PRIMARY CARE CONFERENCE
2018

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"I Don't Want a Total Knee"

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LECOM Health

LEARNING OBJECTIVES

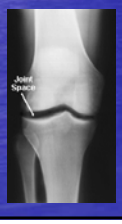
- Understanding the natural history of osteoarthritis of the knee
- Recognizing the signs and symptoms of knee osteoarthritis
- Become familiar with the knee physical exam
- Learn what studies to order to help diagnose knee osteoarthritis
- Understanding the treatment algorithm for knee osteoarthritis

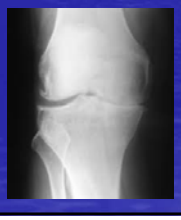
Knee Osteoarthritis

- 52 million Americans suffer from arthritis
- Most common joint disorder in the US
- Knee OA affects 37% of Americans >60 yo
  - 42% Females: 31% Males
- Estimated costs due to hospital expenditures of total knee replacements $28.5 billion (2009)

KNEE ARTHRITIS

- Arthritis is a degenerative joint disease
- Knee arthritis is one of the most common joints effected
- Results in destruction of cartilage progressing to bone on bone in moderate/severe disease



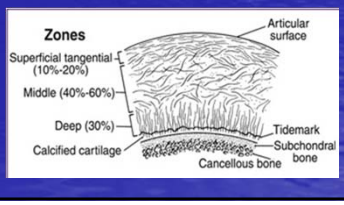


General Principles

- Knee is composed of three joint compartments
  - Medial, lateral and patellofemoral compartments
- Normal knee functions as a complex hinge allowing
  - Flexion, extension, rotation, and gliding
- Weight distribution across the knee with normal alignment
  - 60% through medial compartment
  - 40% through lateral compartment

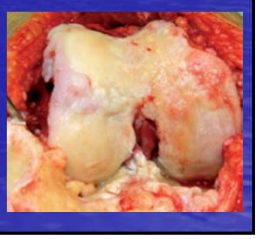
Zones of Articular Cartilage

- **Superficial** (tangential or zone I)
  - Forms the gliding surface
  - Collagen fibers parallel to the articular surface
- **Middle** (transitional or zone II)
  - Thicker with oblique collagen fibers
  - Constitutes most of the cartilage depth
- **Deep** (radial or zone III)
  - Collagen fibers perpendicular to articular surface
- **Calcified cartilage** (zone IV)
  - Radially aligned collagen fibers



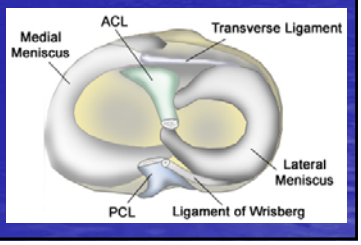
PATHOPHYSIOLOGY
(Degenerative Cascade)

- **Articular Cartilage**
  - Increase water content
  - collagen orientation lost
  - Loss of chondrocytes
- **Synovium**
  - Inflammation (increased thickness & vascularity)
    - Type A (phagocytosis)
    - Type B (produce synovial fluid)
    - Type C (multi-potent precursor cells)



PATHOPHYSIOLOGY
(Degenerative Cascade)

- **Meniscus**
  - Increasing congruency
    - Increases contact area leads to decreased point loading
  - Shock-absorption
    - Meniscus is more elastic than articular cartilage, and therefore absorbs shock
- **Synovial fluid**
  - Decrease of hyaluronin and lubricin



PATHOPHYSIOLOGY
(Degenerative Cascade)

In summary:

- Articular cartilage degeneration
- Meniscus degeneration
- Synovial inflammation
- Synovial fluid with diminished lubrication
- Kidney failure, Heart failure, why not Joint failure?

Presentation

- Patients c/o knee pain worse with walking up or down steps
- Patellofemoral articulation reaction force
  - 2-3x body weight while descending stairs
- Tibiofemoral articulation reaction force
  - 3x body weight with walking

Presentation

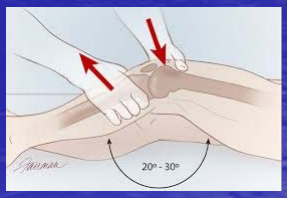
- Symptoms may wax & wane often in correlation with recent activities or body stressors (illness)
- Not uncommon for OA exacerbation to occur during hospital admission for unrelated event
  - Surgery, CHF, COPD, pneumonia, viral illness

Physical Examination

- Joint line tenderness to palpation
  - Degenerative compartment will often correlate to overall alignment
  - Varus deformity = medial joint space narrowing
  - Valgus deformity = lateral joint space narrowing
- Effusion
  - Persistent large/tense effusion may represent degenerative meniscus tear (without specific event)

Physical Examination

- McMurray's test
  - Flex knee & place one hand on medial side of knee
  - Gently externally rotate leg & bring knee into extension
  - Palpable click is a positive test (medial meniscus tear)
- Lachman's test
  - Most sensitive exam to detect ACL tear

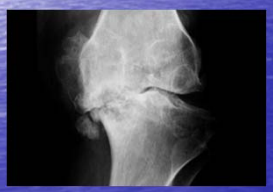
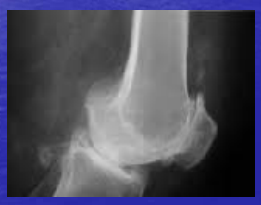
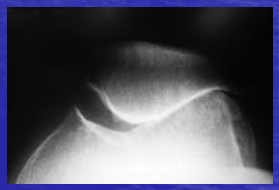


Physical Examination

- Flexion contracture
  - Persistent synovitis and progressive immobility will lead to tight hamstrings
- Joint widening
  - Osteophyte formation is the body's attempt to heal the progressive destruction of cartilage
- Crepitus
  - Patella should glide smoothly over femoral trochlea

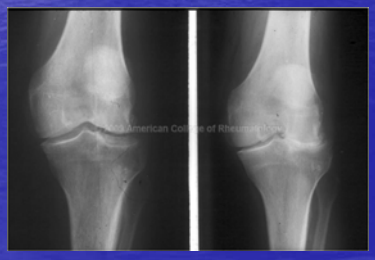
Radiographs

- AP, lateral, and sunrise (merchant) view
  - Osteophyte formation
  - Sclerotic joint margins & subchondral cysts
  - Joint space narrowing
  - Loose bodies

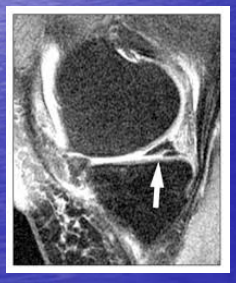
Radiographs

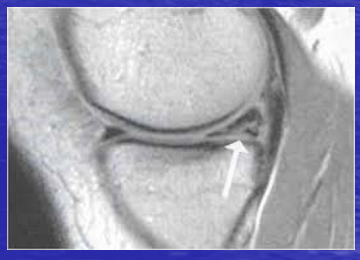
- A clinical pearl is to always order weight bearing AP radiographs of the knee
- Following images is non weight bearing X-ray and weight bearing X-ray of the same knee



MRI

- MRI can be useful in the workup for osteoarthritis of the knee if a degenerative meniscus tear is suspected





MRI

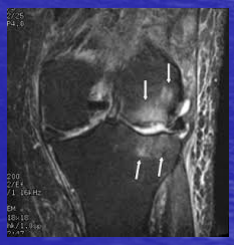
- Degenerative tears in older patients are most commonly found in the posterior horn of the medial meniscus
- Correlation to physical exam findings and/or mechanical symptoms is critical to confirm diagnosis

MRI

- MRI has been shown to find asymptomatic degenerative meniscus tears in over 60% of patients > 65 y.o.
- Diagnosis of symptomatic meniscus tear becomes difficult in the setting of concomitant OA
- Articular cartilage destruction may be the root cause of the patients symptoms

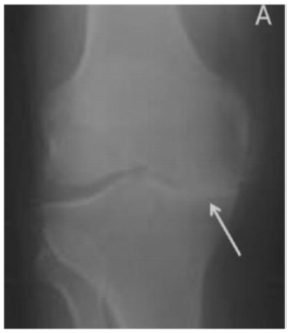
MRI

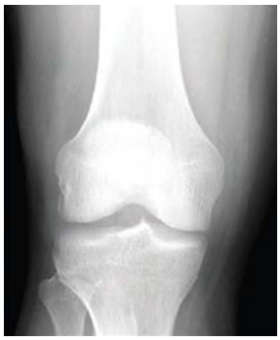
- Adjacent bone marrow lesions can be identified in osteoarthritis
- Representing bone marrow edema of subchondral bone
- BML: Bone marrow lesions



Common Clinical Situation in Knee

- X-ray does not match patient symptoms
- Chronic pain, gait abnormality, worsening QOL





- Clinical picture ≠ radiographic evaluation
  - patient 1: bone on bone but no pain
  - patient 2: preservation of joint space, *severe pain*

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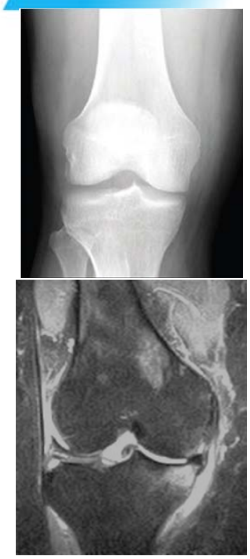
MRI Changes the Picture

- Bone damage not appreciated on radiographs
- As MRI technology improves - helps us better understand this scenario
- MRI demonstrates:
  - Soft tissue causes of pain (meniscal tear, synovitis, etc.)
  - The primary reported source of pain: *chronic* subchondral bone marrow lesions (BML)



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Rothman/Cohen Retrospective Case Series

Cohen, SB, Sharkey, PF. Subchondroplasty for Treating Bone Marrow Lesions, Journal of Knee Surgery, Dec. 2015.

Retrospective Review of 1st 66 Consecutive Patients

General Study Protocol

Patient profile
- Chronic, aching pain (VAS ≥ 4/10)
- ↑ pain with load bearing
- Pain localized to compartment of subchondral bone defect
- ***Failed conservative care***
- Typical candidate for knee replacement

Clinical diagnosis of BML bone defect could be in combination with
- Meniscal tear / extrusion
- Cartilage thinning / fraying / loss
- Mechanical symptoms / loose bodies

Surgical care
- 1 surgeon, 1 center
- *SCP® procedure + arthroscopy*

Postop management
- WBAT w/ crutches 1 wk
- PT started 10-14 d post
- Full activity 4-8 wk post

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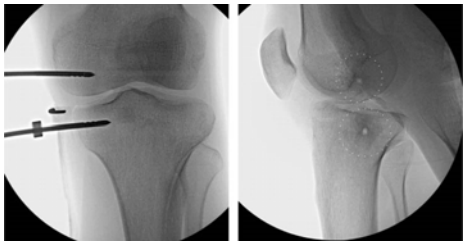
Cohen Clinical Series – Results

Patients followed ≥ 2 years

- Regular follow up visits
- Data points collected
  - VAS Pain
    - Change from baseline
    - Duration of change (years postop at final VAS)
  - IKDC
    - Change from baseline
    - Duration of change
  - Kaplan-Meier survivorship
    - Not converted to TKA/UKA



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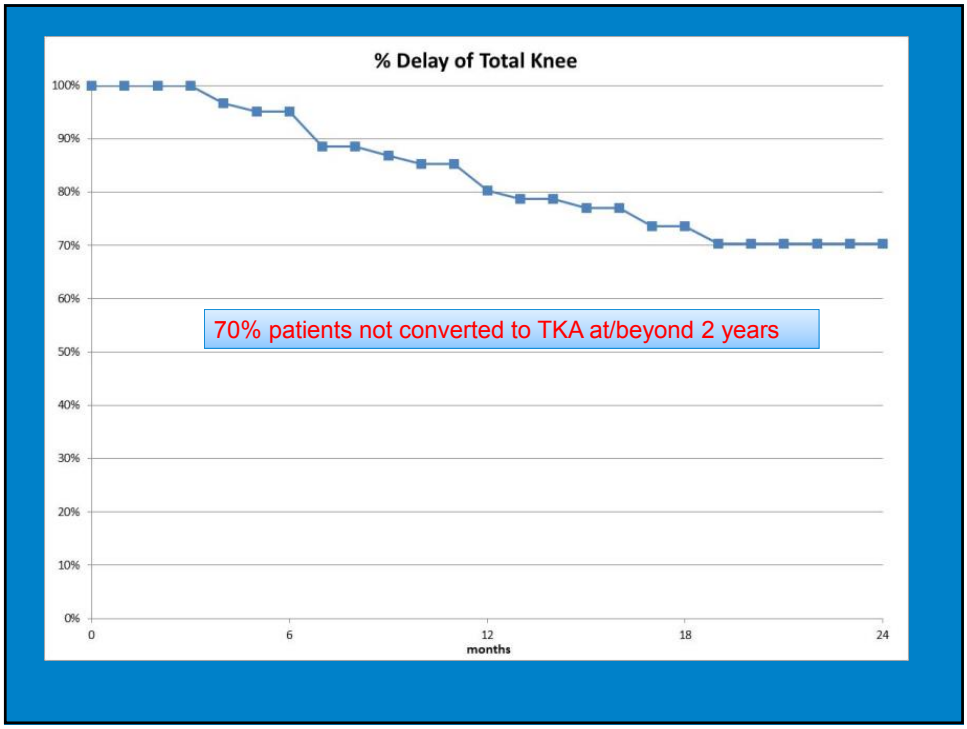


Conservative Treatment

- Ice application
  - 20 minutes on / 20 minutes off for 2 hours
  - May allow patients to continue exercise programs
- Ambulation aids
  - Use in opposite upper extremity

Conservative Treatment

- Weight Loss
  - Indications: symptomatic OA and BMI > 25
  - Improvement in joint pain and function
  - Reducing the risk of progression of OA
  - Each pound of weight loss results in a fourfold reduction in the load exerted on the knee per step during daily activities

Conservative Treatment

- Exercise / Physical therapy
  - First line treatment for all patients with symptomatic arthritis
  - Low impact aerobic exercise
    - Swimming
    - Bicycling
  - Improving flexibility and strengthening muscles improve functional outcome and pain scores

Conservative Treatment

- Exercise / Physical therapy
  - Quadriceps strengthening
    - Improve stability of joints and lessens pain
  - Hamstring stretching
    - Prevention of flexion contracture
  - Combination of supervised exercises and home program show the best results
  - Benefits often lost after 6 months if exercises are stopped

Conservative Treatment

- Viscosupplement intra-articular injections
  - Hyaluronic acid (HA) forms the backbone of aggrecans
  - The macromolecule that makes up cartilage matrix
  - HA at low load speeds acts as a lubricant and faster movements as a shock absorber
  - In OA the concentration of HA is reduced by half to one third of normal

Pharmacologic Treatment

- Acetaminophen at doses of up to 4 g per day have demonstrated to be superior to placebo in relief of pain resulting form OA
- Acetaminophen less effective than NSAIDs
- Tramadol
  - Strongly recommended by AAOS

Pharmacologic Treatment

- **NSAIDS**
  - First line treatment for all patients with symptomatic arthritis
  - Risk factors for adverse reaction
    - Age > 60
    - Multiple medical comorbidities
    - H/o PUD
    - H/o GI bleeding
    - Concurrent corticosteroid use
    - Anticoagulant use

Pharmacologic Treatment

- **NSAIDS**
  - Cox-2 inhibitors limit inflammation without interfering with normal production of protective prostaglandins and thromboxane
    - Decrease the potential gastric toxicity of NSAIDs
  - Cox-2 inhibitors along with all NSAIDs may cause cardiovascular and renal side effects to varying degrees

Conservative Treatment

- Unloader brace
  - Used less frequently
  - Designed to reduce reactive forces in involved compartment
  - Provides 3 point bending force
  - $ 800-1000

Orthotics

- Padded shoe inserts
  - Decrease in joint impact forces to joints
  - $ 8-22
- Varus knee deformity
  - Lateral heel wedges

Hyaluronic Acid vs Corticosteroid Injections

- Meta-analysis, Randomized trial
- Reported effects of intra-articular hyaluronic acid vs corticosteroids on knee osteoarthritis
- 7 eligible trials included 606 patients
- 0 – 4 weeks:
  - Intraarticular corticosteroids appear to be more effective for pain than intraarticular hyaluronic acid
- 4 – 8 weeks:
  - The 2 approaches have equal efficacy
- > 8 weeks:
  - Hyaluronic acid has greater efficacy

Conservative Treatment

- Intra-articular corticosteroid injection
  - Limits inflammation of the joint
  - Injections given typically no closer than Q3 months
  - Useful in controlling acute exacerbation of OA
  - Often injection given in combination with Lidocaine

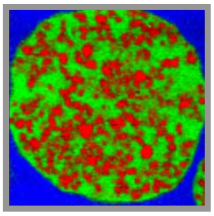
Microsphere Technology: Background

Pain relief associated with IA corticosteroid administration to patients with knee osteoarthritis (OA):

- Can diminish within 1-6 weeks following injection[1-4]
- Is transient due to efflux of drug from the joint within hours of injection[5]

TA-ER is an extended-release formulation of the corticosteroid TA[6-7]

- Small crystals of TA are embedded in a PLGA co-polymer matrix
- Designed with the goal to extend TA joint residency time and reduce systemic exposure to TA following IA injection



Raman Microscopy cross-sectional view of a single microsphere.
Green: PLGA matrix; Red: TA crystals

IA, intraarticular; OA, osteoarthritis; PLGA, poly (lactic-co-glycolic acid); TA, triamcinolone acetonide; TA-ER, triamcinolone acetonide extended-release injectable suspension.

1. Jüni P et al. *Cochrane Database Syst Rev*. 2015; Oct 22;(10): CD005328. doi: 10.1002/1465 1858.CD005328.
2. Ayhan E, et al. *World J Orthop*. 2014;5(3):351–61.
3. Bjordal JM, et al. *BMC Musculoskelet Disord*. 2007;8:51.
4. Godwin M, Dawes M. *Can Fam Physician*. 2004;50:241–8.
5. Derendorf H,et al. *Clin Pharmacol Ther*. 1986;39(3):313–7.
6. Data on File. Flexion Therapeutics, Inc.
7. Conaghan PG et al. *In Press*. NCT02357459.

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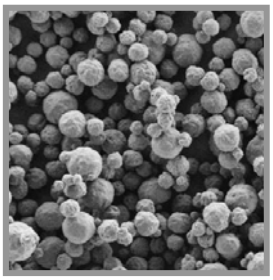
TA-ER Microsphere Characteristics

TA-ER is prepared as an injectable suspension of ~45 µm microspheres[1]

- Active Ingredient: TA
  - FDA-approved for use via multiple routes of administration (including IA)[2]
  - FDA-approved for several diseases/conditions (including OA)[2]
  - One of the most prescribed IA corticosteroids[3]
- Microsphere Scaffold: PLGA[4]
  - Biodegradable polymer
  - Used in several FDA-approved extended-release therapeutics (>20-year history)



Electron micrograph of PLGA microspheres.

FDA, US Food and Drug Administration; IA, intraarticular; OA, osteoarthritis; PLGA, poly (lactic-co-glycolic acid); TA, triamcinolone acetonide; TA-ER, triamcinolone acetonide extended-release injectable suspension.
1. Data on File. Flexion Therapeutics, Inc.
2. Kenalog®-40 injection (triamcinolone acetonide injectable suspension) Prescribing Information. Bristol-Myers Squibb. Jan 2016.
3. Data on File. Flexion Therapeutics, Inc.
4. Makadia HK and Siegel SJ. *Polymers*. 2011;3(3);1377.

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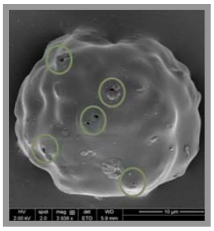
TA-ER Microsphere Function

PLGA microsphere technology allows for extended-release of TA[1]

- **Initial TA release: TA crystals near the surface of the microsphere dissolve upon contact with synovial fluid**
- **Extended TA release: TA crystals that are more deeply embedded within the microsphere are slower to dissolve**
  - Small pores on the surface of the microsphere are created by the dissolving TA crystals
  - ~500 nm channels appear throughout the microsphere; enable TA release from the interior through the surface pores
  - PLGA eventually degrades into lactic acid and glycolic acid, which ultimately metabolize into CO_2 and H_2O



Electron micrograph of PLGA microsphere pores.

PLGA, poly (lactic-co-glycolic acid); TA, triamcinolone acetonide; TA-ER, triamcinolone acetonide extended-release injectable suspension.
1. Data on File. Flexion Therapeutics, Inc.

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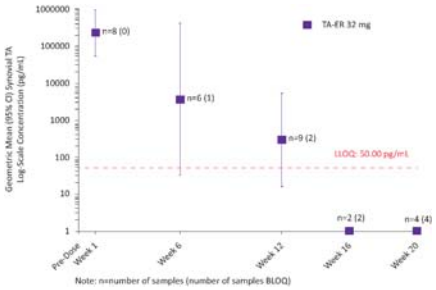
TA-ER Microsphere Characteristics in a Pharmacokinetic Study: Synovial Fluid TA Concentrations

Patients with knee OA received a single IA injection; synovial fluid TA concentrations were measured[1]

- ***TA-ER 32 mg:*** most patients had quantifiable TA through Week 12
  - Week 1: 231,328.9 pg/mL
  - Week 6: 3590.0 pg/mL
  - Week 12: 290.6 pg/mL

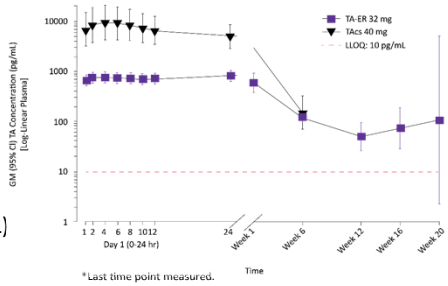


BLOQ, below limit of quantification; CI, confidence interval; LLOQ, lower limit of quantification; TA, triamcinolone acetonide; TAcs, triamcinolone acetonide crystalline suspension; TA-ER, triamcinolone acetonide extended-release injectable suspension.
1. Adapted from Kraus VB et al. *Osteoarthritis Cartilage*. 2018;26(1):34-42.

TA-ER Microsphere Characteristics in a Pharmacokinetic Study: Plasma TA Concentrations

Patients with knee OA received a single IA injection; blood plasma TA concentrations were measured[1]

- ***TA-ER 32 mg:*** **plasma TA**
  - Gradually increased to peak (836.4 pg/mL) over 24 hours
  - Slowly declined to <110 pg/mL over Weeks 12-20
- ***TAcs 40 mg:*** **plasma TA**
  - Peaked at 4 hours (9,628.8 pg/mL)
  - Decreased to 4,991.1 pg/mL at 24 hours
  - Was 149.4 pg/mL at Week 6*

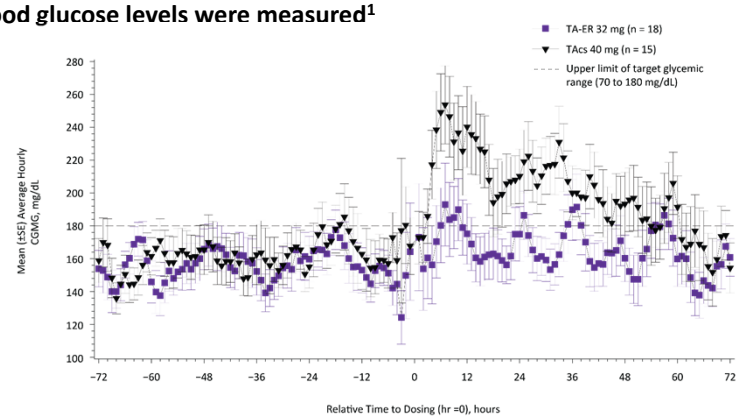


Please see Important Safety Information on slides 21 and 22 and full Prescribing Information available at Zilrettalabel.com.

CI, confidence interval; GM, geometric mean; LLOQ, lower limit of quantification; OA, osteoarthritis; TA, triamcinolone acetonide; TAcs, triamcinolone acetonide crystalline suspension; TA-ER, triamcinolone acetonide extended-release injectable suspension.
1. Adapted from Kraus VB et al. *Osteoarthritis Cartilage*. 2018;26(1):34-42.

TA-ER Microsphere Characterisitics in a Pharmacokinetic Study: Blood Glucose Levels in Patients with T2DM

Patients with knee OA and T2DM received a single IA injection; blood glucose levels were measured[1]



- Change $CGMG_{Days1–3}$ was significantly lower following TA-ER vs TAcs:
  - 14.7 vs 33.9 mg/dL - LSM-difference [95% CI] −19.2[−38.0, −0.4] *P*=0.0452

T2DM, type 2 diabetes mellitus; TAcs, triamcinolone acetonide crystalline suspension; TA-ER, triamcinolone acetonide extended-release injectable suspension.
1. Russell S et al. *Diabetes.* 2017;66(Supplement 1):A289.

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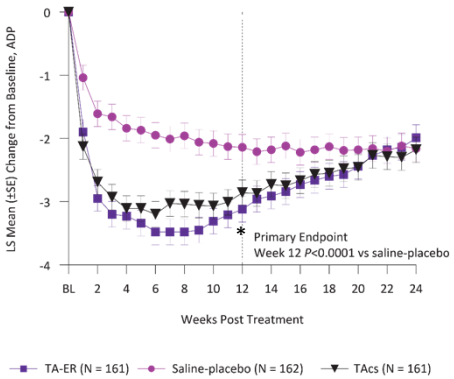
TA-ER: Phase 3 Pivotal Trial *ADP Intensity*



- **Primary endpoint met:** TA-ER pain relief vs saline-placebo at Week 12
  - LSM-difference [95% CI]: -0.98 [-1.47, -0.49]; *P*<0.0001
- **Key secondary endpoint not met:** TA-ER pain relief vs TAcs at Week 12
  - LSM-difference: -0.26; *P*=0.2964
- **Exploratory endpoints:** TA-ER pain relief vs saline-placebo and TAcs at each week
  - Favored TA-ER vs saline-placebo at each week through Week 16
  - Favored TA-ER vs TAcs at each week from Week 2-12 (not statistically significant)

Please see Important Safety Information on slides 21 and 22 and full Prescribing Information available at Zilrettalabel.com.

ADP, average daily pain; CI, confidence interval; LSM, least squares mean; SE, standard error; TAcs, triamcinolone acetonide crystalline suspension; TA-ER, triamcinolone acetonide extended-release injectable suspension.
Conaghan PG et al. *In Press.* NCT02357459.

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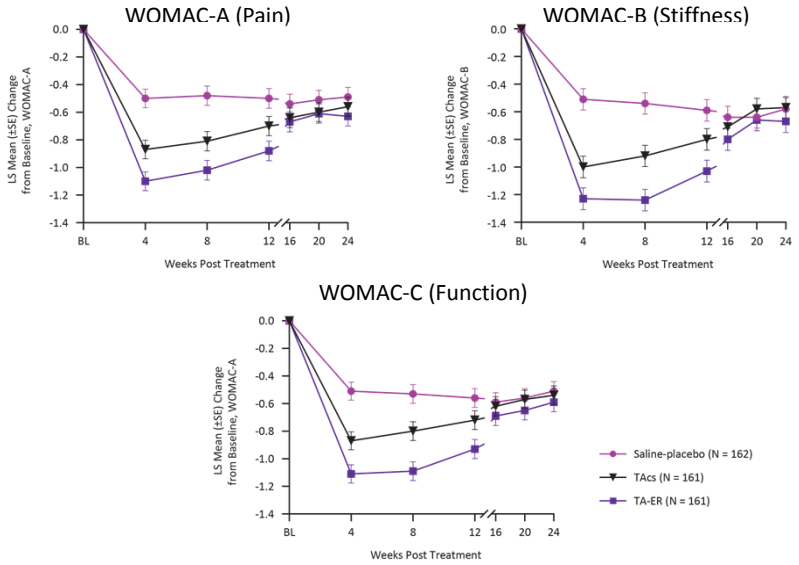
TA-ER: Phase 3 Pivotal Trial
Exploratory endpoints: WOMAC



LSM, least squares mean; SE, standard error; TAcs, triamcinolone acetonide crystalline suspension; TA-ER, triamcinolone acetonide extended-release injectable suspension; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.
Conaghan PG et al. *In Press.* NCT02357459.

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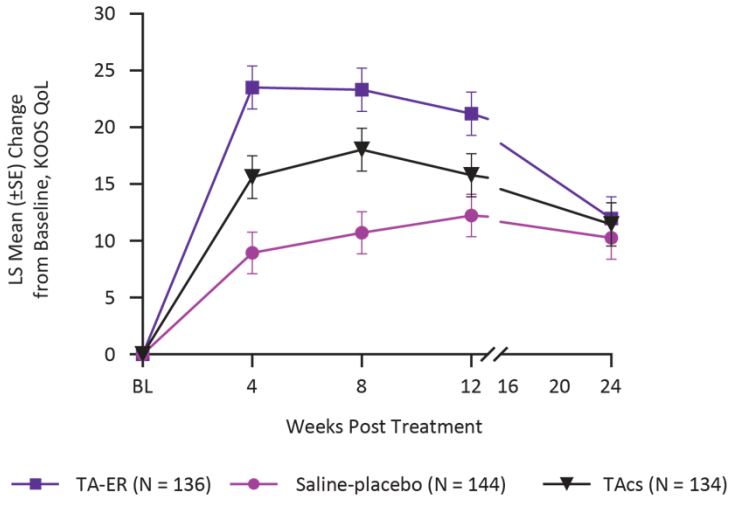
TA-ER: Phase 3 Pivotal Trial
Exploratory endpoints: KOOS QoL Subscale



KOOS QOL, Knee Injury and Osteoarthritis Outcome Score Quality of Life; LSM, least squares mean; SE, standard error; TAcs, triamcinolone acetonide crystalline suspension; TA-ER, triamcinolone acetonide extended-release injectable suspension.
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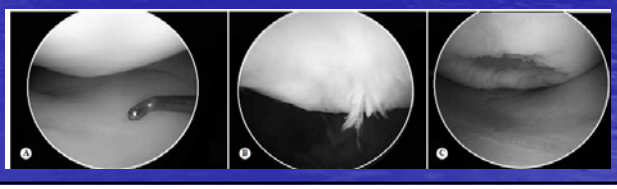
Arthroscopy

- Debridement
  - Synovectomy (plica removal)
  - Removal of loose bodies
  - Chondroplasty
  - Resection of torn/damaged meniscus

Arthroscopy

- Direct Visualization of articular cartilage

Outerbridge Arthroscopic Grading System	
Grade 0	Normal cartilage
Grade I	Softening and swelling
Grade II	Partial thickness defect, fissures < 1.5cm diameter
Grade III	Fissures down to subchondral bone, diameter > 1.5cm
Grade IV	Exposed subchondral bone



Evidence Based Medicine for Arthroscopic Debridement of Knee Osteoarthritis

- Study published in New England Journal of Med (2002)
- 180 patients with knee OA who received arthroscopic débridement, arthroscopic lavage, or placebo surgery (skin incisions)
- Outcomes were assessed at multiple points over a 24-month period
  - Use of 5 self-reported scores for pain, function, walking, and stair climbing
- The outcomes after arthroscopic lavage or arthroscopic debridement were no better than those after a placebo procedure

Arthroscopy

- Partial meniscectomy
  - >80% satisfactory function at minimum follow-up
  - Predictors of success
    - Age <40yo
    - Normal alignment
    - Minimal or no arthritis
    - Single tear

Arthroscopy

- **Total meniscectomy**
  - 70% have arthritic X-ray changes 3 years after surgery
  - 100% have arthrosis at 20 years
  - Severity of degenerative changes is proportional to percent of the meniscus removed

Unicompartmental Knee Arthroplasty

- **Indications**
  - Isolated unicompartmental noninflammatory arthritis
  - Deformity of less than 10 degrees
  - Intact anterior cruciate ligament (ACL)
  - Little or no joint subluxation
  - Little or no patellofemoral disease
  - Weight < 90 kg


Uni Knee Implant

Unicompartmental Knee Arthroplasty

- Data suggests that only 6% of patients meet the criteria for whom knee arthroplasty is indicated
- Indications for this procedure have been expanded for younger patients
- 10 year survival rates range from 87 to 96%
- 15 year survival rates range from 79 to 90%
  - Survivorship declines rapidly in the second decade
- Late failure
  - Opposite compartment degeneration
  - Component loosening
  - Polyethylene wear

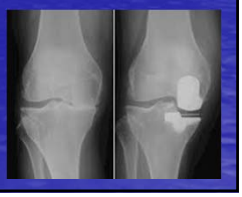


Table 1

American Academy of Orthopaedic Surgeons Evidence-Based Clinical Practice Guidelines for Osteoarthritis of the Knee[1]

Therapeutic Modality	AAOS Position	Strength of Supporting Evidence
Strengthening exercises with neuromuscular education	Recommend	Strong
NSAIDs	Recommend	Strong
Total knee arthroplasty	Recommend	Strong
Appropriate weight loss (body mass index ≥25 kg/m^2)	Recommend	Moderate
Valgus-producing proximal tibial osteotomy	Might recommend	Limited
Intra-articular corticosteroids	Cannot recommend for or against	Inconclusive
Acetaminophen (oral) or opioids (oral or transdermal patch)	Cannot recommend for or against	Inconclusive
Manual therapy	Cannot recommend for or against	Inconclusive
Physical agents, including electrotherapeutic modalities	Cannot recommend for or against	Inconclusive
Arthroscopic partial meniscectomy	Cannot recommend for or against	Inconclusive
Intra-articular hyaluronic acid	Cannot recommend	Strong
Braces (to unload medial compartment)	Cannot recommend	Strong
Arthroscopic intervention (eg, lavage, débridement)	Cannot recommend	Strong
Glucosamine and chondroitin	Cannot recommend	Strong
Acupuncture	Cannot recommend	Strong
Insoles (eg, lateral wedge)	Cannot recommend	Moderate
Needle lavage	Cannot recommend	Moderate
Free-floating (unfixed) interpositional device	Cannot recommend	Consensus (no reliable evidence)

What treatment options exist?

Increasing severity of arthritis

- Activity Modification
- Weight loss
- Self-help/assistive devices
- Heat and Cold Treatments
- Physiotherapy
- Over-The-Counter Medications
- Prescription Medications
- Injections
- **Joint Replacement**

Joint replacement is the final option, once all conservative methods of treatment have been tried

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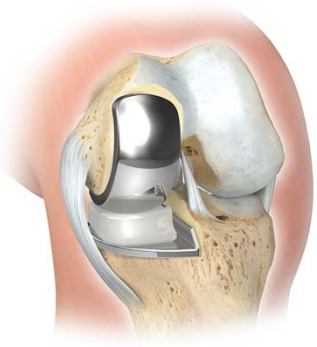
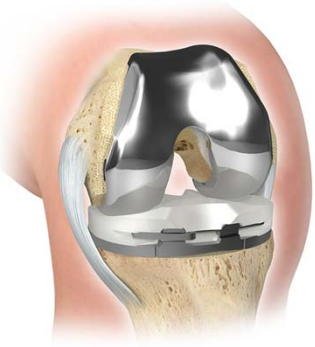
When is someone a suitable candidate for an Oxford?

- 48 out of 100 patients have been shown to be a candidate for an Oxford Partial Knee[2]



Oxford Partial Knee



Traditional Total Knee

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Oxford Microplasty Instrumentation

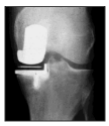
Phase 1 1976 - 1987

- Difficult to balance due to femoral prep
- A lot of eyeballing

Phase 2 1988 - 1997

- Introduction of milling
- Improving reproducibility

Phase 3 1998 - 2011



- Improving milling technique
- Continued focus on reproducibility

Microplasty 2011 - current

- Focus on reproducibility

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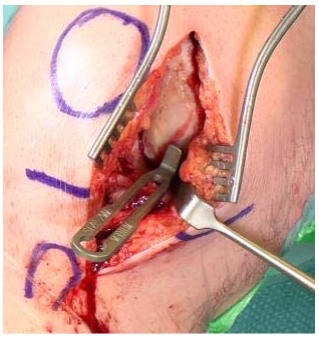
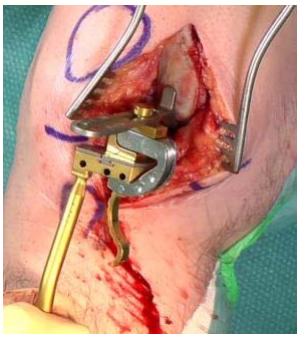
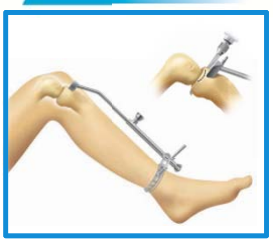
Tibial Preparation







- More reproducible tibial resection using[2]
  - Sizing Spoons – reference intact cartilage
  - G-Clamp
  - Removable Shims

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2. Hurst, *et al.* 2014 (JOA)

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Globally Published Oxford Partial Knee Survivorship
Non-designer results

Author	Year Published	Cohort	Follow-Up	Survival
Svard[6]	2001	124	10-year	95%
Rajasekhar[7]	2004	135	10-year	94%
Yoshida[8]	2013	1279	10-year	95%
Jones[9]	2012	1000	10-year	91%
Lim[10]	2012	400	10-year	94%
Faour-Martin[11]	2013	416	10-year	95%
Price[12]	2011	682	20-year	91%

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6. Svard, *et al.* 2001 (BJJ)
7. Rajasekhar, *et al.* 2008 (Orthopaedic Proceedings)
8. Yoshida, *et al.* 2013 (JOA)
9. Jones, *et al.* 2012 (O&C)
10. Lim , *et al.* 2012 (BJJ)
11. Faour-Martin, *et al.* 2013 (IO)
12. Price, *et al.* 2011 (CORR)

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A shift in focus

- **Traditionally focus has been on**
  - Survivorship
  - Functional Scores
  - Pain Relief
- **Still important, but shifting towards**
  - Patient Satisfaction
  - Activities of Daily Living
  - Happiness with Joint Replacement

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Closing the Revision Gap
PKA Candidacy

- Kozinn & Scott (1989) indications[24] → 5% of patients are PKA candidates[25]
- Globally only 8% of Primary Knee Arthroplasty is a PKA[26,27]

8% current utilisation of PKR

- 2015 publication Scott[28] revisits 1989 publication, and removes the following contraindications
  - Obesity
  - Age
  - PFJ damage limited to the medial facet
  - Chondrocalcinosis

- Study of 200 knees found 47.6% are PKA candidates[30]

47.6% candidates for PKA

- Anteromedial Osteoarthritis
  - Bone-on-bone in the medial compartment
  - Full thickness cartilage in the lateral compartment
  - Functionally intact ACL
  - Functionally normal MCL

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24. Kozinn, *et al* 1989 (JBJS)
25. Pandit, *et al.* 2011 (JBJS BR)
26. EU Millenium 2013
27. US Millenium 2014
28. Berend, *et al.* 2015 (JSOA)
30. Willis-Owen, *et al.* 2009 (Knee)

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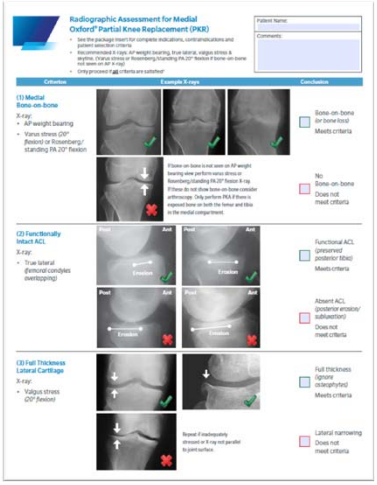
Oxford Radiographic Decision Aid

- Helps surgeons identify whether or not a patient is a candidate for an Oxford Partial Knee
- Validated – *Hamilton, et al BJJ Oct. 2016*[29]
  - Blinded to final device, found w/ pre-op x-rays, 92% sensitivity in predicting suitability for Oxford PKR
  - In patients meeting Decision Aid criteria and receiving PKR, 99% survivorship @ 5 years
- Available via Zimmer Biomet
  - Printed and Digital
- X-Ray Protocol also available
  - Provides an overview of how to perform the required x-rays



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29. Hamilton et al. 2016 (BJJ)

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Benefits of PKA compared to TKA

Benefits

- Better range of motion[32-34]
- Preserving more healthy bone than TKA[34]
- More physiological functionality[34] and near normal gait[35] than TKA
- Faster return to a more functional level and shorter hospital stay than TKA[32]
- Fewer and less severe postoperative complications including less morbidity compared with TKA[36,37]

And for society…

- Substantial cost savings over TKA[30] ($3,261 per knee)
- Registry data reports that TKAs are 2.6 times more likely to have risk of reoperation for infection[37]
- Average reduction in length of stay, at least 0.8 days in favour of PKA (variation between 0.8 – 4 days)[36-41]
- Additional cost savings when associated with an accelerated recovery protocol[42]

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30. Willis-Owen, *et al.* 2009 (Knee)
32. Lombardi, *et al.* 2009 (CORR)
33. Amin, *et al.* (2006)
34. Deshmukh, *et al.* (2001)
35. Wiik, *et al.* (2013)
36. Brown, *et al.* (2012)
37. Robertsson, *et al.* 1999 (AOS)
38. Shakespeare, *et al.* 2003 (Knee)
39. Yang, *et al.* 2003 (SMJ)
40. Xie, *et al.* 2009 (EJHE)
41. Koskinen, *et al.* 2008 (AO)
42. Reilly, *et al.* 2005 (Knee)

Lifetime Warranty

- Every Oxford Partial Knee implanted on or after April 29, 2013 is covered under the only Lifetime Knee Implant Replacement Warranty in the US*
- If a patient receives an Oxford Partial Knee, and it has to be revised for any reason, Zimmer Biomet will cover the cost of the Zimmer Biomet replacement knee implant.

*Subject to terms and conditions within the written warranty.
- Applies to Oxford Partial Knees implanted on or after 4-29-2013
- Covers the replacement of Oxford Partial Knee components for any reason
- Covers the cost of the replacement implant only; does not cover hospital costs, co-pays, or other related expenses
- Limited to no more than one complete replacement of the product
- Any additional costs associated with surgery or follow-up are not covered – only the implant components

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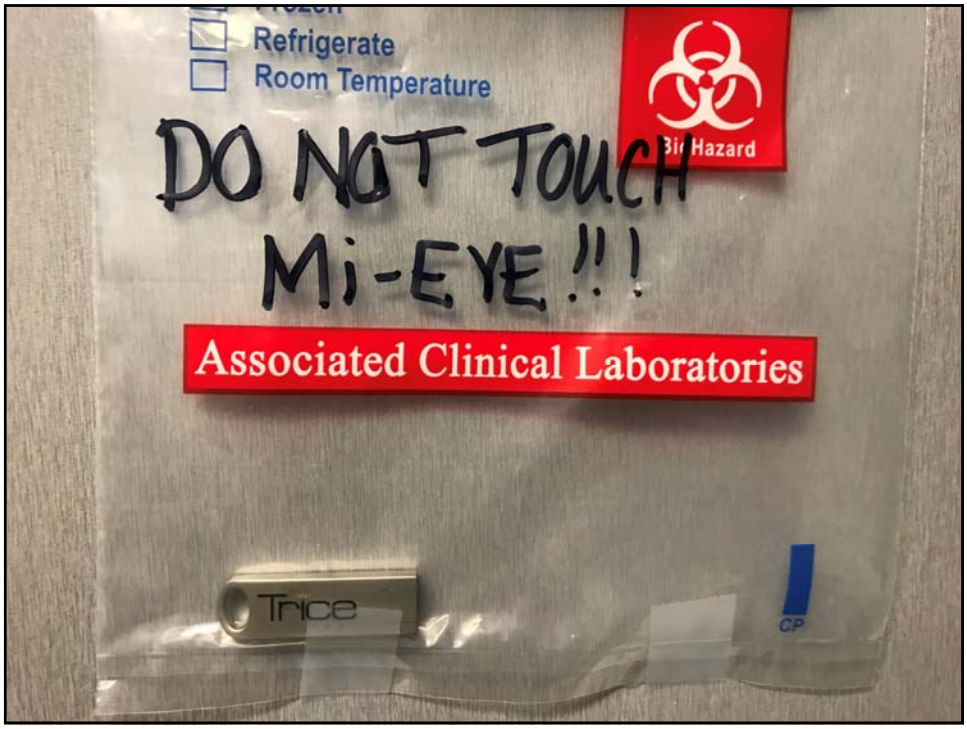
Refrigerate
Room Temperature
DO NOT TOUCH
Mi-EYE!!!
Associated Clinical Laboratories
Trice
CP

THE END

References

- Bannuru,R., Natov, N., Obadan, I., Price, L, Schmid, C., McAlindon, T. (2009). Therapeutic trajectory of hyaluronic acid versus corticosteroids in the treatment of knee osteoarthritis: a systematic review and meta-analysis. Journal of Arthritis Rheumatology. Dec 15;61(12):1704-11
- Boyer, M. (2014) Primary Knee Arthroplasty. Wellman, S., Bolognesi, M. *AAOS Comprehensive Orthopaedic Review* (pp 1289-1304) Rosemont, IL: American Academy of Orthopaedic Surgeons.
- Fischgrund, J. (2008). Knee Reconstruction and Replacement. Peters, C., Crofoot, C. *Orthopaedic Knowledge Update* (pp 457-472). Rosemont, IL: American Academy of Orthopaedic Surgeons.
- Hoshino, A., Wallace, W. (1987). Impact-absorbing properties of the human knee. Journal of Bone Joint Surgery British, 69(5), 807-811.
- Miller, M., Thompson, S., Hart, J. (2012). Total Knee Arthroplasty. Review of Orthopaedics (pp 394-398). Philadelphia, PA: Saunders Elsevier.

References

- Moore, D. Orthobullets: Basic Science. Linage Medical. 2015. March, 29. www.orthobullets.com.
- Moore, D. Orthobullets: Adult Reconstruction. Linage Medical. 2015. March, 29. www.orthobullets.com.
- Moore, D. Orthobullets: Sports. Linage Medical. 2015. March, 29. www.orthobullets.com.
- Moseley, J., O'Malley, K., Petersen, N., Menke, T., Brody, B., Kuykendall, D., Hollingsworth, J., Ashton, C., Wray, N. (2002). A controlled trial of arthroscopic surgery for osteoarthritis of the knee. New England Journal of Medicine: 347(2):81-8
- Sheth, N., Lonner, J. (2009). Total Knee Arthroplasty. Pill, S. *Gowned and Gloved Orthopaedics* (pp 251-267). Philadelphia, PA: Saunders Elsevier

Question 1

Which of the following non-operative treatments for osteoarthritis has the best evidence to support its use?

- 1. Combination of supervised and home exercise programs
- 2. Hyaluronic acid injections
- 3. Lateral heel wedge
- 4. Acetaminophen
- 5. Glucosamine

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Question 2

A 62-year-old female undergoes an uncomplicated primary total knee replacement. Her knee range-of-motion pre-operatively was 0-135 degrees of flexion. Which of the following is true regarding the immediate post-operative use of a continuous passive motion machine in this patient?

- 1. Reduced risk of venous thromboembolism
- 2. No long-term difference in ROM compared to patients not using CPM
- 3. Increased passive knee flexion at 6 months
- 4. Increased length of hospitalization
- 5. Decreased risk of surgical site infection

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Question 3

The following are risk factors for developing knee osteoarthritis EXCEPT:

- 1. Knee articular trauma
- 2. Metabolic syndrome
- 3. Female gender
- 4. Increased age
- 5. Participating in physical fitness

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Question 4

- All the following are common complaints associated with knee osteoarthritis EXCEPT?

- 1. Knee pain at night
- 2. Knee pain while climbing stairs
- 3. Knee stiffness
- 4. Instability, clicking, or locking sensation
- 5. Numbness in the ankle or foot

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Question 5

Which radiographic images are most commonly used to identify the degree of degenerative joint disease caused by knee osteoarthritis?

1. Knee MRI to identify meniscal pathology
2. Knee CT scan
3. X-ray images of knee with patient lying down
4. Ultrasound images of the knee joint
5. X-rays: Standing AP, lateral, and sunrise views of the knee

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