides many benefits when considered against the cost in time, money and risk of a Total Knee Arthroplasty.

1. Total cost of major TKA surgery and extended recovery is massive as compared to a short iKnee outpatient procedure.
2. Immediately weight bearing and motion preservation in PT and OT predict iKnee return to work and sport in weeks, not months or years.
3. Almost zero risk of infection or rejection compared to TKA, since the bones are not resected exposing subcortical bone and because the arthroscopic process inherently washes out the joint via sterile fluid flow.
4. Preservation of bone, cartilage and ligaments with the iKnee as opposed to a radical removal of tissues with TKA give the chance for patients to keep and use their own body parts.
5. Higher potential for full knee mobility and naturally improved quality of life as opposed to restrictions caused by a prosthetic device with its inherent design motion and resection-mandating limitations.

The images below show the PFD/iOI story to date. *Top row (l-r)* 1. RAD/iKnee Inventor and iOI Co-Founder Dr. Thomas Grotz is shown with a surgical team. 2. The first patent for the iKNee technology was granted in 2014, 3. Shown is a first prototype 3D printed version of the iKnee. 4. A bench-top test model of the iKnee attached to a distal femur with printed patella is tested for range of movement. 5. The custom fit of a second generation iKnee to a distal femur is shown. *Bottom row (l-r)* 1. PFD/iOI's Chief Investigator Dr. Christopher Woodson performs a TKA on a patient with chronic OA. 2. Dr. Woodson shows an example of the large amount of tissue that gets removed in a TKA. Dr. Woodson is shown with PFD/iOI Clinical Director and Patient 1 Eric Hansen. Dr. Woodson shows Eric Hansen how the iKnee procedure he will be undergoing works. 5. Eric Hansen demonstrates the new Arburg Freeformer printer installed at PFD/iOI's Clean room in Los Angeles, CA.



the Company
Changing a paradigm

PFD/iOrthopedics (PFD/iOi) is a medical technology company focused on creating innovative orthopedic devices that can better address targeted issues to provide alternatives for improved outcomes, lower cost, and overall better quality of life for the patient.

Within their device technology platforms, PFD/iOI has developed a 21st Century, personalized, patient driven, novel and highly disruptive restorative, joint salvage outpatient approach to fill the gaping, costly and inefficient void between pills, bracings, physical therapies and complete joint replacement that limits the daily activity; as well as the quality of life, for patients suffering from osteoarthritis.

PFD/iOI was formed in 2021 to combine the innovative and pioneering work of Dr. Thomas Grotz, who under his iOrthopedics company banner, had developed several novel orthopedic-based medical devices that each provided a major step forward from their respective current art technologies, and PFD Capital Partners, LLC, who had built a highly successful company in helping the professional medical community in managing their medical receivables assets as it related to their personal injury cases. The principals in both companies saw a potentially very lucrative path forward in joining efforts in order to create a WIN-WIN-WIN scenario for advancing the goals of both companies, but more importantly, in providing an effective lower-cost, faster recovery solution for the millions of patients who could benefit fro their discoveries.

With its lead technology, the Resilient Arthroplasty Device (RAD), and its first product candidate the iKnee, the company has already received a Non-Significant Risk (NSR) designation from the FDA as well as an Investigational Device Exemption (IDE) which has cleared the path for an IRB authorized human use in trial for the first 10,000 qualified patients in an upcoming iKnee Comfort Study (see iKnee Comfort Study on page 25).

Executive Management Team

The PFD/iOI Executive Management Team consists of highly experienced individuals who have a proven track record of success in medical device technology creation, orthopedic medicine, scalable business management, technology sales and marketing, regulatory compliance and IP and trademark protection. As such, the company is strongly positioned strategically to ensure the company's objective of achieving investor value, achieving benchmark goals, and meeting the growing patient demand for a better solution.

Dr. R. Thomas Grotz, MD
Founder Inventor and
Chief Executive Officer

Dr. Christopher J. Woodson, MD
Chief Investigator

Gary L. Ermoian
Chief Operating Officer

Robert Pryke
Chief Technology Officer
and Fund Manager

Dr. Daniel Rastien, MD
FDA IRB Consultant

Ryan Helber
Regulatory Consultant

Eric Hansen
Clinical Director
and Patient #!

Mitch Graffeo
Patent Attorney

ADVARRA
advancing better research

ADVARRA, Inc.
IRB Sponsor

The PFD/iOI RAD/iKnee Lab

PFD/iOI has established a state-of-the art lab at its Los Angeles facility to facilitate the continued research and development of its RAD/iKnee technology as it moves towards the start of its initial Comfort Study. The RAD/iKnee Lab is part of a facility that has a long legacy of supporting proven IP development and commercialization success.

The RAD/iKnee Lab was constructed to meet EPA Class 10 ISO-4 Clean Room standards. The RAD/iKnee Lab was engineered to maintain a very low concentration of airborne particulates. It was specifically designed to keep everything from dust to airborne organisms, or vaporized particles, away from the materials the PFD/iOI engineering teams are handling inside the lab. As a Class 10 cleanroom, the RAD/iKnee Lab meets the following requirements:

- Air filtration to allow only up to 1,200 0.3-µm sized particles per square meter.
- Average airflow velocity of to be maintained at 0.254 – 0.457 meters/second (or 50 – 90 ft/ min).
- Provide complete volume changes of air between 300 – 540 per hour.
- Deliver fan/filter unit (FFU) coverage of 50 – 90%
- Utilize Ultra-low Penetration Air (ULPA) Filters .
- Perform and maintain a regular cleaning and disinfecting program.
- Test particle count every 6 months; airflow and air-pressure differential every 12 months.

In addition to the above, the RAD/iKnee Lab contains 3-phase electrical with compressed air, oxygen, and nitrogen service. The lab consists of three different spaces that allow the engineering team the ability to test prototype designs, perform quality control checks and establish operational and test protocols while gathering the important analytical and comparative clinical data needed to further its regulatory approval strategy.

3D Printing Capabilities

In the RAD/iKnee Lab, PFD/iOI has installed a top-of-the-line medical-grade 3-D printer to provide in-house fabrication of its iKnee prototype and Comfort Study custom-made implants. The Arburg Freeformer 300-3X is revolutionary regarding its proprietary technology as the only 3D printer in the world that can print using the Quadrathane

ARBURG
freeformer
300-3X

The Freeformer 300-3X control panel allows complete operator control of the system operation, diagnostics and system testing.

The Freeformer 300-3X mixing chamber allows the use of up to three separate materials to be mixed or layered into a production piece.

The Freeformer 300-3X uses an additive printing process which allows for highly complex part with multi-dimensional angles and curves to be produced.

Polymer from Biomerics; which is the main material used in the production of the iKnee.

The ARBURG Freeformer 300-3X is an industrial quality free-form injection molding system that is capable of taking up to three qualified granulate materials and using a proprietary jetting method that heat melts and discharges the materials with a high level of precision to fabricate thermoplastic parts. The large 23 x 13 x 20 build chamber allows the printer to build complex structured parts and its unique three-port injection system allows a separate support material to be simultaneously printed where the material thickness or the vertical angle of the printed part might be compromised without an underlying material to maintain the integrity of the finished product shape design.

Arburg GmbH + Co KG (ARBURG) is one of the world's leading manufacturers of high-end injection molding machines for plastics processing. Founded in 1923 and located in Lossburg, Germany. The company operates out of 33 locations in 25 countries employing more than 3,000 workers along with trading partners in more than 50 countries. The company generates more than $80M in revenue per year.

Strategic Partners

The development, validation, marketing and support for a disruptive technology such as the RAD and the iKnee device requires the efforts of not only a strong visionary, management professionals, and a dedicated engineering team; but also the support of strong supply and technology partners, as well as experts and leaders in the corollary medical fields, and federal and international regulatory requirements. PFD/iOI continues to work on building these necessary partnerships in order to make sure each step forward is positioned for success.

Our Strategic Partners

BIOMERICS
FUTUREMATRIX INTERVENTIONAL

Quadrathane is a polyurethane-based thermoplastic that offers superior bio-compatibility, superior chemical resistance and oxidative stability for use in long-term body implantable applications. Quadrathane is used across a wide range of medical applications including chronic indwelling catheters, feeding catheters, pacemaker leads, coatings, orthopedics and other applications where superior chemical resistance is required. For the iKnee, PFD/iOI is using the ARC 80 A Quadrathane which is a naturally clear material that is both USP Class VI and ISO-10993 compliant. The hemocompatibility of the material is perfect for the iKnee in that it provides for safe long-term integration of the iKnee implant into the blood-rich environment of the knee joint with minimal risk of adverse reaction.

materialise
innovators you can count on

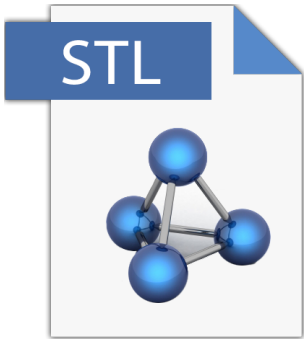
In furtherance to complete comprehensive personalized medicine, PFD/iOI has utilized Materialise, as the industry-standard medical image-based engineering software and service. Their Mimics Innovation Suits (MIS) puts us in control with the most advanced tools to support our mission to improve patient care. Medical image data thus serves as a powerful basis for engineers and researchers striving for solutions that will lead to safer and more predictable personalized patient outcomes.

The MIS was designed to make using medical image data for engineering purposes as easy and rewarding as possible. PFD/iOI uses the data gathered from the patients CT scan and generates their "Digital Twin" of the distal femur to be used in a virtual surgery to generate a virtual mold to manufacture the comprehensive, personalized, customized, one of a kind distal femur iKnee.

AMT has developed a proprietary Vapor Smoothing post-processing required to finish the 3D-printed iKnee implant. A green plant-based consumable, called PURE, was found to produce exceptional results for the smoothing process.

- Fully green sustainable manufactured from cellulosic biomass (plant-based)
- Safe and non-toxic
- Non-halogenated
- Low acute toxicity
- Readily biodegradable
- Environmentally friendly
- Non-benzene or phenol derivative

Enginuity Works provides our engineering consultation for the iKnee. Enginuity Works provides the final design of the patient specific STL file of the iKnee design that gets imported into the Freeformer 300-3X 3D Printer. They offer PFD/iOI a full range of product development services, Industrial Design, Mechanical Engineering, Electrical Engineering, Prototyping, R&D and Manufacturing Management.



The STL file format is the most used file format for 3D printing. When used in conjunction with a 3D slicer, it allows a computer to communicate with the 3D printer hardware. The STL file format has been adopted and supported by many CAD software packages. Today it is widely used for rapid prototyping, 3D printing, and computer-aided manufacturing.

PFD/iOI's RAD/ iKnee technology has been IRB authorized for human use as an IDE for the first 10,000 qualified patients in an upcoming iKnee Comfort Study to gather the longitudinal data required to move the iKnee application of the RAD technology to FDA approval and commercialization.

The iKnee Comfort Study The study has been authorized by the FDA certified review process under an Investigational Device Exemption (IDE) which permits a clinical trial to gather data on the technology's efficacy and safety based on its qualification of being a Non-Significant Risk (NSR) device, provided to patients who seek to avoid TKA after failed conservative management. Surgeons and patients are informed and should understand reasonable expectations for iKnee RAD procedures.

Description

The iKnee seeks to provide temporary comfort and improved function for patients awaiting a TKA. Reasons to delay a TKA include, but are not limited to, the need for weight loss, wound infection healing, implant availability and required medical or psychological patient preparations. The iKnee use determinations are made between the patient and caretaker. The subject population for the iKnee Comfort Study are individuals with refractory disabling knee pain who failed other conservative measures and are on track for a TKA. The purpose of the iKnee is to provide comfort and is not intended to treat a disease, or the underlying causes leading to TKA.

Objective

The objective of the iKnee Comfort Study is to determine the iKnee's impact on quality of life issues and its ability to allow normal activities of daily living in patients awaiting TKA. The data will be used to improve possible designs to enhance ideal patient comfort.

The First-In-Human (FIH) implant of the iKnee will be conducted at the Memorial Care Surgical Center in Long Beach, CA. later this year. Eric Hansen, who is PFD's Director, Co-Founder, and Clinical/Asc Operations Manager, has been selected as Patient One in the study's cohort group.

Eric has suffered from debilitating knee pain for more than eight years due to injuries sustained from both sports and heavy use issues and is currently at the point where a TKA would be the traditional next step.

As such Eric meets all the criteria established by the Institutional Review Board (IRB) for the iKnee Comfort Study's protocols as a candidate for the iKnee implant. The surgery will be performed by PFD/iOI's Chief Investigator, Dr. Christopher Woodson, who is a board-certified orthopedic surgeon and sports medicine physician and founder of Beach Orthopedic Specialty Institute.

Dr. Woodson will also be serving as the Principle Investigator for the iKnee Comfort Study's ongoing trials.

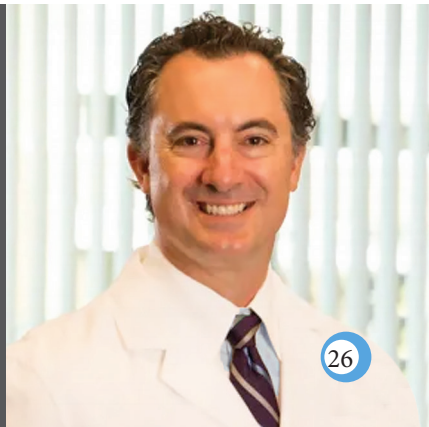
Study Criteria

The PFD/iOI Comfort Study is designed to allow the company to gather critical data in three major areas:

1. The ability of the patient to tolerate the iKnee implant both from a bio-compatibility standpoint and an ortho-comfort level.
2. The ability of the iKnee implant to decrease or eliminate the patient's pain level as it applies to the use of the impacted joint.
3. The ability of the iKnee to maintain or expand the patient's quality of life as it pertains to daily activity, leisure and recreational movement and/or active sports engagement.

The PFD/iOi FIH Comfort Study

The PFD/iOI Comfort Study is a major milestone for the company as it will be a First-In-Human test of the iKnee's ability to meet the objective for which it was designed. The two primaries in the study have each been a part of the PFD/iOI vision from the start, and as patient and surgeon, are both very excited to see the results. Pictured on the left is iKnee's Patient One Eric Hansen and on the left is Surgeon One, Dr. Christopher Woodson.



In addition, the study will be looking at additional areas of impact including the iKnee's ability to provide:

- better patient outcomes
- faster recovery
- lower cost
- lower risk

Candidate Selection

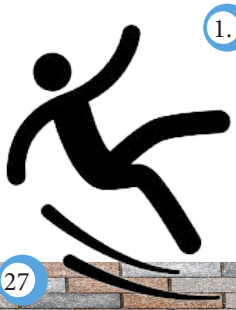
Candidate selection for the study will be done by PFD/iOI's IRB which is being sponsored and managed by Advarra, who is a global leader in supplying IRB allowances, institutional bio-safety committee and research compliance services to clinical trial sponsors, CROs, hospital systems, academic medical centers and investigators. Candidates for the trial must meet the following criteria:

- Debilitating knee pain and disability after failed conservative treatment.
- Be a candidate for TKA but show a reasonable expectations of temporary comfort with an iKnee implant.
- Have a BMI of 30 or less.
- Have had continual and chronic adverse issues with their knee joint.
- Have a pre-operative Visual Analogue Pain Scale (VAS) score of ≥4.
- Be referred to the study by their Primary Care Physician (PCP) or by a qualified referring orthopedic specialist.
- Have no disqualifying health conditions or risks.

Once prospective candidates have submitted their applications, they are vetted by the PFD/iOI IRB for potential inclusion into the study. The application screening process consists of a series of steps to ensure that the candidate will be a viable cohort for the program and that there is an anticipated benefit to the patient's knee condition and

The iKnee Comfort Study Path

PFD/iOI along with its IRB has designed an exemplary First-In-Human clinical trial to examine the efficacy of the RAD/iKnee technology to provide reduced pain and restoration of movement to qualified candidates who are facing TKA. The graphic below shows the path to participation for the iKnee Comfort Study candidates.



1. Candidate has suffered a debilitating knee injury

2. Candidate has exhausted treatment options and is facing a TKA

3. Candidate applies and is interviewed for participation in the Comfort Study

quality of life as a result of participation. The application review consists of an initial patient consult with a PFD/iOI-certified physician that includes:

1. Initial patient background history (HPI, PMH, FH, ROS).
2. Physical examination including a VAS and joint mobility assessment.
3. Initial consult on study overview, implantation procedure and benefit/risk assessment.
4. Correlation of assimilated data and ancillary lab/imaging leading to predicted beneficial iKnee outcome.

Based on this evaluation, a request for medical records, copies of the latest radiological films, which can include X-rays, CT and MRI scans, and any needed lab work is made. Once procured, an in-depth review of the applicant's records, films and labs is made by the qualified PFD/iOI surgeon along with the IRB.

If at this point the applicant is deemed to be a viable cohort, a second consult is scheduled during which the study protocols and the implant procedure are once again thoroughly reviewed. If the applicant decides to move forward, a detailed Informed Consent document is signed along with any related additional release and medical information paperwork. Once processed the patient is given a case ID and a surgery date is scheduled.

iKnee Implant Procedure

At this point, the patient's latest CT scan is digitized and brought into PFD/iOI's 3D imaging platform utilizing the Materialise Mimics Suite to conduct a virtual surgery using the patients Digital Twin to construct an STL file of the patient's distal femur. Based on this model, the patient's iKnee is modeled for printing. The custom-tailored iKnee is created by the PFD/ iOI Arburg Freeformer 300-3X printer using Quadrathane™ ARC, a polycarbonate-based thermoplastic polyurethane that offers superior bio-compatibility, superior chemical resistance and

4. Candidate has second interview and an agreement to participate is signed.

5. Candidate is scheduled for and undergoes the outpatient implant of their iKnee.

6. Candidate participates in post-implant follow-up to monitor progress.

oxidative stability for use in long-term body implantable applications. Quadrathane™ ARC is a USP Class VI and ISO-10993 compliant histo-compatible material that is used across a wide range of medical applications and is felt to be the perfect material to provide the protective cushioning for the iKnee expectations.

After printing the patient's iKnee, the piece is sent for AMT PostPro processing. At this stage, the implant is vapor smoothed to refine the surface and seal it for easier cleaning and sterilization. Turnaround time from film digitization to implant in hand takes only a few days.

One week prior to their scheduled surgery, the patient is again evaluated for the most current VAS assessment, mobility range and review of any significant changes that may have occurred.

The procedure itself is done on an outpatient basis at a qualified PFD/iOI-authorized surgery center. The surgery takes an hour to perform and barring any complications, the patient is released and able to bear weight on the implanted knee that day. On the day of surgery, the patient is admitted and prepped. They are then given a general anesthetic and once stabilized, the knee is prepared for an arthroscopically facilitated debridement. A small incision is made, and an osteotome is used to remove any osteophytes, loose materials, or bony protrusions on the femur, the tibia, and the patella. Ligaments or tendons are preserved, although realignment and ligament lengthening procedures may be indicated. Healthy cartilage is preserved while a specimen may be sent to the Carticel lab for later ACI use.

Once the joint is prepared, the iKnee, which has been compressed and rolled to a fraction of its size, is inserted into the knee. The iKnee is then opened up and maneuvered into its correct position by the surgeon to cover the distal and anterior femoral surfaces.

Because of the elasticity of the iKnee polymer material, the implant creates a virtual hand-in-glove fit to the distal femur. Sutures and biodegradable screws are then used to secure the iKnee to the femur. Efforts directed toward bone in-growth and long-term stabilizer are invoked. Once the iKnee is in place, a range of motion test is performed on the joint and any adjustments are done to provide the best positioning for maximum flexibility and comfort.

The patient's incision is then closed, and they are moved to post-op to recover from the anesthesia. Peri-operative analgesia is preplanned to enable immediate limb use and motion.

Once awake, a post-operative evaluation is made on the patient. Since the iKnee enables immediate weight-bearing, once cleared, the patient is released to return home. The patient may have some limited post-op restrictions on use but remarkable recovery is days rather than weeks or months is anticipated.

Patient follow-up for the study is performed at 10 days, week six, week 12, week 24, and at one year plus annually thereafter, in order to assess the patient's response to the iKnee care. In these post-operative follow-ups, the patient is assessed for:

- Comfort and level of pain
- Joint mobility
- Infection or inflammation
- Evaluation of post-op imaging
- Quality of life changes.

Post-Operative Follow-Up

The data is carefully recorded at each step and becomes part of the ongoing evaluation to ascertain several criteria including:

- iKnee design for possible improvements.
- Material integrity and bio-compatibility.
- The ability of the implant to lower or eliminate joint pain.

DR. R. THOMAS GROTZ, MD
A PROFILE IN VISION

For over fifty years, Dr. Robert Thomas Grotz has been working and pioneering innovation in diagnostic, therapeutic and restorative care for his orthopedic patients. He has established one of the largest and best know orthopedic surgery clinics in the San Francisco Bay area and to date has performed over 10,000 surgeries and treated more than 25,000 patients for100,000 injuries.

Dr. Grotz graduated with Honors in Psychology from Oberlin College in Ohio, where he built a mass spectrometer, and taught trumpet performance, then proceeding through Case Western Reserve School of Medicine for his MD. Internship in 1975, and first year residency at the University of California, San Francisco Hospitals, involved General Surgery, followed by three years of Orthopedic Surgery residency, and a Microsurgery Fellowship. Since 1981 Dr, Grotz has practiced orthopedic surgery for decades. In recent years, he became passionate about inventing, as experience revealed better solutions to Heal Mankind. He is an active member of more than a dozen medical societies and has been widely published in peer reviewed journals.

To date Dr. Grotz has filed over 30 patents for his inventions in restorative joint technologies for orthopedic patients. Chief amongst these is his work in developing a novel expandable spine cage for patients with chronic back pain issues and of course his extensive work in developing the RAD platform and its first product candidate, the iKnee.

In his work, Dr. Grotz once commented, "As a surgeon, researcher, and educator since 1981, I've embraced orthopedic evolution. Standards and regulation permitted little change in total joint replacements. Advanced arthritis currently leads to joint resection, then implantation of metal components, sacrificing cartilage and ligaments. There remains a gap between pills and prostheses, for severely debilitated knee patients. I remain dedicated to finding better solutions for my patients."

Note: In cases where an iKnee revision or replacement is warranted, since it is a cap of the bone, the process should be relatively simple as opposed to major revision TKA manifestations.

Though the study is focused on the iKnee's ability to provide comfort and relief for a minimum six-month period, PFD/iOI will continue to perform multi-year follow-ups with those cohorts who maintain their implants until such a time as they have a TKA procedure performed.

If, as expected, the initial FIH procedure is successful as defined by the study's criteria of comfort, reduced pain, and bio-acceptance, enrollment of the next group of cohorts will begin immediately and evaluation and approval of other surgical centers across the US will proceed.

The study is designed to increase the patient's quality of life, functionality, and comfort while they await the knee replacement operation (TKA). The iKnee procedure poses little medical risk to the patient, either as a procedure or as a risk to the patient's knee structures per se, as the decision has already been made to remove the joint where a TKA is required.

Investigational Device Exemption (IDE)

An investigational device exemption (IDE) allows the investigational device to be used in a clinical study to collect safety and effectiveness data. Clinical studies may be conducted to support a PMA. However, when devices are determined "substantially equivalent" they may qualify for 510k clearance. The iKnee was designed to mimic the normal cartilage covering of the distal femur – to resurface the natural shape and cover of the arthritic bone. The iKnee is also substantially equivalent to the femoral components of TKAs in that the external radii or medial and lateral femoral condylar surfaces and the troclear connecting groove of the normal femur is 'designed like' the outer TKA surface and the RAD iKnee.

As for materials in RAD/iKnee construction, the polyurethanes are substantially equivalent to that in Active Implant NuSurface menisci positioned between the femur and tibia and identical to the Bryan cervical disc material PU. That Quadrathane/Bionate type material is FDA cleared or approved and has been used for several decades with valid and reliable results, yielding "negligible wear debris". Investigational use also includes clinical evaluation of certain modifications or new intended uses of legally marketed devices. All clinical evaluations of investigational devices, unless exempt, must have an approved IDE before the study is initiated. An IDE has been awarded and recently renewed for RAD/iKnee.

Clinical evaluation of devices that have not been cleared for marketing requires an investigational plan approved by an IRB. If the study involves a significant risk device, the IDE must also be approved by FDA; informed consent from all patients; labeling stating that the device is for investigational use only. Monitoring of the study and, records and reports are required. Clinical studies and devices approved by IRB IDE as iKnees are legally and ethically permitted to bill for services including but not limited to surgical center, physician, and implant costs.

First In Human (FIH)

A FIH trial is a clinical trial in which a new drug, procedure, or treatment is tested in humans for the First time. Also called First-In-Human study.

Non-Significant Risk (NSR)

The FDA does not regulate Non-Significant Risk (NSR) devices.

The Sponsor has the responsibility of making a Significant Risk (SR) or NSR determination and may utilize the services of an IRB, though this is not required.

The RAD/iKnee device does not intend to cure or treat any disease. We are implanting this minimally invasive device for a patient's quality of life issues while they await a full TKA. This may be for comfort, mobility, or many other non-disease-related terms that seek improved ADL.

NSR device studies must follow the abbreviated requirements at 21 CFR 812.2(b).

An IRB's NSR determination is important because the IRB serves as the FDA's surrogate for review, approval, and continuing review of the NSR device studies.

An NSR device study may start at the institution as soon as the IRB reviews and approves the study and without prior approval by FDA.

THE PATH TO MARKET

In the U.S., the FDA regulates the efficacy and safety of a medical device before it is allowed to go into the marketplace. Before a device can be legally sold in the U.S., the developer that wants to sell the device must seek approval from the FDA by presenting evidence that the device is reasonably safe and effective for a particular use. The majority of medical devices subject to FDA regulation, progress to market via one of two pathways: Premarket Notification (commonly known as 510(k) Clearance), and Premarket Approval (PMA). Each of these pathways are extremely rigorous, time-consuming and expensive to pursue. This can be problematic in the case where a new device might serve a humanitarian need, or a device that is designed to treat an under-served, but real population, for which no current therapies exist. Each of these are important areas for providing cure, but because of the time and cost to get 510k or PMA approval, a company may not feel incentivised to pursue development as the ROI may pencil out to be too low. For such devices the FDA has created additional categories that dramatically shorten the time table and cost to approval to help encourage developers who want to create solutions to help these under-served patients. These include Humanitarian Device Exemption (HDE), Breakthrough, Expedited Access, De Novo, and the Investigational Device Exemption, which is the path the PFD/iOI team is seeking for its RAD/iKnee platform.

PFD/iOI is in discussion to engage with Frost & Sullivan to undertake a market validation project to support the both the RAD and iKnee viability in the space in which it will be competing and to identify the addressable needs of both the surgeon, healthcare provider and patient.

Frost & Sullivan is a business consulting firm that offers market research and analysis, as well as growth strategy consulting. Based in California, Frost and Sullivan has grown to become a global presence with 45 offices in the Americas, Africa, Asia and Europe and annual revenue close to $200 million. Frost and Sullivan is recognize as a leading strategic partner in helping business that are entering a marketplace with a new technology to gather the data needed to accurately gauge both the need and the barriers to acceptance a company may face.

Frost & Sullivan is in an ideal position to support PFD/iOI on this project because of its extensive expertise in assessing new medical technologies, including those in the orthopedic sector. The company's team of med-tech subject matter experts, combined with consultants, focused on deploying and analyzing qualitative and quantitative research make it an idea partner for this important engagement.

In initial discussions, Frost & Sullivan has agreed to the value of gathering insights from U.S. surgeons and patients to assess the disruptive market potential for the RAD/iKnee technology and is preparing a proposal for the study.

PFD/iOI and Frost & Sullivan have agreed that the mutual goal is to assure the greatest possible success for PFD/iOI as it moves forward with its strategic growth plans. Frost and Sullivan is convinced the project, as proposed, would significantly enhance the effectiveness of PFD/iOI's plans.

As PFD/iOI was created to develop and commercialize the RAD technology and the iKnee implant with the hope that the treatment will be a faster, less invasive and less costly alternative to TKA, and that it could also be used for other treatments associated with cartilage repair in the joint.

The iKnee procedure would be a valuable addition to a surgeon's portfolio of approaches for managing a patient's knee pain filling a gap between arthroscopy and intra-articular injections and a complete knee replacement.

With more than one million primary TKAs expected to be completed by the end of 2023 in the USA, and another million performed worldwide, it is felt that a significant portion of these patients, as well as others with less advanced knee degeneration, are likely candidates for the iKnee procedure. Young patients who seek limb preservation and patients with severe illness seeking to stand or walk may all benefit from the procedure.

As PFD/iOI is in the early stage of clinical trials for the iKnee product for clinical evaluation of the technology, it also wishes to gather insight into the market value of the product and the size of the addressable market sector through conversations with prospective implanting surgeons as well as prospective patients. These insights will be used for internal planning purposes but will also be presented in a final document suitable for presenting to prospective investors and partners.

PFD/iOI expects the RAD/iKnee technology will evolve and improve overtime to help mobilize humans, analogous to tires on automobiles that have undergone revisions and improvements for more than 120 years – both concepts involving polymers that sustain compressive and shear forces through millions of cyclic loads.

The United States is the single largest market for knee surgery in terms of revenue potential, so this research will be focused on orthopedic surgeons and patients in this country.

Market Research Project Objectives

As PFD/iOI and Frost & Sullivan have currently discussed, the project of the study will be designed to address five different areas of analysis and to gather relevant data from both a significant sample base of surgeons and patients in each of the areas.

The first objective will be to gather respondent data from the sample groups on their background, history and important demographic statistics. The second area will be t assess the current and perceived future needs of both sample groups. The third phase will involve introducing the RAD/iKnee technology to the participants in the study to get an initial response to the technology and its ability to be a partial if not complete solution to the needs advanced in the second objective. The fourth area will look at how the RAD/iKnee technology would impact the current economics of the marketplace for both the surgeon, the patient, the insurance providers, the healthcare organizations and current vendor provider entities, such as manufacturers of hardware and supplies for current TKA procedures. Finally the study will look at emerging competitors in the space and the respondents preference for the RAD/iKnee solution or other potential options.

The table below provides an outline of the objective of the study.

Objective	Surgeons	Patients
Respondent Background	Demographics; Practice Setting; Geography;Case Mix Surgical volumes for 2023 broken by type of patient, severity, patient journey. Attitudes toward different surgical intervention (aggressive vs. conservative, etc.).	Patient journey (timeline). Current treatment methods used for knee pain. Knee pain impact on function and quality of life; desire for alternatives.
Needs Assessment/ Gap Analysis (Unprompted)	Perceived needs for less invasive treatment alternatives. Satisfaction with current approaches in terms of outcomes, economics, throughput, etc. Current bottlenecks to providing better care for knee pain Surgeon perspective on patient experience.	Satisfaction with past/current treatment methods. Desire for alternatives.
Feedback on Product	Perceived iKnee advantages / disadvantages (responding to prepared iKnee description). Expected adoption rate under different “evidence scenarios”.	Perceived feedback on value of the iKnee surgery vs. TKA surgery expressed as benefits to patient, e.g. pain, procedure time, recovery time, risk, ability to revise, etc. Patient adoption of the iKnee compared to other interventions at varying degrees of knee pain/ function.
Economics and Reimbursement	Influence of TKA reimbursement on treatment pathway. Do surgeons view iKnee as cannibalizing TKA or just delaying? How would surgeon adoption be impacted by different billing codes allowed? Does the iKnee align with bundled payment approaches? What would facilities and payors think about the iKnee?	Current insurance status. Out-of-pocket payment for knee pain interventions. Feedback on the iKnee out-of pocket expense compared to TKA. Degree to which patients might select facilities and surgeons specifically for offering iKnee.
Competitive Strategies	Feedback on similar/alternative treatments. Surgeon preference for direct support from PFD/iOI vs. partner. Optimal marketing/positioning strategy for the iKnee.	Preference of competing approaches vs. the iKnee. Optimal marketing/positioning strategy for the iKnee.

Project Methodology and Deliverables

In moving this study forward, PFD/iOI and Frost & Sullivan have set the following milestones as progress markers for meeting the intended goals.

Pre-Study Needs:	• Internal PFD/iOI interviews • Develop discussion guide, including iKnee description and evidence scenarios
P1: In-Depth Surgeon Interviews	• Completion of 10 one-hour telephone interviews with U.S. orthopedic surgeons: ~50% reconstructive surgeons, ~50% sports medicine surgeons • Surgeons will be asked to review corporate video in link below prior to call, consolidate findings in PowerPoint presentation and feed into Web survey design.
P2: Surgeon Web Survey	• Develop, program, field and analyze a 20-25 min Web survey of 50 U.S. orthopedic surgeons with >30 performing TKA and >30 performing meniscectomy.
P3: Patient Web Survey	• Develop, program, field and analyze a 15-20 min Web survey of 500 U.S. adults representative of iKnee patients~200 ALREADY received TKA • ~150 Severe Knee Pain (TKA likely in <1 year, been told they need TKA soon) • ~150 Moderate Knee Pain (TKA likely in <3 years, receiving advanced treatments, e.g. arthroscopy, injections, etc.)
P2/P3: Deliverables	• Findings from both survey will be presented in a single PowerPoint presentation combined with P1 surgeon insights • Deliverables will also include a simple Excel model showing size of addressable U.S. market based on different customer segmentation, adoption and pricing scenarios for iKnee
P4: White-paper	• Frost & Sullivan will produce a ~6 page, fully-designed, static summary white-paper consolidating relevant findings from all three project phases focusing on the unique and disruptive qualities of the iKnee as well as Frost & Sullivan's estimated market size for the product. • No additional lead generation, public relations or digital media support is included.

As PFD/iOI moves ahead with both its iKnee Comfort Study to gather needed clinical data, and its Frost & Sullivan research project to acquire important market data, the Executive Management Team will be assessing the best path forward for its commercialization of the RAD/iKnee technology based on the current FDA regulatory pathways.

Currently the FDA has developed seven pathways to bring a medical device to market . The pathway for commercialization of the RAD/iKnee technology will be determined based on the commercialization path of the purchaser of the IP. It is important to note that with the iKnee Comfort Study, the first 10,000 RAD/iKnees will be eligible for standard reimbursement to entities caring for iKnee patients with added payment allowances for the surgical procedures and manufacturing costs of iKnee customized implants.

The Seven FDA Pathways To Bring a Medical Device to Market

1.) Premarket Notification 510(k)

The Premarket Notification 510(k) pathway is the most common route taken when launching a medical device. Almost all Class II devices and certain Class I devices will require a 510(k).

The purpose of a 510(k) submission is to provide the FDA with documented evidence showing that a medical device is substantially equivalent in terms of safety and effectiveness to a predicate device.

A predicate device is one that is already legally marketed and shares the same intended use and technological characteristics as the new device. The requirement is to compare the new device with the predicate by summarizing information from the design controls process, such as design features and verification testing.

The FDA typically processes 510(k) applications in 30-90 days. Depending on the robustness of the initial application, there may be a period of back-and-forth discussions, which can delay the process. It is important to plan and provide all appropriate documentation at the time of initial submission.

510(k) "departments" may pertain to variable aspects of implants. E.g. RADs delivering stem cells could qualify under Biologics that control Carticel or under Devices without pharmacologic or cell adjuncts.

2.) Premarket Approval (PMA)

Class III devices, and any device that cannot provide substantial equivalence to a Class I or Class II device through the 510(k) process, must use the Premarket Approval (PMA) pathway.

The PMA process is the most involved as scientific evidence, typically in the form of a clinical trial, is needed to prove the safety and effectiveness of the new device. The FDA will either approve or reject the application within 180 days.

The different steps of the review process include:

- FDA staff will determine completeness through an administrative and limited scientific review
- FDA staff will conduct an in-depth scientific, regulatory, and Quality System review
- An advisory committee will review and offer any recommendations.
- Any final deliberations will occur and the FDA will document and notify the applicant of their final decision.

Although the premarket approval process sounds intimidating, it is the right option for a high-risk, Class III device. However, when devices are substantially equivalent to market use comparisons, the lengthy PMA routes are not needed.

3.) De Novo

If the applicant is developing a lower-risk, "novel" device and struggling to find a predicate, the De Novo pathway might be the best option.

The De Novo pathway has been around since 1997 but many people do not know about it since it is not very commonly used. Companies that do not qualify for 510(k) clearance, since they cannot provide substantial equivalence to a device on the market, should learn more about the De Novo pathway.

Since comparison to a predicate is not needed, companies have a "blank canvas" when it comes to labeling and can set a standard that may give them a competitive advantage over others. One of the key things to remember about the De Novo pathway is that the device must present low to moderate risk through a robust risk mitigation strategy.

4.) Humanitarian Device Exemption

The Humanitarian Device Exemption (HDE) pathway is for devices that are intended to treat or diagnose conditions or diseases that affect small or rare populations.

This pathway involves a two-step process. The FDA must grant a Humanitarian Use Device (HUD) exemption and the device company must then submit an HDE application to the appropriate review center.

Another important requirement is that there cannot be another comparable device on the market that shares the same intended use. The FDA will consider the following when determining if there are comparable devices on the market:

- The device's indications for use and technological characteristics.
- The patient population to be treated or diagnosed with the device.
- Whether the device meets the needs of the identified patient population.

Part of the rationale for providing this pathway is there may not be a large enough patient population with clinical data to satisfy regular FDA requirements of safety and efficacy. Since these devices may be very crucial to patients with rare conditions, the FDA put them in place to do a proper review to determine if the device can be sold.

5.) Custom Device Exemption (CDE)

Is the company developing a custom device for a specific patient? If so, the device falls under the Custom Device Exemption (CDE) pathway and must meet a very narrow set of criteria.

The device must be created or modified to comply with the order of an individual physician or dentist, typically in the form of a prescription. Not only must the clinician order the device, but it must also be used in

the normal course of the professional practice of that physician or dentist.

The product should be specifically designed to treat a unique pathology or physiological condition that no other device is domestically available to treat. It must be assembled from components or manufactured and finished on a case-by-case basis to accommodate the unique needs of the patient.

The FDA even states that companies are limited to no more than 5 units per year of a particular device type.

CDE devices are exempt from PMA or 510(k) submission process, but the company still needs to comply with the following regulations:

- Design Controls (21 CFR Part 820)
- Medical Device Reporting (21 CFR Part 803)
- Labeling (21 CFR Part 801)
- Corrections and Removals (21 CFR Part 806)
- Registration and Listing (21 CFR Part 807)

6.) Expanded Access Program

The Expanded Access Program (EAP), often referred to as the compassionate use or emergency use provision, is fairly self-explanatory.

It allows an investigational device to be used, outside of a clinical trial, in situations where a seriously ill patient has few if any alternatives.

Although there are often ethical considerations, it may be appropriate to evaluate this option to get early feasibility data for high-risk devices, especially when suitable animal models are unavailable. Like the HDE, this data could then be used to expand the label in the future.

Expanded access may be an appropriate pathway for you to choose when all the following apply:

- Patient has a serious disease or condition, or whose quality of life is immediately threatened by their disease or condition.
- There is no comparable or satisfactory alternative therapy to diagnose, monitor, or treat the disease or condition.
- Patient enrollment in a clinical trial is not possible.
- Potential patient benefit justifies the potential risks of treatment. Providing the investigational medical product

will not interfere with investigational trials that could support a medical product's development or marketing approval for the treatment indication.

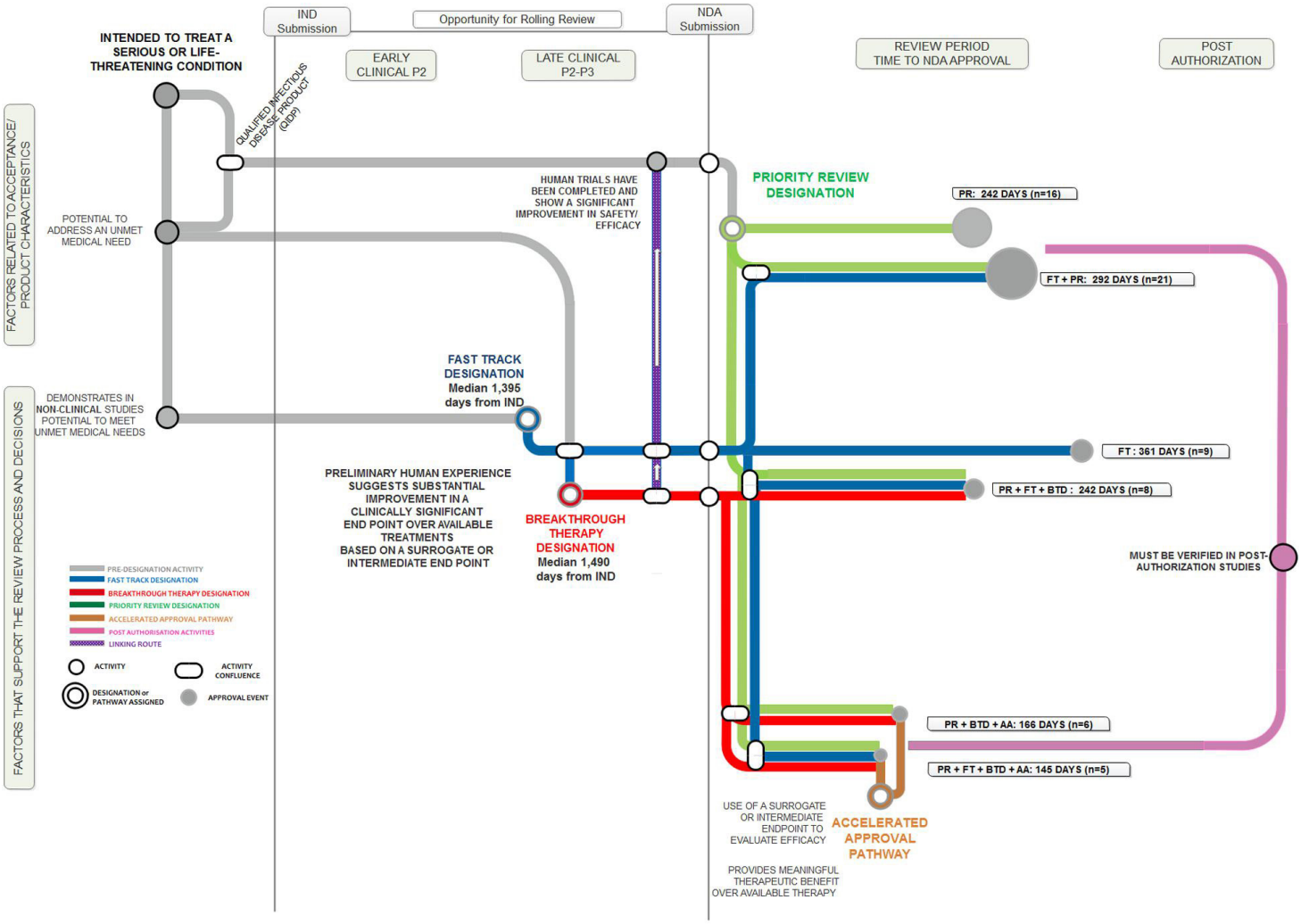
7.) Product Development Protocol

The Product Development Protocol (PDP) is a subset of the PMA process that allows for another pathway for companies with devices in which the technology is well established in the industry.

This pathway allows the company to come to an early agreement with the FDA about how the safety and effectiveness of the device will be shown. The two parties are essentially creating a contract that describes design and development activities, including the outputs of these activities, and acceptance criteria for these outputs.

The company can follow the plan on its own time and report back to the FDA on the agreed-upon milestones. At the end of the process, the company is considered to have "completed" a PDP, which gives them an "approved" PMA.

The flowchart below shows some of the complexity involved in making the determination on how best to proceed for regulatory approval of a new medical device, as well as the milestones and decision that must be managed depending upon the pathway chosen.



FREQUENTLY ASKED QUESTIONS

The following is being provided to answer some of the most common questions about the RAD/iKnee technology. If you have a question for which an answer is not provided, please contact PFD/iOI and we will be happy to answer.

1. ***What is the RAD/iKnee made of?***

The iKnee is made of a polycarbonate-based thermoplastic polyurethane that offers superior bio-compatibility, superior chemical resistance, and oxidative stability for use in long-term body implantable applications. Biomerics Quadrathane™ ARC is a USP Class VI and ISO-10993 compliant, FDA approved hemocompatible material that is used across a wide range of medical applications and is the perfect material to provide the protective cushioning for the RAD/iKnee expectations. It is stronger than Kevlar and will retain its form and shape under extreme pressures and temperatures. The RAD/iKnee caps the bottom of the femur and attaches to the bone giving immediate relief and functionality to the patient. The RAD/iKnee material can be combined with bio-active substances: viscolubricants and chondrocytes. (Stem Cells). The RAD/iKnee device is 3-D printed to exactly match each patients unique bone structure.

FREQUENTLY ASKED QUESTIONS

2. *How is the RAD/iKnee made?*

The RAD/iKnee is made by taking a patient's latest CT scan and digitizing it into PFD/iOI's 3D imaging platform utilizing the Materialise Mimics Suite to create a "Digital Twin" of the patient's distal femur. At this point, the surgeon along with the Materialise engineers conducts a virtual surgery to remove the visible osteophytes and perform a debridement in order to visualize what the patient's joint will look like before the iKnee implant is positioned. This not only allows the patient's iKnee to be custom-tailored to their specific joint topography but it also provides a pre-surgical road-map to the surgeon to facilitate the actual implant procedure. Once the virtual surgery is completed, a 3D STL file of the patient's distal femur is constructed. Based on this model, the patient's iKnee is finalized for printing. The custom-tailored iKnee is created by the PFD/ iOI Arburg Freeformer 300-3X printer using Quadrathane™ ARC. After printing the patient's iKnee, the piece is sent for PostPro processing. At this stage, the implant is vapor smoothed to refine the surface and seal it for easier cleaning and sterilization. Turnaround time from film digitization to implant in hand takes only a few days.

3. *How is RAD/iKnee different than a Total Knee Replacement?*

Total Knee Arthroplasty, or TKA, is one of the most invasive and disruptive options for patients with chronic knee joint issues. TKA's require the removal of significant portions of the patient's distal femur and tibia, as well as damage to ligaments, tendons,

and surrounding cartilage in order to make room for a prosthetic device. TKAs require a large incision to be made to expose the joint open to allow for the removal of the arthritis plus the normal remnant cartilage, ACL, and bone. As a result, large portions of the femoral/tibial/patellar interfaces are destroyed to allow for the insertion of the metal and hard polyethylene hardware. The cost for a TKA is enormous and the chances of rejection, side effects, limited increase in mobility, and even death are potential risks.

Instead of cutting away and removing significant portions of the patient's bone and cartilage, the RAD/iKnee implant will cover and protect the damaged surfaces, in effect, sparing the joint from resection. The RAD/iKnee implant does no harm. It has a non-significant risk designation and it does not use a metal robot to insert metal implants. There is no irreversible destruction of tissue.

The procedure itself is done on an outpatient basis at a qualified PFD/iOI-authorized surgery center. The surgery takes under an hour to perform and barring any complications, the patient is released and able to bear weight on the implanted knee that day. There is no disturbance of any of the patient's ligaments or tendons and the remaining healthy cartilage is preserved. This means:

- No more metal.
- No irreversible destruction of tissue.
- No invasive surgery.

and the patient receives the following benefits:

- Protective restorative bio-compatible polymeric implant.
- Preservation of remnant cartilage and the ACL ligament.
- Joint salvage with regeneration potential.
- Minimally invasive arthroscopic procedure.
- Potential stem cell adjuncts.

4. *Who else makes a product like the RAD/iKnee?*

There are currently no 3D printed patient-specific non-metal, bio-compatible polymeric implants. The iKnee is a non significant risk conservative therapy measure. The iKnee can and should be used as an adjunct therapy and precursor to TKA. Four companies (Stryker, Zimmer, Smith & Nephew, DePuy Synthes) account for an 82% market share in the current Total Knee Market. The current technologies are archaic if not barbaric.

5. *How long will it last?*

Though the PFD/iOI Comfort Study is focused on the iKnee's ability to provide comfort and relief for a minimum six-month period, PFD/iOI will continue to perform multi-year follow-ups with those cohorts who maintain their implants until such a time as they have a TKA procedure performed. At that time, the RAD/iKnee is designed and studied as a temporary comfort device. It is of interest that weight bearing in vivo devices made from PU as Active Implant menisci and Bryan discs have lasted for decades.

FREQUENTLY ASKED QUESTIONS

6. *How long is the procedure?*

The procedure itself is done on an outpatient basis at a qualified PFD/iOI-authorized surgery center. The surgery takes under an hour to perform and barring any complications, the patient is released and able to bear weight on the implanted knee that day.

7. *How long is the rehab?*

Once awake, a post-operative evaluation is made on the patient. Since the RAD/ iKnee enables immediate weight-bearing, once cleared the patient is released to return home. The patient will have some limited post-op restrictions on use, but full recovery time is days rather than weeks or months as they would have had with a TKA.

8. *When should I consider the RAD/iKnee?*

The RAD/iKnee seeks to provide temporary comfort and improved function for patients awaiting TKA. Reasons to delay a TKA include, but are not limited to, the need for weight loss, wound infection healing, implant availability, and required medical or psychological patient preparations. The decision to pursue a RAD/iKnee implant is made between the patient and caretaker. The subject population are individuals with refractory disabling knee pain who failed other conservative measures and are on track for TKA. The iKnee was developed to provide comfort, and it is not intended to treat a disease, or any underlying cause leading to TKA.

FREQUENTLY ASKED QUESTIONS

9. ***Where is the RAD/iKnee available?***

The procedure itself is done on an outpatient basis at a qualified PFD/iOI-authorized surgery center. The First-In-Human (FIH) implant of the RAD/iKnee will be conducted at the Memorial Care Surgical Center in Long Beach, CA. later this year.

10. ***Who invented the RAD/iKnee?***

The RAD technology and the iKnee, the first product candidate using the RAD technology, are the results of the innovative vision of Dr. Robert Thomas Grotz. Dr. Grotz is a noted orthopedic surgeon who has developed several novel inventions for advancing orthopedic care for a variety of patient issues. The RAD technology and the iKnee are two of those inventions that were created to provide an orthopedic surgeon a better alternative than the current TKA procedure or traditional prosthetic hardware provides. Dr. Grotz also developed the first expanding hydraulic spine cage (AccuLif) and the Stabilizer for Human Joints, both of which earned patents, 510(k)s, and FIH to acquisition.

11. ***What surgeons use the RAD/iKnee?***

The surgery will be performed by PFD/iOI's Chief Investigator, Dr. Christopher Woodson, who is a board-certified orthopedic surgeon and sports medicine physician, and founder of Beach Orthopedic Specialty Institute. Dr. Woodson will also be serving as the Principle Investigator for the iKnee Comfort Study's ongoing trials. As patients qualify and applicant surgeons obtain PFD/iOI certification, other centers for use may offer care.

12. *How do I get the RAD/iKnee implant?*

Once a prospective candidate has submitted their applications for the iKnee Comfort Study, they are vetted by the PFD/iOI IRB for possible inclusion into the study. The application screening process consists of a series of steps to ensure that the candidate will be a viable cohort for the program and that there is an anticipated benefit to the patient's knee issue and quality of life as a result of participation. The application review consists of an initial patient consult with a PFD/iOI-certified physician to include:

1. Initial patient background review.
2. Physical examination including a VAS and joint mobility assessment.
3. Initial consult on study overview, implantation procedure, and benefit/risk assessment.
4. Evaluation of other recalcitrant knee problems indicating the need for a TKA.
5. Have a BMI of 30 or less.
6. Have had a continual and chronic issue with their knee joint.
7. Have a pre-operative Visual Analogue Pain Scale (VAS) score of ≥4.
8. Have failed all standard therapeutic care and treatment and are now candidates for a TKA.

9. Be referred to the program by their Primary Care Physician (PCP) or by a qualified referring orthopedic specialist.
10. Have no disqualifying health conditions or risks.

Based on this evaluation, a request for medical records, copies of the latest radiological films, which can include X-rays, CT and MRI scans, and any needed lab work is made. Once procured, an in-depth review of the applicant's records, films, and labs is made by the qualified PFD/iOI surgeon along with the IRB.

If at this point the applicant is deemed to be a viable cohort, a second consult is scheduled during which the study protocols and the implant procedure are once again thoroughly reviewed. If the applicant decides to move forward, a detailed Informed Consent document is signed along with any related additional release and medical information paperwork. Once processed the patient is given a case ID and a surgery date is scheduled.

13. ***Do you have this technology for other joints?***

The first application of the RAD technology is for the knee, where the femur interacts with the tibia and patella. The intent was that this principle would be used in all mammalian joints in need; think animal and human including the knee, hip, shoulder, etc throughout all the long bone interfaces (appendicular skeleton). The RAD/iKnee platform will change the pain profile by covering the dominant surface of the damaged joints.

14. *How long will the study last?*

The iKnee as a temporary device will have different study time frame dependent on the patient and related physician(s). We expect a duration of one month minimum and 6 months maximum. Data reports from each participant will be collected and analyzed. It is planned that up to 10,000 adult male and female study participants will be involved in the iKnee Comfort Study.

15. *Do you collect data on each patient?*

Yes. The iKnee Comfort Study is designed to allow the company to gather critical data in three major areas:

- The ability of the patient to tolerate the iKnee implant both from a bio-compatibility standpoint and an ortho-comfort level.
- The ability of the iKnee implant to decrease or eliminate the patient's pain level as it applies to the use of the impacted joint.
- The ability of the iKnee to maintain or expand the patient's quality of life as it pertains to daily activity, leisure and recreational movement, and/or active sports engagement.

16. *How often is the follow up with patients?*

Patient follow-up for the study is performed at day 10, week six, week 12, and week 24, and then yearly, in order to assess the patient's reaction to the iKnee. In these post-operative follow-ups, the patient is assessed for:

- Comfort and level of pain
- Joint mobility
- Infection or inflammation
- Evaluation of post-op imaging
- Quality of life changes.

17. ***Do you track results on patient outcomes?***

The data is carefully recorded at each step and becomes part of the ongoing evaluation to ascertain several criteria including:

- iKnee design for possible improvements.
- Material integrity and bio-compatibility.
- The ability of the implant to lower or eliminate joint pain.

Along with accomplishing:

- Better patient outcomes
- Faster recovery
- Lower cost
- Lower risk

We hope the preceding offers some insight into our process in introducing this personalized, patient-driven, novel, and highly disruptive, and restorative technology. We wish you the best in your therapeutic journey. Regardless of the path you choose to take, we will continue to execute our process and focus on our mission to heal mankind and "Do No Harm". Onward…

Sincerely,
The PFD/iOI Team

Glossary Of Terms

GLOSSARY

Ablative: In medicine, the removal or destruction of a body part or tissue or its function. Ablation may be performed by surgery, hormones, drugs, radio-frequency, heat, or other methods.

Activities Of Daily Living (ADL): The activities of daily living (ADLs) is a term used to collectively describe fundamental skills required to independently care for oneself, such as eating, bathing, and mobility.

Arthritis: Arthritis is the swelling and tenderness of one or more joints. The main symptoms of arthritis are joint pain and stiffness, which typically worsen with age. The most common types of arthritis are osteoarthritis and rheumatoid arthritis.

Arthroplasty: Arthroplasty is a surgical procedure to restore the function of a joint. A joint can be restored by resurfacing the bones. An artificial joint (called a prosthesis) may also be used. Various types of arthritis may affect the joints.

Arthroscopy: Arthroscopy is a procedure for diagnosing and treating joint problems. A surgeon inserts a narrow tube attached to a fiber-optic video camera through a small incision — about the size of a button hole. The view inside your joint is transmitted to a high-definition video monitor.

Arthrosis: Arthrosis, often referred to as osteoarthritis, is the most common type of arthritis. According to estimates, 32.5 American adults suffer from osteoarthritis. With arthritis and osteoarthritis, the cartilage that covers the end of your bones either becomes damaged or disappears altogether.

Autologous chondrocyte implantation (ACI): A relatively new, state-of-the-art procedure used to treat isolated full-thickness (down to bone) articular cartilage defects of the knee. It has been approved by the Food and Drug Administration for cartilage defects located at the end of the femur bone (thigh).

Bio-compatible: (especially of materials used in surgical implants) not harmful to living tissue.

Debilitating: Something that's debilitating seriously affects someone or something's strength or ability to carry on with regular activities.

Debridement: Arthroscopic debridement is a surgical procedure that removes the broken down bits of cartilage and tissues to help reduce pain and improve movement. It is most commonly performed to help reduce the symptoms of arthritis so that you can regain much of the function of your knee while reducing pain.

Degenerative: Characterized by progressive, often irreversible deterioration, and loss of function in the joint. Tending to decline and deterioration.

Efficacy: The ability to produce a desired or intended result.

Femoral: Relating to the femur or the thigh.

First in human (FIH): A type of clinical trial in which a new drug, procedure, or treatment is tested in humans for the first time. First-in-human studies take place after the new treatment has been tested in laboratory and animal studies and are usually done as phase I clinical trials. Also called FIH study.

Hyaline Articular Cartilage: Articular cartilage is hyaline cartilage and is 2 to 4 mm thick. Unlike most tissues, articular cartilage does not have blood vessels, nerves, or lymphatics. It is composed of a dense extracellular matrix (ECM) with a sparse distribution of highly specialized cells called chondrocytes.

Ligamentous: Relating to the ligaments (= strong fibers that hold bones in place, especially around joints).

Minimally Invasive Surgery: In minimally invasive surgery, doctors use a variety of techniques to operate with less damage to the body than with open surgery.

NSAIDs: Non-steroidal anti-inflammatory drugs, or NSAIDs (pronounced en-saids), are the most prescribed medications for treating conditions such as arthritis.

Osteoarthritis: Osteoarthritis is the most common form of arthritis, affecting millions of people worldwide. It occurs when the protective cartilage that cushions the ends of the bones wears down over time. Although osteoarthritis can damage any joint, the disorder most commonly affects joints in your hands, knees, hips and spine.

Outpatient: A patient who receives medical treatment without being admitted to a hospital.

PE - Polyethylene: Polyethylene is a member of the important family of polyolefin resins. It is the most widely used plastic in the world, being made into products ranging from clear food wrap and shopping bags to detergent bottles and automobile fuel tanks.

Pharmacological: Relating to the branch of medicine concerned with the uses, effects, and modes of action of drugs.

Physiologically: In a way that relates to the functions of living organisms and their parts.

Polymeric/Polymers: A polymer is any of a class of natural or synthetic substances composed of very large molecules, called macromolecules, which are multiples of simpler chemical units called monomers. Polymers make up many of the materials in living organisms and are the basis of many minerals and man-made materials.

Proprioception: Proprioception, otherwise known as kinesthesia, is your body's ability to sense movement, action, and location. It's present in every muscle movement you have. Without proprioception, you wouldn't be able to move without thinking about your next step.

Regenerating: To regrow (new tissue) to replace lost or injured tissue.

Resected: To cut out (of tissue or part of an organ).

Resilient: Able to recoil or spring back into shape after bending, stretching, or being compressed.

Restorative: Promoting a return to health or strength. A remedy that aids in restoring health, vigor, or consciousness.

Synovial Lining: A layer of connective tissue that lines the cavities of joints, tendon sheaths, and bursae (fluid-filled sacs between tendons and bones). The synovial membrane makes synovial fluid, which has a lubricating function.

Therapeutic: The branch of medicine concerned with the treatment of disease and the action of remedial agents, a treatment, therapy, or drug.

Total Knee Arthroplasty or TKA: Knee replacement, also called total knee arthroplasty or total knee replacement, is a surgical procedure to resurface a knee damaged by arthritis. Metal and plastic parts are used to cap the ends of the bones that form the knee joint, along with he kneecap.

NOTES:

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