# Washington State Health Care Authority, HTA Program
## Final Key Questions

## Osteochondral Allograft Transplantation and Autograft Transfer System (OATS/mosaicplasty)

### Introduction

HTA has selected Osteochondral Allograft Transplantation and Autograft Transfer System (OATS/mosaicplasty) to undergo a health technology assessment where an independent vendor will systematically review the evidence available on its safety, efficacy, and cost-effectiveness. HTA originally posted the topic as Osteoarticular Transfer System Cartilage Surgery (OATS), now modified to the more generic title above, and gathered public input on all available evidence. HTA published the Draft Key Questions to gather public input about the key questions and any additional evidence to be considered in the evidence review. Key questions guide the development of the evidence report. HTA seeks to identify the appropriate topics (e.g. population, indications, comparators, outcomes, policy considerations) to address the statutory elements of evidence on safety, efficacy, and cost effectiveness relevant to coverage determinations.

Osteoarticular Autograft Transfer System cartilage surgery (OATS) is an open joint or arthroscopic procedure used to repair localized cartilage injuries, usually caused by trauma or acquired defect of a joint (knee, ankle, hip, shoulder, elbow), such as an anterior cruciate ligament (ACL) deficiency. In the procedure, one (or more) plugs of healthy cartilage are harvested from a less important area of the cartilage within the same joint or from preserved cadaver tissue, and inserted into the center the damaged area, with the idea that surrounding cartilage will grow over the edges of the insert without the reduction of quality to fibrocartilage cells found in other cartilage repair procedures (sub-chondral bone marrow stimulation by drilling or microfracture, abrasion arthroplasty).

#### *Draft Key Questions*

When used in patients with cartilage damage:

1. What is the case definition of a patient suitable for OATS/mosaicplasty surgery, and are there measures of reliability and validity for case identification?
    a. What are the maximum, minimum, and optimum size (volume) of the damage that is suitable for repair using OATS/mosaicplasty?
    b. What are the maximum and optimum number of lesions that can be repaired in a single OATS/mosaicplasty procedure?
    c. Are there other considerations that make OATS/mosaicplasty suitable or unsuitable (age, mobility, comorbidities, BMI).
    d. Is there a distinction between OATS and mosaicplasty, and a related case definition difference between the two?

e. Is there a distinction between cases where autograft vs. allograft OATS/mosaicplasty is preferable?

f. Of the joints where OATS/mosaicplasty has used (knee, ankle, hip, shoulder, elbow), are any more or less suitable to this procedure?

2. What are the expected treatment outcomes of OATS/mosaicplasty, and are there validated instruments and scores to measure clinically meaningful improvement?

3. What is the evidence of efficacy and effectiveness of OATS/mosaicplasty (open or arthroscopic)? Including consideration of short term and long term:

   a. Delay or avoidance of progression to osteoarthritis
   b. Impact on function, pain, range of motion, quality of life, activities of daily living and return to work
   c. Longevity of treatment effect
   d. Need for continuing and/or subsequent intervention
   e. Need for extended or continuing physical therapy
   f. Recovery time considering harvest site recovery issues
   g. Differential results from multiple versus single grafts, patterning for multiple grafts (linear arrangement vs. circular arrangement)
   h. Differential results between allograft and autograft procedures
   i. Differential results between open and arthroscopic procedures
   j. Differential results in centers of excellence

4. What is the evidence of the safety of OATS surgery? Including consideration of:

   a. Adverse events type and frequency (peri-operative, cartilage plug detachment, cartilage rejection, graft fit, harvest site issues, development of fibrocartilage, mortality, other major morbidity such as DVT, deep infection, and excessive intraarticular bleeding)
   b. Revision/re-operation rates (if not addressed in efficacy)

5. What is the evidence that OATS surgery has differential efficacy or safety issues in sub populations? Including consideration of:

   a. Gender
   b. Age
   c. Psychological or psychosocial co-morbidities
   d. Baseline functional status: e.g. type of injury or lesion, extent of cartilage damage, specific damage site size, number of damage sites
   e. Other patient characteristics or evidence based patient selection criteria, especially comorbidities of diabetes and high BMI
   f. Provider type, setting or other provider characteristics
   g. Payor/ beneficiary type: including worker's compensation, Medicaid, state employees

6. What is the evidence of cost implications and cost-effectiveness for OATS/mosaicplasty? Including consideration of:

   a. Costs (direct and indirect) and cost effectiveness
   b. Short term and long term

*Policy Context:*

Injury or damage to cartilage can be resistant to healing due to low vascularization, and in joints, may lead to pain and loss of function. The resulting irritation and inflammation of the joint may also be associated with further degeneration and osteoarthritis. Treatments for injured cartilage include arthroscopic removal of damaged cartilage, stimulation of the underlying bone to encourage cartilage growth, injection of chondrocytes to encourage repair, and/or grafts of cartilage from other parts of the joint or from preserved cadaver tissue. Advanced joint degeneration is treated with other approaches, such as the injection of cushioning material (hyaluronic acid), bone shaping to reduce wear and joint replacement.

Injuries suitable for repair using OATS/mosaicplasty often occur in young, athletic individuals. Treatment that allows a continued healthy lifestyle and avoids long term joint damage and eventual more invasive procedures is of great benefit. Though definite causes for osteoarthritis have not been identified, there are indications that minor joint damage followed by years of continuous wear may be the major cause.

**Technology Description:**

Osteochondral Autograft Transfer System surgery is a graft procedure that uses one or more "plugs" of healthy cartilage to fill in damaged areas. It can be done as an open or arthroscopic procedure, and is sometimes combined with other joint operations such as arthroscopic debridement or ACL repair. The grafted cartilage is harvested from another area within the joint, and the harvest site as well as the repair site need to heal properly, so a period of physical therapy is required after the operation.

Osteochondral Allograft Transplant Surgery is a graft procedure similar to Osteochondral Autograft Transfer System, but using graft material from preserved cadaver cartilage. There is some indication that allograft cartilage does not integrate as well, and transplantation involves some risk of infection. However, adequate healthy cartilage tissue is not always available within the joint under repair.

Mosaicplasty is a more generic term that covers either Osteochondral autograft or allograft, open or arthroscopic.

**Issues:**

Significant questions remain about the safety, efficacy and effectiveness, and cost effectiveness of OATS/mosaicplasty cartilage surgery. The choice of suitable patients for OATS/mosaicplasty surgery is controversial because the size and number of damage sites for which it is functional are not well defined, because the harvesting of cartilage from another site or cadaver tissue adds risk and healing issues, and because other, less invasive procedures may be equally effective in the short term (autologous chondrocyte injection). Effectiveness questions particularly center on whether the potential beneficial outcomes of long term pain and functional improvement, prevention of osteoarthritis or further joint deterioration occur with this surgical intervention.

Joseph M. Czerniecki, MD is the Associate Director, of the VA Research Center of Excellence in Limb Loss Prevention and Prosthetic Engineering at Seattle and Professor of Rehabilitation at the University of Washington. He is a clinical specialist in Physical Medicine and Rehabilitation, with a clinical focus in the area of amputee rehabilitation. He has an active ongoing research program, studying many facets of amputee rehabilitation including, the biomechanics of amputee gait and prosthetic components, pain after amputation, and most recently the prediction of outcomes in veterans who are about to undergo amputation secondary to diabetes or vascular disease. He has published over 60 scientific papers.

Washington State Health Care Authority

## Disclosure

Any unmarked topic will be considered a "Yes"

| | Potential Conflict Type | Yes | No |
|---|---|---|---|
| 1. | Salary or payments such as consulting fees or honoraria in excess of $10,000 | | x |
| 2. | Equity interests such as stocks, stock options or other ownership interests | | x |
| 3. | Status or position as an officer, board member, trustee, owner | | x |
| 4. | Loan or intellectual property rights | | x |
| 5. | Research funding | | x |
| 6. | Any other relationship, including travel arrangements | | x |

If yes, list name of organizations that relationship(s) are with and for #6, describe other relationship:

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| | Potential Conflict Type | Yes | No |
|---|---|---|---|
| 7. | Representation: if representing a person or organization, include the name and funding sources (e.g. member dues, governmental/taxes, commercial products or services, grants from industry or government). | | x |

7. If yes, Provide Name and Funding Sources: _____

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If you believe that you do not have a conflict but are concerned that it may appear that you do, you may ***attach additional sheets*** explaining why you believe that you should not be excluded.

**I certify that I have read and understand this Conflict of Interest Form and that the information I have provided is true, complete, and correct as of this date.**

X [redacted] Oct 12, 2011 Joseph A. Czerwiecki

*Date* *Print Name*

**FOR QUESTIONS:** Denise Santoyo, Health Care Authority, 360-923-2742,
PO Box 42712, Olympia, WA 98504-2712

Rev. July 2011

# CURRICULUM VITAE


**Name** Joseph M. Czerniecki, M.D.

**Date of Birth** August 19, 1953

**Place of Birth** Nelson, British Columbia, Canada

**Current Address** 4232 Bagley Ave. N.
Seattle, Washington 98103

**Telephone**
(206) 277-1812 (Work)


## Undergraduate Education

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|---|---|
| 1971-1975 | Bachelor of Science in Rehabilitation (Physical Therapy and Occupational Therapy) University of British Columbia, Vancouver, B.C. |

## Medical School

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| 1977-1981 | M.D., University of British Columbia, Vancouver, B.C. |

## Post Graduate Training

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| 1981-1982 | Internal Medicine Internship, University of Toronto, Sunnybrook Medical Centre, Toronto |
| 1982-1985 | Residency Training in Physical Medicine and Rehabilitation Medicine University of Washington, Seattle, WA |
| 1985 | Masters of Science, University of Washington, Seattle, WA<br>Thesis Entitled: An Electrogoniometric Analysis of Rotational Motion at the Knee in Normal Subjects and those with Anterior Cruciate Ligament Injury |
| 1985-1986 | Research Fellowship, Department of Rehabilitation Medicine University of Washington, Seattle, WA |

## Faculty Appointments

| | |
|---|---|
| July '86-Feb '89 | Acting Assistant Professor, Dept. of Rehabilitation Medicine<br>University of Washington, Seattle, WA |
| Feb '89-July '95 | Assistant Professor, Dept. of Rehabilitation Medicine<br>University of Washington, Seattle, WA |
| July ’90-Present | Member, Graduate Faculty<br>University of Washington, Seattle, WA |
| July '95-July ‘03 | Associate Professor, Department of Rehabilitation Medicine<br>University of Washington, Seattle, WA |
| July ’03-Present | Professor, Department of Rehabilitation Medicine<br>University of Washington, Seattle, WA |

**Hospital Appointments**

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|---|---|
| July '86-July‘04 | Attending Physician, STAMP/PACT Service, Physical Medicine and Rehabilitation Medicine Service, Seattle V.A. Medical Center, Seattle, WA |
| July '88-July‘07 | Director, Motion Analysis Laboratory, Seattle VA Medical Center, Seattle, WA |
| July '88-Present | Director, VA Regional Amputee Clinic |
| July '88-Present | Associate Medical Staff, Harborview Medical Center |
| July '88-Present | Associate Medical Staff, University of Washington Medical Center |
| July '88- July'92 | Attending Physician, University Hospital Child Myoelectric Clinic |
| Feb '91- Dec '93 | Co-Director, STAMP (Special Team for Amputation, Mobility & Prosthetics/Orthotics), Seattle VA Medical Center, Seattle WA |
| Dec '93-July‘04 | Co-Director PACT Program (Preservation Amputation Care Team), Seattle VA Medical Center, Seattle WA |
| May '95-Jan'97 | Director Outpatient Clinics, Physical Medicine and Rehabilitation Service, Seattle VA Medical Center, Seattle WA |
| Jan '97- Jan’99 | Director Electrodiagnostic Services, Physical Medicine and Rehabilitation Service, Seattle VA Medical Center, Seattle WA |

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| Aug'05–May'10 | Director of Rehabilitation Care Service Line, VA Puget Sound Health Care System, Seattle WA |

**Academic Honors Scholarships**

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| 1971 | Norman A. MacKenzie Scholarship |
| 1978 | Dr. and Mrs. S. Schaffer Memorial Scholarship |
| 1979 | Cornelius Leonard Mitchell Scholarship |
| 1980 | Samuel Diamond Scholarship |
| 1981 | Peter Bain Scholarship Dr. and Mrs. J. Nemetz Memorial Scholarship |
| 1989 | Teacher of the Year, Dept of Rehabilitation Medicine<br>University of Washington, Seattle, WA |
| 1992 | Physical Medicine and Rehabilitation, Education and Research Foundation Award<br>Best publication by a Physiatrist in 1992 (role: co-author)<br><br>Gitter A., **Czerniecki JM**, DeGroot DM; Biomechanical Analysis of the Influence of Prosthetic Feet on Below Knee Amputee Walking. *American Journal of Physical Medicine and Rehabilitation*, 70(3):142-148, 1991. |
| 1994 | Teacher of the Year, Dept. of Rehabilitation Medicine<br>University of Washington, Seattle, WA |
| 1996 | Physical Medicine and Rehabilitation, Education and Research Foundation Award<br>Best publication by a Physiatrist in 1996 (role: co-author)<br><br>Gitter A., **Czerniecki JM**, Weaver K; A Reassessment of Center of Mass Dynamics as a Determinant of the Metabolic Inefficiency of Above Knee Amputee Ambulation. *American Journal of Physical Medicine and Rehabilitation*, 74(5):332-338, 1995. |
| 2003 | Visiting Professor, University of Geneva, Geneva, Switzerland |
| 2004 | Visiting Professor, Dalhousie University, Halifax Canada.<br>Presented the Arthur H. Shears Lectureship "Critical Issues in the Rehabilitation of People with Amputations". |

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| 2006 | Professional Achievement of the Year Award, awarded by the Amputee Coalition of America. |
| 2009 | Visiting Professor, University of Colorado, Denver Colorado, Gersten Lectureship "Innovations in Lower Extremity Amputee Rehabilitation and Prosthetic Technology: The near term and more distant horizon". |
| 2011 | 2010 Ernest W. Johnson / AAP Excellence in Research Writing Award honorable mention winner. (role: senior author) |
| | Morgenroth D, Orendurff M, Shakir A, Segal A, Schofer J. **Czerniecki JM**; "The Relationship Between Lumbar Spine Kinematics during Gait and Low-Back Pain in Transfemoral Amputees". published in the August 2010 issue of the American Journal of Physical Medicine & Rehabilitation. |

**Specialty Board Status**

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| 1986 | Fellow of the Royal College of Physicians (Canada)<br>Physical Medicine and Rehabilitation |
| 1987 | American Board of Physical Medicine and Rehabilitation |
| 1988 | American Board of Electrodiagnostic Medicine |

**Medical Licensure**

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| 1982 - Present | Washington State Medical License |

**Professional Membership**

American Academy of Physical Medicine & Rehabilitation

Royal College of Physicians (Canada)

**Teaching Responsibilities**

*Courses*

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| 1986 – Present | Rehab 685/687 Chronic Disease and Disability<br>Four times/ year two week clinical rotation for medical students |

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| 1986-1994 | Rehab 529 Prosthetic Orthotic Conference<br>Bi-monthly clinical/didactic case centered conference on amputation related issues. |
| 1986-1988 | Ortho 585 Sports Medicine for Medical Students<br>2-3 lectures on biomechanics in sports medicine |
| 1987-1994 | Rehab 654 Medical Student Introduction to Rehabilitation Medicine<br>2 hour lecture in this course to introduce medical students to issues related to amputation prevention and amputation rehabilitation |
| 1988-1991 | ICM II Introduction to Clinical Medicine II<br>I provided a single 2 hour lecture in this course |
| 1986-1991 | Hubio 553 Medical Student Anatomy<br>One quarter per year of Anatomy Lab supervision. This involved approximately 28 hours of involvement in a quarter. |
| 1987-1992 | Rehab 445 Therapy Students Anatomy<br>One quarter per year three lectures and 3 hrs of anatomy lab participation |
| 1987-1992 | Rehab 545 Rehabilitation Medicine Resident Anatomy Course<br>One quarter per year three lectures and anatomy lab participation. |
| 1993-1997 | Rehab 442 Advanced Clinical Kinesiology and Biomechanics<br>Co-course chair complete redesign of course and administrative responsibility for the course as well as 3-4 lectures in the quarter. |
| 1995-2008 | Rehab 593 Principles of Prosthetic Use in Rehabilitation<br>Designed a new course for 3rd year Rehab Residents consisting of 11 lectures in a quarter. Full administrative responsibility and ½ of the lectures. Development of the course to include Web based materials. |
| 1998 | Chair Educational Symposium. Biomechanics of Prosthetic Components. *American Academy of PM&R Meeting*, Seattle. |
| 2001 | Chair Educational Course. Post Amputation Pain Syndromes and their Management. *American Academy of PM&R Meeting*, New Orleans. |
| 2001 | Co-chair. Department of Rehabilitation Medicine, University of Washington Review Course. Coordinated all aspects of this 10 day review course. |

*Local CME Lectures*

1. Patient Factors that Influence Prosthetic Fitting. Presented at 5th Annual Physical Medicine Short Course, Tacoma, Washington, March 1988.

2. Vocational Aspects of Amputation Rehabilitation, Presented at, Medical Aspects of Severe Disability for Vocational Rehabilitation Councilors, Seattle, Washington, 1988.

3. The Role of Rehabilitation Medicine in the Pre-Operative Evaluation of the Amputee Patient. STAMP, Continuing Education Course, Seattle, Washington, June 1988.

4. A Comparison of the Energy Generation Absorption Characteristics of Energy Storing Prosthetic Feet. STAMP, Continuing Education Course, Seattle, Washington, June 1988.

5. Gait Analysis in the Evaluation of Energy Storing Prosthetic Feet. Presented at STAMP Continuing Education Course, Seattle, Washington, April, 1989.

6. Phantom Limb Pain a Rehabilitation Perspective. Presented at University of Washington, Pain Service Grand Rounds, Seattle, Washington, August, 1989.

7. Energy Storing Prosthetic Feet: A Critical Review of the Literature, Presented at STAMP Regional Continuing Education Course, Seattle, Washington, March 1990.

8. Vocational Aspects of Amputation Rehabilitation, Presented at Medical Aspects of Severe Disability for Vocational Rehabilitation Counselors, Seattle, Washington, May 1990.

9. The Management of Amputations: An Update, Highline Hospital Continuing Medical Education series, March 29, 1991.

10. Metabolic issues that impact the rehabilitation care of the amputee. Presented at the Northwest Chapter of the American Academy of Orthotists Prosthetists Meeting, Seattle, WA, September, 1996.

11. The role of exercise in low back pain. Presented at Rheumatology Research Rounds University of Washington, Seattle, WA, June, 1997.

12. The etiology and clinical features of phantom limb phenomona. Presented at Rehabilitation Medicine Grand Rounds, University of Washington, Seattle, WA, March 1999.

13. Americans with Disabilities Ready for the Global Workforce, The role of the VAPSHCS Polytrauma Program. Seattle, October, 2006.

14. Amputee Rehabilitation Expanding function and Quality of Life. University of Washington, Minimed School Program. February, 2007.

15. Rehabilitation of the Combat Injured Amputee. Seattle, February, 2007.

*National CME Lectures*

1. The Impact of Energy Storing Prosthetic Feet on Below Knee Amputee Gait. Presented at the 67th Annual Session of the American Academy of Physical Medicine and Rehabilitation, October 1990.

2. Early Post Operative Care of the Lower Extremity Amputee, Presented at the 13th Annual University of Washington Physical Medicine and Rehabilitation Review Course, Seattle, Washington, April 1990.

3. Late Post Operative Care of the Lower Extremity Amputee, Presented at the 13th Annual University Physical Medicine and Rehabilitation Review Course, Seattle, Washington, April, 1990.

4. Upper Extremity Orthotics. Presented at 14th Annual Physical Medicine and Rehabilitation Review Course, Bellevue, Washington, April 1991.

5. Upper Extremity Prosthetics. Presented at 14th Annual Physical Medicine and Rehabilitation Review Course, Bellevue, Washington, April 1991.

6. Lower Extremity Amputations, Preoperative and Post Operative Management. Presented at 14th Annual Physical Medicine and Rehabilitation Review Course, Bellevue, Washington, April 1991.

7. Normal Kinematic, Kinetic and Electromyographic Analysis of Human Walking. Presented at 15th Annual Physical Medicine and Rehabilitation Review Course, Bellevue, WA, March 1992

8. Prosthetic Prescription in the Below Knee Amputee. Presented at 15th and 16th Annual Physical Medicine and Rehabilitation Review Courses, Bellevue, WA, March, 1992-1993

9. Prevention of amputation through an understanding of the pathophysiology and management of the diabetic foot. Presented at 15th and 16th Annual Physical Medicine and Rehabilitation Review Course, Bellevue, WA, March, 1992-1993

10. The role of Rehabilitation Medicine in the preoperative evaluation of the patient pending amputation. Presented at 15th and 16th Annual Physical Medicine and Rehabilitation Review Course, Bellevue, WA, March, 1992-1993.

11. Unique characteristics of amputee rehabilitation in the VA Health Care System. Presented at the *Association of Rehabilitation Nurses Educational Conference*. Seattle, WA, October, 1996.

12. Pathomechanics of Amputee Gait Patterns. VA *Orthotist/Prosthetist National Training Program*. Indianapolis, Indiana, July 1996.

13. The metabolic costs of amputee ambulation. Presented at the University of Washington Physical Medicine and Rehabilitation Review Course, Seattle, WA, March, 1996.

14. Prosthetic alignment in the below knee amputee. Presented at the University of Washington, Physical Medicine and Rehabilitation Review Course, Seattle, WA, March, 1996.

15. Phantom limb pain; theoretical and clinical considerations. Presented at *Neurosciences Grand Rounds*, University of Calgary, Calgary Alberta January 1997.

16. The normal function of the ankle plantarflexors; Implications for Prosthetic development. Presented at Northwest Chapter American Academy of Orthotists Prosthetists, Portland, Oregon. October, 1997.

17. Diabetes as a risk factor for amputation. Presented at the 18th University of Washington Review Course in Physical Medicine and Rehabilitation, Seattle, WA, March, 1999.

18. Post Amputation Pain Syndromes and their management. Presented at the 18th University of Washington Review Course in Physical Medicine and Rehabilitation, Seattle, WA, March, 1999.

19. The metabolic costs of ambulation after lower extremity amputation. Presented at the 18th University of Washington Review Course in Physical Medicine and Rehabilitation, Seattle, WA, March, 1999.

20. Diabetes as a risk factor for amputation. Presented at the 19th University of Washington Review Course in Physical Medicine and Rehabilitation, Seattle, WA, March, 2001.

21. Post Amputation Pain Syndromes and their management. Presented at the 19th University of Washington Review Course in Physical Medicine and Rehabilitation, Seattle, WA, March, 2001.

22. Low Back Pain in the transfemoral amputee: evaluation and management. Presented at Orthopedic Rounds, University of Geneva, Geneva, Switzerland, March, 2003

23. The evaluation of pain in the amputee. Presented at Orthopedic Rounds, University of Geneva, Geneva, Switzerland. March 2003.

24. Pain after Lower Extremity Amputation. Presented at the Lower Extremity Amputee Workshop. Halifax, Canada. October, 2004.

25. The Metabolic Costs of Amputee Ambulation: Functional Significance and Therapeutic Interventions. Keynote Address at the Lower Extremity Amputee Workshop, Halifax, Canada. October, 2004.

26. Amputation Care within the VA Health Care System. American Academy of Physical Medicine and Rehabilitation Meeting, Philadelphia, Pennsylvania, October, 2005.

27. Amputation Rehabilitation: The provision of care throughout the lifespan of the amputee. American Academy of Physical Medicine and Rehabilitation Meeting, Philadelphia Pennsylvania, October, 2005.

28. Amputee Rehabilitation: Current treatment and new research directions. War Illness and Injuries Study Center, New Jersey, May, 2006

29. VAPSHCS Polytrauma Network Site: Development and Implementation, National Polytrauma Care Meeting, Las Vegas, NV, August, 2006.

30. Aging with an amputation; challenges and issues. National Veterans Administration Amputation Conference, Tampa, FL, Dec, 2007

31. The effect of Microprocessor Controlled Knees on the metabolic costs and biomechanics of Transfemoral Amputee Gait, AAOPA meeting, Atlanta, March, 2009.

32. VA National Amputation System of Care, VISN 3 Regional Amputation Conference, Bronx, NY, March 2010.

33. VA / DoD, L/E Amputation Clinical Practice Guidelines:Development and Utility, in Patient Care, VISN 3 Regional Amputation Conference, Bronx, NY, March 2010.

34. VA National Amputation System of Care, VISN 20 Regional Amputation Conference, Seattle WA, July 2010.

35. VA / DoD Lower Extremity Clinical Practice Guidelines: Development and Utility in Patient Care, Seattle WA, July 2010.

36. The Utilization of the VA/DoD Lower Extremity Clinical Practice Guidelines, CARF International Webinar, Seattle, October 2010.

*Graduate Students Supervised*

1. Samuel Bierner, MD, Masters of Rehabilitation Medicine June 1988, Thesis entitled: "Phantom Pain: Status Questionis" Role: Chairman of Committee.

2. Ib Odderson, MD, Masters of Rehabilitation Medicine June 1988, Thesis entitled: "RSD in an Amputee: Case Study" Role: Chairman of Committee

3. David Smithson, MD, Masters of Rehabilitation Medicine.Sept. 1989, Thesis entitled: "The Role of Flexion vs Extension Exercises in Low Back Pain". Role: Chairman of Committee

4. Margaret Forgette, MD, Masters of Rehabilitation Medicine, June, 1989. Thesis entitled: "Reflex Sympathetic Dystrophy in a Child, A single subject study design of the Role of Calcium Channel Blockers". Role: Member of Committee.

5. Jonathan Ritson, MD, Masters of Rehabilitation Medicine. Sept. 1989, Thesis entitled: "Trapezius Palsy and Arm Abduction in the Scapular Plane: A Biomechanical and Electromyographic Analysis." Role: Member of Committee.

6. Brooke Greiner, Masters of Science in Occupational Therapy, Thesis entitled: "A Biomechanical Analysis of the Posture Control Walker on Cerebral Palsy Gait." Role: Member of Committee.

7. Terry Parsons, MD, Masters of Rehabilitation Medicine, Sept. 1992, Thesis entitled: "Use of lumbo-sacral orthoses in the treatment of painful conditions of the lumbar spine." Role: Chairman of Committee.

8. James Beck, Masters of Science in Engineering, March 1993, Thesis entitled: A computer modeling approach to the optimization of prosthetic shank mass". Role: Principal Preceptor, Member of Committee.

9. Raymond Villalobos, MD, Masters of Rehabilitation Medicine, July 1993, Thesis entitled:" Fibrillation potentials and prolonged post-synaptic neuromuscular blockade with curare analogs: Case report and literature review". Role: Chairman of Committee.

10. Mary Zdrojewski, MD, Masters of Rehabilitation Medicine, July 1994, Thesis entitled: Is the self-selected walking speed of AK amputee ambulation their most efficient. Role Chairman of Committee.

11. Heather Kroll, MD, Masters of Rehabilitation Medicine, July 1998,Thesis entitled: The cardinal events in the initiation of Gait. Role: Chairman of Committee.

12. Brian Hafner, PhD Bioengineering. Thesis: Alterations in limb stiffness with changes in prosthetic foot stiffness. Role: Member of Dissertation committee. Completed 2002.

13. Jocelyn Berge, MSc Bioengineering. Thesis: Evaluation of impact absorbing prosthetic pylons. Role: Chair Thesis Committee. Completed March 2002

14. Greg Darlington, MSc Mechanical Engineering. Thesis: Development of an upper limb assistive robot for individuals with hemiparesis. Role: Member of Thesis Committee/Principal Preceptor. July 2000 Not Active.

15. Eric Baker, MSc Medical Engineering. Thesis; Development of a novel in shoe orthotic system. Role: Member of Thesis Committee/Principal Preceptor. November 2000,

16. Dan Norvell, PhD Epidemiology. Thesis: Knee Pain and Osteoarthritis in Veterans with Lower Extremity Amputations: A Retrospective Cohort Study. Role: Member of Dissertation Committee Completed July 2003.

17. Dan Ferris, PhD Post Doc Biorobotics: Co-Principal Preceptor with Blake Hannaford Electrical Engineering. The Use of Artificial Muscle Actuators in Lower Extremity Orthoses and their effect on Motor Control Strategies. Mentor, Completed July 2001.

18. Joel Perry, MSc in Mechanical Engineering. Thesis: The development of Actuator and Control System to reduce mechanical impacts during gait. Role: Member of Thesis Committee. Completed October 2003.

19. David Morgenroth, MD. K12 Research Fellowship. Rehabilitation Medicine Scientist Training Program. Grant Number. K12HD01097. Biomechanical Loading and Knee Degenerative Changes in Transfemoral Amputees. August 2007 to August 2010.

20. Andrew Sawyers, PhD Candidate, Rehabilitation Sciences, University of Washington, August 2008 to present, Member of Dissertation Committee.

21. David Morgenroth, MD. CDA-2 Awardee. Effect of Prosthetic Foot Stiffness on Intact knee loading in transtibial amputees. October 2010-October 2015.

**Editorial Responsibilities**

May '91-Present Ad Hoc manuscript reviewer
Journal of Biomechanics

May '89-Present Ad Hoc manuscript reviewer

Archives of Physical Medicine and Rehabilitation

June '97-July ‘00 Ad Hoc manuscript Reviewer
Clinical Orthopedics and Related Research

July '99-Present Ad Hoc manuscript reviewer
VA Journal of Rehabilitation Research and Development

Aug '00-Mar ‘04 Editorial Board member
Archives of Physical Medicine and Rehabilitation

**Special National Responsibilities**

Apr ‘89-Apr ‘96 Oral Board Examiner
American Board of Electrodiagnostic Medicine

Jan '89-Sept '92 Member, Self-Assessment Examination Subcommittee
American Academy of PM&R

May '92-May ‘02 Guest Oral Board Examiner, American Board of PM&R

June '92 Grant Review Panel Member, Biomedical Engineering to Aid the Disabled, National Science Foundation

March'94-June'95 Study Guide Committee (Prosthetics/Orthotics Section)
American Academy of PM&R

May '94 Grant Review Panel Member, Biomechanics and Rehabilitation, National Science Foundation

Jun '97 - Present Associate Director, VA Rehabilitation Research and Development Center (Limb Loss Prevention and Prosthetic Engineering). A specialized research center of excellence in the Veterans Administration Health Care System.

Mar’99-Jul ‘02 Grant Review Panel Member, NIH Small Business Innovation Research Grant, Rehabilitation Special Emphasis Panel.

Oct’99-Jul ‘01 Question Writer for American Board of PM&R Re-certification Examination

June '01 Invited Participant in a National Conference (Veterans Administration and NIH ) to establish future directions and research priorities for Prosthetic Research.

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| Apr '02-Apr'03 | Member of Executive Committee of the US- ISPO. This is the US division of the International Society of Prosthetics and Orthotics. |
| Oct '03 | Invited Member National VA committee to evaluate and enhance amputee care in the VA Health Care System. |
| June '05 | Invited Member Consensus Conference on the Biomechanics of Prosthetic Feet, sponsored by the American Academy of Orthotists and Prosthetists, Dallas. |
| Sept '04- Jan'08 | VA National Advisory Board for Physical Medicine and Rehabilitation |
| Dec '06 | Invited to participate in a conference to develop international accreditation standards for Amputee Specialty Programs, CARF International, Washington, DC |
| Dec '06 | Participated in a committee to develop clinical practice guidelines for amputation care within the VA health care system, Denver, CO. |
| July '07-present | Member VA National Research Advisory Committee, review and advise on VHA's research portfolio regarding OIF/OEF combat injured. |
| July '07 | NIH grant review panel member, Musculoskeletal Rehabilitation Study Section. Bethesda, MD. |
| Feb'08 – Sept'08 | National Technical Advisory Team, develop and implement a plan for Post Deployment Health Care for returning combat exposed patients. |
| Sept'09 – May'10 | Interim National Director VA Amputation System of Care, |

**Special Local Responsibilities**

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| July '87-July '90 | Member, Advisory and Evaluation Committee for Physical Therapy, University of Washington, Dept of Rehab Medicine |
| Aug '87-July '99 | Departmental Career Advisor<br>University of Washington, School of Medicine |
| July '88-April '89 | Chairman, Committee to Evaluate Residency Training in Musculoskeletal Medicine |
| July '88-July'92 | Member, Standing Committee on Prosthetics and Orthotics Undergraduate Education, University of Washington, Dept of Rehab Medicine |

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| July '89-July '90 | Member, Departmental Physician Search Committee |
| Sept '90-May '93 | Member, Rehabilitation Medicine Quality Improvement Committee, Seattle VA Medical Center |
| July '91-July '92 | Member, Departmental Residency Training Advisory Committee University of Washington, Dept of Rehab Medicine |
| July '91-July '02 | Member, Advisory Committee Medical Rehabilitation Research Training Program,University of Washington, Dept. of Rehab Medicine |
| Dec '91-May '04 | Chair, Credentialing & Privileging Committee Rehab Medicine Service, Seattle VA Medical Center |
| July '92-May '93 | Chair, Committee to Reformulate Kinesiology 442 Course University of Washington, Dept of Rehab Medicine |
| May '93- July '98 | Chair, Rehabilitation Medicine QI Committee Seattle VA Medical Center |
| Mar '95-July '96 | Member, Search Committee, Head of the Division of Prosthetics/Orthotics, Dept of Rehab Medicine, University of Washington |
| Mar '95-Mar'97 | Member, Search Committee, Head of the Division of Physical Therapy, Dept of Rehab Medicine, University of Washington |
| Jan '97- July '03 | Member, Departmental Physician Search Committee |
| July '97-Oct '03 | Member, Standing Committee on Prosthetics and Orthotics Undergraduate Education University of Washington, Dept of Rehab Medicine |
| Oct '97-Oct '01 | Member, Washington State Department of Health, Advisory Committee on Prosthetics and Orthotics |
| Apr '99-Oct '99 | Member, Search Committee, Associate Chief of Staff for Research. VA Puget Sound Health Care System, Seattle Washington |
| Nov '99-July '02 | Member, Veterans Affairs Medical Center, Research and Development Committee |
| Sept '00-Mar'01 | Chair, Department of Rehabilitation Medicine, Physical Medicine and Rehabilitation Review Course |

| | |
|---|---|
| Aug '03-Aug '04 | Member Departmental Graduate School Council, evaluation of need for doctoral program in Physical Therapy |
| May '06-July '07 | Member Search Committee, for the Chair, Department of Rehabilitation Medicine, University of Washington |
| May '09-May'10 | Member VAPSHCS Credentialing and Privileging Committee |
| July '07-Present | Member VAPSHCS Physician Compensation Panel |
| Nov '10-Present | Member VAPSHCS IRB Committee |

**Grant Support**

1. Use of Tri-Axial Electrogoniometer in the Study of the
   Anterior Cruciate Deficient Knee, Associate Grantee
   Co-Grantees: Sigvard Hansen, MD, Frederick Lippert, MD, John Olerud, MD.
   Date: January 1, 1984 - January 1985, Extended to June 1986
   Agency: Orthopedic Research Education Foundation
   Amount: $8,950

2. Clinical Measurement and Modeling of Residual Limb/Prosthetic Socket Interface Forces in Below Knee Amputees.
   Role: Principal Investigator
   Funding Period: Sept.l, 1988 - Sept.l, 1989
   Agency: Whitaker Foundation
   Amount: $58,005

3. Biomechanical Power Output Analysis of Prosthetic Feet
   Role: Co-Investigator
   Funding Period: September 1988 - September 1989
   Amount: $26,000
   Agency: VA Regional Advisory Group Proposal

4. A Metabolic and Biomechanical Analysis of Above Knee Amputee Gait
   Role: Co-Principal Investigator
   Date: October 1990 - October 1992
   Amount: $145,000
   Agency: VA Merit Review

5. Management of Chronic Pain in Rehabilitation, Principal Investigator, Mark Jensen PhD
   Project Title: Management of Chronic Pain in Persons with Amputations
   Role: Co-investigator
   Amount: $2,857,349 Direct Costs
   Funding Period: August 1996 - August 2001

6. RR&D Center for Amputation Prosthetics and Limb Loss Prevention.
   Role: Co-Principal Investigator
   Amount: $3,719,000
   Funding Period: October 1997 - October 2002
   Agency: Veterans Administration, Rehabilitation Research and Development

7. Effect of Motor imbalance on bony deformity and plantar pressure in the foot.
   Role: Co-investigator
   Amount: $231,400
   Date: October 1999 – October 2001
   Agency: Veterans Administration, Merit Review

8. Management of Chronic Pain in Rehabilitation
   Role: Co-investigator 5%, Principal Investigator, Mark Jensen PhD
   Amount: $3,640,609
   Date: Resubmission June 2001
   Agency: NIH

9. Performance of Shock Absorbing Pylons: Laboratory and Clinical Evaluation
   Role: Co-Principal Investigator
   Amount: $287,400
   Date: October, 2000 submission. Funding period Apr 2001- Apr 2004
   Agency: Veterans Administration, Merit Review

10. RR&D Center for Amputation Prosthetics and Limb Loss Prevention.
    Role: Co-Principal Investigator
    Amount: $3,429,000
    Date: Submitted March 2001, Funding Period: Oct. 2002 – Oct. 2007
    Agency: Veterans Administration, Rehabilitation Research and Development

11. A Longitudinal Study of Social Support Following Limb Loss
    Role: Co- Investigator 5%, Principal Investigator Dawn Ehde PhD
    Amount: $325,502
    Date: June, 2000
    Agency: CDC

12. The Effects of Novel Prosthetic Knees on the Function of Veterans with Transfemoral Amputation
    Role: Principal Investigator
    Amount: $100,000
    Agency: VA Merit Review;
    Funding Period Apr 2002- Apr 2004

13. Transtibial Amputation Management Strategies
    Role: Co-Investigator 5%

Amount: $96,000
Agency: VA Merit Review;
Funding Period Oct 2003 – Oct 2005

14. Controlled Plantar Pressure Re-Distribution
Role: Co: Investigator 5%
Principal Investigator: Glenn Klute, PhD
Agency: VA Merit Review;
Funding Period Aug 2004 – July 2005

15. Turning Corners: prosthetic components and stability in amputee gait(A3611I)
Role: Co-investigator 5%
Amount: $487,162
Agency: VA Rehabilitation Research and Development Merit Review
Funding Period: July 2005 – July 2008

16. Controlled plantar pressure re-distribution (A3217P)
Role: Co-investigator 5%
Amount: $45,097
Agency: VA Rehabilitation Research and Development, Pilot Project
Funding Period July 2004-July 2005

17. Vacuum suspension: effect on tissue oxygenation, activity, and fit (A3666I)
Role: Co-investigator 5%
Amount: $719,261
Agency: VA Rehabilitation Research and Development, Merit Review
Funding Period: July 2005-July 2008

18. Ankle equinus and plantar pressure in individuals with diabetes
Role: Principal Investigator
Agency: VA Rehabilitation Research and Development, Merit Review
Amount: $403,440
Funding Period: July 2005-July 2008

19. Functional Outcome Prediction in the Dysvascular/Diabetic Amputee during the Preamputation Period.
Role: Principal Investigator
Agency: VA Rehabilitation Research and Development, Merit Review
Amount: $738,607
Funding Period: April 2006- April 2010

20. RR&D Center for Amputation Prosthetics and Limb Loss Prevention.
Role: Co-Principal Investigator(A4843C)
Amount: $4,750,000
Date: Funding Period: Oct. 2007 – Oct. 2012

Agency: Veterans Administration, Rehabilitation Research and Development

21. Metabolic Cost Savings for Transtibial Amputees Wearing the CESR Foot.
    Role: Principal Investigator
    Agency: VA Rehabilitation Research and Development, Merit Review
    Amount: 749,632
    Funding Period: June 2006 – June 2010

22. Distributed sensing in prosthetic sockets
    Agency: NIH R21
    Role: Consultant
    Amount: $193,454
    Funding Period: February 2008- February 2010

23. Prosthetic Knee-Ankle-Foot System with Biomechatronic Sensing, Control, and Power Generation - (DR081177)
    Agency: DoD – DRMRP
    Role: Co-investigator
    Amount: $8,712,373
    Funding Period: July 2009 – July 2014

24. Ampredict; A prognostic System for Selecting Appropriate Level of Amputation(O7119R)
    Agency: VA Merit Review
    Role: Principal Investigator
    Amount: $995,000
    Funding Period: July 2010 – July 2014

25. Optimizing Stiffness in a Multi-Component Prosthetic Foot
    Agency: VA Merit Review
    Role: Investigator (Mike Hahn, PhD Principal Investigator)
    Amount: $822,142
    Funding Period: Oct 2010 – Sept 2013

26. Prosthetic foot characteristics and Knee osteoarthritis in Amputees
    Agency: VA Career Development
    Role: Mentor (David Morgenroth, MD Career Development Awardee)
    Amount $1,156,250
    Funding Period: Oct 2010 – Sept 2015

*For complete CV (includes bibliography) – please request from HTA program at: shtap@hca.wa.gov*

| OATS - Scheduled Public Comments (5 minutes per presenter) | | | | |
|---|---|---|---|---|
| **#** | **Name** | **Representing** | **COI** | **PPT** |
| 1 | Paul Just, PharmD, BCPS | Smith & Nephew | Yes | Yes |
| 2 | Samir Bhattacharyya, PhD | Depuy Mitek, Johnson & Johnson | Yes | Yes |

Washington State Health Care Authority

## Disclosure

Any unmarked topic will be considered a "Yes"

| | Potential Conflict Type | Yes | No |
|---|---|---|---|
| 1. | Salary or payments such as consulting fees or honoraria in excess of $10,000 | ✓ | |
| 2. | Equity interests such as stocks, stock options or other ownership interests | ✓ | |
| 3. | Status or position as an officer, board member, trustee, owner | | ✓ |
| 4. | Loan or intellectual property rights | | ✓ |
| 5. | Research funding | | ✓ |
| 6. | Any other relationship, including travel arrangements | ✓ | |

If yes, list name of organizations that relationship(s) are with and for #6, describe other relationship:

Employee of Smith & Nephew, Inc., Advanced Surgical Devices

| | Potential Conflict Type | Yes | No |
|---|---|---|---|
| 7. | Representation: if representing a person or organization, include the name and funding sources (e.g. member dues, governmental/taxes, commercial products or services, grants from industry or government). | | |

7. If yes, Provide Name and Funding Sources: _____

If you believe that you do not have a conflict but are concerned that it may appear that you do, you may ***attach additional sheets*** explaining why you believe that you should not be excluded.

**I certify that I have read and understand this Conflict of Interest Form and that the information I have provided is true, complete, and correct as of this date.**

X [redacted] 10/262011 Paul M. Just, PharmD,BCPS

*Signature* *Date* *Print Name*

**FOR QUESTIONS:** Denise Santoyo, Health Care Authority, 360-923-2742,
PO Box 42712, Olympia, WA 98504-2712

# Comments On Spectrum Research's Final Report of a Health Technology Appraisal of Osteochondral Autograft Transplantation (OAT)

Washington State Health Care Authority
Health Technology Clinical Committee
Seattle, WA

November 18, 2011

Paul M. Just, PharmD, BCPS
Director, Healthcare Economics
Advanced Surgical Devices Division
Smith & Nephew, Inc.
Andover, MA

## Overview of the surgical continuum for osteochondral defects

| Category* | Procedure | Result |
|---|---|---|
| Palliative (Temporizing) | • Intraarticular lavage | Not applicable |
| | • Debridement | Not applicable |
| Marrow stimulation (Reparative) | • Abrasion | Fibrocartilage |
| | • Subchondral drilling | Fibrocartilage |
| | • Microfracture | Fibrocartilage |
| Restorative | • OAT | Pure hyaline cartilage |
| | • Mosaicplasty | Pure hyaline cartilage |
| | • ACI | Mixed Type I/II collagen cartilage |
| Replacement | • Total joint | |

*Adapted from Farr, etal, 2004

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## Level I/II Evidence (Level IIb in the report)

- **OAT/MP to ACI**
  - ACI superior to OAT/MP (Bentley)
  - ACI inferior to OAT/MP (Horas)
  - ACI equivalent to OAT/MP (Dozin)
- **OAT/MP to MF**
  - OAT/MP > MF (Gudas, 2005)
  - OAT/MP > MF (Gudas, 2009)
- **ACI to MF** (Knutsen 2004 & 2007)
  - MF = ACI at 2y by clinical outcome / superior humanistic
  - MF = ACI at 5y by clinical outcome / humanistic evaluation

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## Return to sport data

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| Good and excellent repair ratings | |
|---|---|
| Microfracture | 67% ± 7% |
| ACI | 82% ± 7% |
| OAT | 93% ± 5% , P=0.01 to MF |

| Overall return to sports | |
|---|---|
| Microfracture | 66% ± 6% |
| ACI | 67% ± 17% |
| OAT | 91% ± 2%, P=0.01 to MF |

| Time to return to sports | |
|---|---|
| Microfracture | 8 ± 1 months |
| ACI | 18 ± 4 months |
| OAT | 7 ± 2 months |

(Mithoefer etal 2009)

*Although those who do return to sport after ACI have greater "durability", those with OAT are 36% more likely to return to sport and do so on average 11 months sooner.*

The authors stated that the best "durability" was associated with ACI (96% ± 4%) followed by microfracture (52% ± 6%, P=0.079) and OAT (52% ± 21%, P=0.002)

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## Other points of differentiation

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OAT/MP to ACI

- OAT/MP alone results in Type II hyaline cartilage (Radulescu, et.al 2010; Melton & Cossey, 2011)
- NICE ok with MP (Interventional Procedure Guidance 162) but does not recommend ACI (Technology Appraisal Guidance 89)
- ACI is a two-stage procedure (one AS, one open)
- 

| | Clinical/modified | Manual | When |
|---|---|---|---|
| Arthroscopic | 7-10 days | 28 days | Once only for OAT/MP First ACI surgery |
| Open | 21 days | 49 days | Second ACI surgery |

- From: Work Loss Data Institute, 2011, for Knee and Leg Guideline summary NGC-8516

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## Comparing cost ACI and OAT/MP

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- Mosaicplasty costs (corrected) from State Agency Data 1 (p28)
  - 4y average = $11,061 per patient
  - 29 patients in 2010
  - About $310,000 in 2010 (across PEB, L&I and DSHS)
- ACI estimated to cost $20,000 to $30,000 per patient
- Estimated incremental cost for ACI in 30 patients / year
  - $268,000 to $568,000 (double or more present cost)
- Why ACI not MF to replace OAT/MF if coverage denied
  - OAT/MP superior to MF and ACI equivalent to MF
  - ACI equivalent to OAT/MP

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## Summary: Results from prospective RCTs: Microfracture, OAT/MP and ACI

- OAT/MP to ACI RCTs (Dozin & Horas) — about equivalent in 2 prospective
- OAT/MP to ACI (Bentley) — ACI superior in 1 prospective RCT (caveats: too large, proud, rehab issues)
- OAT/MP to MF (Gudas x 2) — OAT/MP superior
- ACI to MF and 5y; (Knutsen) — Clinical OC about equivalent at 2y; Humanistic OC for MF superior

- OAT/MP is superior to microfracture

7

**Paul M. Just, PharmD, BCPS**
**Advanced Surgical Devices Division**
Smith & Nephew, Inc.
150 Minuteman Road
Andover, MA 01810
USA

T 1 978 749 1594
F 1 978 749 1212
paul.just@smith-nephew.com
www.smith-nephew.com

We are smith&nephew

Josh Morse
Program Director, Washington State Health Care Authority
Health Technology Assessment Program
P.O. Box 42712
Olympia, WA 98504-2712

VIA E-MAIL

October 26, 2011

Dear Mr. Morse:

Smith & Nephew, Inc. is a global medical technology business specializing in Orthopaedics (Trauma and Total Joint Reconstruction), Endoscopy and Advanced Wound Management. Smith & Nephew is a global leader in the development and manufacture of devices used in arthroscopic surgery.

We would appreciate your consideration of the following comments on the final Health Technology Assessment (HTA) report on Osteochondral Allograft/Autograft Transplantation (OAT) conducted by Spectrum Research, Inc.

We applaud the fact that Spectrum Research, Inc. has incorporated many of the recommendations we provided in our comments on the draft report to improve the final report's factual accuracy and some of the recommendations to improve the report's balance. Factual accuracy alone is an insufficient element of a critical appraisal. It is the integration of facts into an unbiased analysis reflecting the evolution of medical knowledge that makes for a strong technology appraisal. This latter element appears not universally present in the final report. A reader must be able to easily comprehend without undue distraction the knowledge gained from the past and present body of evidence and how it is integrated into the fabric of everyday patient care decisions. When done well, health care decision makers are best able to objectively assess the most appropriate way to apply the best evidence to make available the highest quality health care for the largest number of patients.

If one accepts the premise identified on page 71 of the final report that case series were not considered because comparative studies of safety and effectiveness were available for autograft procedures, this analysis should be considerably easier to review. It is not. When evaluating therapies, one must reach decisions with the best interests of patients in mind by using the best available evidence. Throughout the final report, the available level I/II prospective randomized controlled trials (RCTs) are repeatedly

referred to as poor quality. It appears that these were considered better evidence than case series and became the *defacto* best quality evidence available.

Therefore, five prospective RCTs (1-5) (final report references 3-7) form the basis of this appraisal and the analyses provided in virtually all relevant systematic reviews presented. Among the latter, authors' interpretations may differ but the source of the data links to the same original trials. The manner in which statements or interpretations from these systematic reviews were selected for inclusion in the final report may influence a reader's perception of the source evidence.

For example, on page 46 of the final report it states, "Some reviews found evidence suggestive of autologous chondrocyte implantation (ACI) being a superior treatment than OAT or mosaicplasty." This statement is referenced by report references 15(6) and 77(7). Both of these references were systematic reviews that included the same evidence evaluated in six other systematic reviews that did not report such a conclusion.(8-13) One might contend that report reference 15 itself does not actually support the statement.

The only prospective RCT to directly conclude ACI was superior to OAT/mosaicplasty (5) was based on application of the latter surgery for large lesions of a size subsequently not recommended for primary treatment with OAT mosaicplasty. The other two prospective RCTs or quasi-RCT comparing OAT/mosaicplasty to ACI did not find ACI to have a clinically superior outcome.(3;4)

Another example of flawed context is found on page 41 of the final report. It states, "However, to date, few comparative studies have examined the efficacy of ACI compared to another treatment." This is misleading because three of the prospective randomized controlled trials, rated level IIb evidence in the report, compared OAT or mosaicplasty to ACI, as described above. Additionally, a level I prospective RCT of ACI to microfracture is unmentioned in the report, but frequently included in systematic reviews of ACI used in the report. Spectrum has taken the position in its response to comments on the draft report that this appraisal is for OAT/mosaicplasty and detail on ACI is not in scope. Nonetheless, the comparisons of OAT/mosaicplasty to ACI are common throughout the report and in point of fact are highly relevant.

When objectively evaluating the role of OAT and mosaicplasty in the treatment of cartilage damage, one must consider the treatment alternatives and the place of OAT/mosaicplasty within the continuum of surgical options. The most reasonable comparative alternatives are microfracture and ACI as described in the literature. Their comparative effectiveness to OAT/mosaicplasty is relevant if the true purpose of this appraisal is to evaluate the role of OAT/mosaicplasty among surgical treatment options for patients with damaged cartilage. Fortunately, level I/II prospective RCTs are available comparing OAT/mosaicplasty to microfracture (1;2) and ACI to microfracture (14;15). A large prospective cohort study is available to evaluate clinical outcomes from microfracture.(16) These last three were not considered in the final report.

Of the three comparisons between OAT/mosaicplasty and ACI, one finds ACI to result in superior outcomes (5), another finds OAT/mosaicplasty to result in superior outcomes (3) and the last finds no

difference in clinical outcomes (4). As mentioned, the study reporting ACI to have superior outcomes was the earliest and used OAT/mosaicplasty for lesion sizes that were larger than are recommended based upon today's knowledge as well containing other methodological challenges (13).

When mosaicplasty was evaluated in a prospective cohort study, the two-year outcome was favorable, however, knee function thereafter deteriorated.(16) In two prospective RCTs comparing OAT/mosaicplasty to microfracture, response to the former was superior (1;2). In a single prospective RCT comparing ACI to microfracture, at two years microfracture was reported to have equivalent clinical outcomes but superior humanistic outcomes (14). At five years clinical outcomes were still equivalent but there was no significant difference in humanistic outcomes (P=0.054) despite microfracture alone having a significant improvement in humanistic outcomes compared to baseline (P <0.001) while ACI did not (P= 0.309) (15).

Comparing clinical outcomes results from prospective RCTs, OAT/mosaicplasty is superior to microfracture (1;2), ACI is equivalent to microfracture (14;15) and two of three studies (3;4) found OAT/mosaicplasty to have no significant outcome difference from ACI. In the only prospective to find ACI superior to OAT/mosaicplasty, the latter surgery is not performed today as a primary treatment for lesions as large as it was used for in that early trial.(5) It appears unreasonable to conclude that ACI offers clinical advantages over OAT/mosaicplasty for cartilage defects of 4 $cm^2$ or smaller. Because OAT/mosaicplasty has superior outcomes over time to microfracture, its use is preferred in many patients.

**What other factors might distinguish OAT/mosaicplasty and ACI?**

Mithoefer etal 2009, provides a systematic review of return to sport in athletes following articular cartilage surgery of the knee.(17) Data from 20 studies reporting on 1363 patients was included. Principal comparisons completed were between microfracture, OAT and ACI (they called it ACT). Good and excellent repair ratings were: Microfracture 67% ± 7%; ACI 82% ± 7%; and OAT 93% ± 5% (P=0.01 to MF). Overall return to sports was: Microfracture 66% ± 6%; ACI 67% ± 17%; and, OAT 91% ± 2% (P=0.01 to MF). Time to return to sports was: Microfracture 8 ± 1 months; ACI 18 ± 4 months; and, OA 7 ± 2 months. The authors stated that the best "durability" was associated with ACI (96% ± 4%) followed by microfracture (52% ± 6%, P=0.079) and OAT (52% ± 21%, P=0.002). (17)

OAT/mosaicplasty is a single stage procedure. If arthroscopy is used as the definitive tool to diagnose cartilage damage, the repair can be immediately completed. ACI, however, is a two-stage procedure requiring an initial arthroscopy for harvesting and an open arthrotomy several weeks later to implant the cultured chondrocytes. According to the Official Disability Guidelines for Knee and leg (Guideline Summary NGC-8516 and reference 68 of the final report), arthroscopic repair of osteochondral defects results in 7-10 days and 28 days of disability, respectively, for clerical/modified and manual work.

For open joint surgery, as required for the second implantation surgery for ACI, disability days are 21 and 49, respectively. Since both procedures require arthroscopy, these latter days of disability are incremental to that of the arthroscopic portion of either surgery. It is unreasonable to ignore the fact that

a second surgery must be performed openly and has increased days of disability. A very reasonable expectation is that these circumstances add cost compared to a single-stage arthroscopic procedure.

After correcting the error in the State Agency Data Table listed on pages 28-29 of the final report, OAT/mosaicplasty is reported to cost about $11,061 per patient. Because ACI costs between $20,000 and $30,000 per patient, a transition to ACI would require an additional $268,000 to $568,000 for 30 patients per year. This is consistent with work showing the surgical costs for ACI to be twice that of mosaicplasty.(18)

While microfracture is a less costly surgery than either OAT/mosaicplasty or ACI, would access to this alone in the absence of OAT/mosaicplasty offer patients a reasonable surgical alternative? It is unlikely because microfracture is considered inferior to OAT/mosaicplasty and ACI in terms of overall response and duration of sustained response. If OAT/mosaicplasty becomes unavailable, surgeons are most likely to replace it with ACI.

Beyond the prospective RCTs alone, the final report details case series documenting the success and safety of OAT/mosaicplasty when used in appropriately selected patients with symptomatic cartilage defects. We urge you to do what is right for patients and continue coverage for OAT and mosaicplasty as safe and effective surgical procedures.

Yours Truly,

Paul M. Just, PharmD, BCPS
Director, Healthcare Economics

Reference List


(1) Gudas R, Kalesinskas RJ, Kimtys V, et al. A prospective randomized clinical study of mosaic osteochondral autologous transplantation versus microfracture for the treatment of osteochondral defects in the knee joint in young athletes. Arthroscopy 2005 Sep;21(9):1066-75.

(2) Gudas R, Simonaityte R, Cekanauskas E, Tamosiunas R. A prospective, randomized clinical study of osteochondral autologous transplantation versus microfracture for the treatment of osteochondritis dissecans in the knee joint in children. J Pediatr Orthop 2009 Oct;29(7):741-8.

(3) Horas U, Pelinkovic D, Herr G, et al. Autologous chondrocyte implantation and osteochondral cylinder transplantation in cartilage repair of the knee joint. A prospective, comparative trial. J Bone Joint Surg Am 2003 Feb;85-A(2):185-92.

(4) Dozin B, Malpeli M, Cancedda R, et al. Comparative evaluation of autologous chondrocyte implantation and mosaicplasty: a multicentered randomized clinical trial. Clin J Sport Med 2005 Jul;15(4):220-6.

(5) Bentley G, Biant LC, Carrington RW, et al. A prospective, randomised comparison of autologous chondrocyte implantation versus mosaicplasty for osteochondral defects in the knee. J Bone Joint Surg Br 2003 Mar;85(2):223-30.

(6) Bekkers JE, Inklaar M, Saris DB. Treatment selection in articular cartilage lesions of the knee: a systematic review. Am J Sports Med 2009 Nov;37 Suppl 1:148S-55S.

(7) Vavken P, Samartzis D. Effectiveness of autologous chondrocyte implantation in cartilage repair of the knee: a systematic review of controlled trials. Osteoarthritis Cartilage 2010 Jun;18(6):857-63.

(8) Harris JD, Brophy RH, Siston RA, Flanigan DC. Treatment of chondral defects in the athlete's knee. Arthroscopy 2010 Jun;26(6):841-52.

(9) Vasiliadis HS, Wasiak J, Salanti G. Autologous chondrocyte implantation for the treatment of cartilage lesions of the knee: a systematic review of randomized studies. Knee Surg Sports Traumatol Arthrosc 2010 Dec;18(12):1645-55.

(10) Nakamura N, Miyama T, Engebretsen L, et al. Cell-based therapy in articular cartilage lesions of the knee. Arthroscopy 2009 May;25(5):531-52.

(11) Magnussen RA, Dunn WR, Carey JL, Spindler KP. Treatment of focal articular cartilage defects in the knee: a systematic review. Clin Orthop Relat Res 2008 Apr;466(4):952-62.

(12) Ruano-Ravina A, Jato DM. Autologous chondrocyte implantation: a systematic review. Osteoarthritis Cartilage 2006 Jan;14(1):47-51.

(13) Safran MR, Seiber K. The evidence for surgical repair of articular cartilage in the knee. J Am Acad Orthop Surg 2010 May;18(5):259-66.

(14) Knutsen G, Engebretsen L, Ludvigsen TC, et al. Autologous chondrocyte implantation compared with microfracture in the knee. A randomized trial. J Bone Joint Surg Am 2004 Mar;86-A(3):455-64.

(15) Knutsen G, Drogset JO, Engebretsen L, et al. A randomized trial comparing autologous chondrocyte implantation with microfracture. Findings at five years. J Bone Joint Surg Am 2007 Oct;89(10):2105-12.

(16) Mithoefer K, Williams RJ, III, Warren RF, et al. The microfracture technique for the treatment of articular cartilage lesions in the knee. A prospective cohort study. J Bone Joint Surg Am 2005 Sep;87(9):1911-20.

(17) Mithoefer K, Hambly K, Della VS, et al. Return to sports participation after articular cartilage repair in the knee: scientific evidence. Am J Sports Med 2009 Nov;37 Suppl 1:167S-76S.

(18) Derrett S, Stokes EA, James M, et al. Cost and health status analysis after autologous chondrocyte implantation and mosaicplasty: a retrospective comparison. Int J Technol Assess Health Care 2005;21(3):359-67.

Washington State
Health Care Authority

## Disclosure

Any unmarked topic will be considered a "Yes"

| | Potential Conflict Type | Yes | No |
|---|---|---|---|
| 1. | Salary or payments such as consulting fees or honoraria in excess of $10,000 | X | |
| 2. | Equity interests such as stocks, stock options or other ownership interests | | X |
| 3. | Status or position as an officer, board member, trustee, owner | | X |
| 4. | Loan or intellectual property rights | | X |
| 5. | Research funding | | X |
| 6. | Any other relationship, including travel arrangements | X | |

If yes, list name of organizations that relationship(s) are with and for #6, describe other relationship:

Salaried employee of DePuy Mitek, A J&J Company. Company pays for travel.

| | Potential Conflict Type | Yes | No |
|---|---|---|---|
| 7. | Representation: if representing a person or organization, include the name and funding sources (e.g. member dues, governmental/taxes, commercial products or services, grants from industry or government). | X | |

7. If yes, Provide Name and Funding Sources:

DePuy Mitek, A Johnson & Johnson Company

If you believe that you do not have a conflict but are concerned that it may appear that you do, you may ***attach additional sheets*** explaining why you believe that you should not be excluded.

**I certify that I have read and understand this Conflict of Interest Form and that the information I have provided is true, complete, and correct as of this date.**

X [redacted]

10.28.11
Date

Samir K. Bhattacharyya
Print Name

FOR QUESTIONS: Denise Santoyo, Health Care Authority, 360-923-2742.
PO Box 42712, Olympia, WA 98504-2712

# *Osteochondral Allograft/Autograpt Transplantation (OATS/Mosaicplasty): Health Technology Review*

*October 2011*

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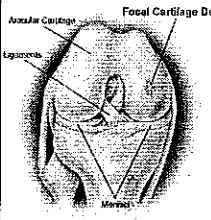
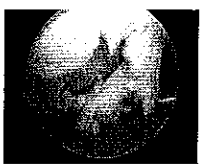
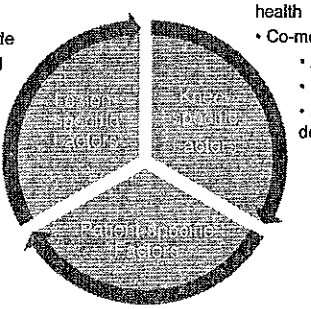
## *Cartilage Damage & Treatment: Multifactorial Decision Making Process*



- Size & shape
- Location
- Classification/Grade
- Depth/subchondral bone involvement
- Containment
- Chronicity
- Prior treatment/response




- Global knee/cartilage health
- Co-morbidities
  - Alignment
  - Ligament stability
  - Meniscal deficiency

- Age
- BMI
- Goals & expectations
- Insurance
- Rehabilitation compliance

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## Unique Role of Osteochondral Allograft and Autograft


| Techniques | Role in Cartilage Repair Paradigm |
|---|---|
| Debridement & Lavage | Palliative option; targets pain relief without structural repair (low activity, older patients) |
| Marrow Stimulation | Single-stage, arthroscopic procedures for focal, contained lesions (1-6 $cm^2$) only |
| Autologous chondrocyte implantation (ACI) | Two-stage, high cost, technically challenging option for second-line repair of larger lesions (2-10 $cm^2$) |
| Osteochondral Autograft | Single-stage option to provide immediate hyaline cartilage repair with bony graft fixation for small (1-4 $cm^2$) contained & uncontained lesions |
| Osteochondral Allograft | Single-stage option to provide immediate hyaline cartilage repair with bony graft fixation for large (3-12 $cm^2$) contained & uncontained lesions, including OCD & AVN |

- Osteochondral autograft and allograft maintain a unique role in the cartilage repair paradigm
  - Only techniques that support treatment of uncontained lesions and restoration of subchondral bone architecture
  - Only techniques that provide immediate defect filling with mature, hyaline cartilage



## Validity and Reliability of 5 Instruments for Measuring Clinically Meaningful Outcomes (Key Question 2)

- HTA concluded **validity** has not been shown for 5 selected clinical measures (ICRS cartilage repair assessment, Lysholm, MCRS, IKDC SKF, and KOOS)
  - Content validity of the IKDC was investigated by Hambly et al (2008) in the target population. The authors concluded that the majority of IKDC items were both important and occurred frequently among the majority of patients. (The HTA did not reference this study.)
  - Construct validity of the IKDC was demonstrated by Irrgang (2001) in a study of over 500 patients with various conditions including ligament, meniscal, OA and cartilage issues.
  - Construct validity of the KOOS was assessed in comparison to the SF-36, EQ-5d, and Lysholm (Bekkers, 2009) in the target population. Moderate correlations were found for all subscales.
  - Construct validity of the Lysholm was confirmed in a study involving 157 patients with cartilage defects (Smith, 2009). After removal of the swelling item via Rasch analysis, a summation of the remaining 7 items was determined to provide a good measure.
- HTA concluded that **reliability** was inadequately tested and **samples were too small** to meet quality criteria

*Reliability*

- IKDC: Irrgang et al (2001) found high levels of internal consistency (coefficient α = .92) and test-retest reliability (assessed over an average of 49.7 days; intraclass correlation coefficient = .95).
- KOOS: In a study of 40 patients with focal cartilage lesions, Bekkers (2009) reported acceptable to excellent test-retest reliability (ICC ranging from .87 to .97), and good internal consistency reliability for all subscales (ranging from .74 to .96).
- Lysholm: Internal consistency was demonstrated to be 0.73 in a study involving 157 patients with cartilage defects (Smith, 2009). There was high agreement between patient and physiotherapists (ICC = .90).

*Sample Size*

- Small sample sizes are irrelevant if analysis results are statistically significant or meet predefined criteria for reliability.

## *Level of Evidence Determination Shows Inconsistencies Between HTA and Other Systematic Reviews*

| | Bentley 2003 | Dozin 2005 | Gudas 2005 | Horas 2003 |
|---|---|---|---|---|
| HTA | IIb | IIb | IIb | IIb |
| Bekkers et al | Ib | IIb | Ib | IIb |
| Magnussen et al | I | - | I | II |
| Ruano-Ravina and Diaz | I | - | - | I |
| Safran and Seiber | I | - | I | II |

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## *OAT Repairs Articular Cartilage Lesions*

"Gudas et all performed a level I prospective randomized controlled study to evaluate treatment with all-arthroscopic OAT versus microfracture.... Patients treated with OAT had significantly better results than did the microfracture group at 1, 2, and 3 years postoperatively according to modified HSS evaluation (P = 0.03, P = 0.006, and P = 0.006, respectively)"

*- Safran and Seiber (2010)*

**TABLE 4 (Gudas 2005).** ***Macroscopic Evaluations on Second-Look Arthroscopy at an Average of 12.4 Months for 33 Patients***

| ICRS Repair Grade | OAT No. (%) | MF No. (%) |
|---|---|---|
| 1 excellent | 7 (50%) | 3 (15%) |
| 2 good | 4 (29%) | 6 (30%) |
| 3 fair | 3 (21%) | 6 (30%) |
| 4 poor | — | 5 (25%) |
| Total | 14 | 20 |

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ICRS: International Cartilage Repair Society
HSS: Hospital for Special Surgery

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## References


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Washington State Health Care Authority

# Agency Medical Director Comments
# Health Technology Clinical Committee
# Osteochrondral Transplant

Dr. Steve Hammond
Medical Director
Department of Corrections
Nov 18, 2011

## Osteochondral Transplantation Background

Several techniques exist for repair of focal, full-thickness chondral defects. Osteochondral autograft/ allograft transplantation techniques have been developed over the past 10-20 years

- Various techniques include transplantation of chondral/subchondral bone plugs, either as single or multiple units or in a larger mosaic pattern of smaller implants
- Implants may be autologous or allogeneic
- Other techniques include bone marrow stimulation/microfracture, chondrocyte transplantation, and debridement
- The evidence base for these techniques is rudimentary, leaving unanswered basic questions such as what technique is most efficacious in which clinical settings



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## Osteochondral Transplantation Background

### AMDG Perspective

Topic concerns

- **Safety = Medium**
  - Paucity of long-term follow-up data
- **Efficacy = High**
  - Poor definition of appropriate indications/case selection
  - Outcome measures not well developed
  - Long-term outcomes not known
- **Cost = Low**
  - Modest costs to WA State agencies
  - Given uncertainties around case selection, potential for overuse or inappropriate application



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## Osteochondral Transplantation Current State Agency Policy

**UMP/PEB Coverage**

Covered

**L&I Coverage**

Covered

**Medicaid Coverage**

- Open procedure covered with prior auth
- Arthroscopic procedure not covered

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## Osteochondral Transplantation Billing Codes

| Related Medical Codes | | |
|---|---|---|
| **Code Type** | **Codes** | **Short Description** |
| Comorbidity | ICD-9 | |
| | 715-715.9 | Osteoarthritis |
| Treatment | CPT | |
| | 27415 | Osteochondral allograft, knee, open |
| | 27416 | Osteochondral autograft(s), knee, open (eg. mosaicplasty) (includes harvesting of autografts) |
| | 29866 | Arthroscopy, knee, surgical; osteochondral autograft(s) (eg. mosaicplasty) (includes harvesting of the autografts) |
| | 29867 | Arthroscopy, knee, surgical; osteo--chrondral allograft (eg mosaicplasty) |

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## Osteochondral Transplantation State Agency Utilization

**Combined Agency Mosaicplasty Costs and Counts, 2007-2010**

| Member/ Clmts | 2007 | 2008 | 2009 | 2010 | 4 yr Total |
|---|---|---|---|---|---|
| **PEB** | 4 | 5 | 5 | 6 | 20 |
| **L&I** | 18 | 17 | 19 | 21 | 73 |
| **Medicaid** | 2 | 2 | 1 | 2 | 7 |
| **All Agencies** | **24** | **24** | **25** | **29** | **100** |
| **Total Amt Paid** | **2007** | **2008** | **2009** | **2010** | **4 yr Total** |
| **PEB** | $36,111 | $78,893 | $115,758 | $72,266 | $303,028 |
| **L&I** | $180,701 | $181,999 | $196,137 | $237,408 | $796,245 |
| **Medicaid** | $11,558 | $13,392 | $3,886 | $90 | $28,926 |
| **All Agencies** | **$228,370** | **$274,284** | **$315,781** | **$309,764** | **$1,128,199** |
| **Avg Pd / Mbr** | **2007** | **2008** | **2009** | **2010** | **4 Year Avg** |
| **PEB** | $9,028 | $15,779 | $23,152 | $12,044 | $10,451 |
| **L&I** | $10,039 | $10,706 | $10,323 | $11,305 | $10,907 |
| **Medicaid** | $5,779 | $6,696 | $3,886 | $45 | $4,132 |
| **All Agencies** | **$9,515** | **$11,429** | **$12,631** | **$10,682** | **$11,282** |

PEB - Public Employee Benefits L&I – Labor and Industry

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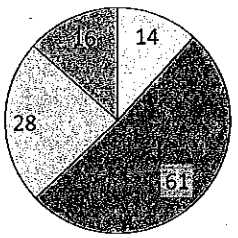
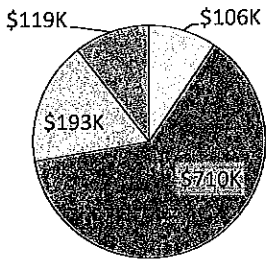
# Osteochondral Transplantation
# State Agency Utilization

**All Agency Mosaicplasty Claim Counts by Procedure Type, 2007 - 2010**




**All Agency Mosaicplasty Claim Payments by Procedure Type, 2007-2010**




Arthroscopic Allograft | Open Allograft | Arthroscopic Autograft | Open Autograft

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# Osteochondral Transplantation
# State Agency Utilization

**All Agency Top 10 Diagnosis Codes, 2007-2010**

| Diagnosis Description | Payment Total | % Total Payments | Claim Count | % Total Claims |
|---|---|---|---|---|
| OSTEOCHONDRIT DISSECANS | $407,860 | 36.2% | 41 | 41.0% |
| ACQ DEFORMITY NEC | $90,104 | 8.0% | 10 | 10.0% |
| BONE & CARTILAGE DIS NEC | $73,789 | 6.5% | 5 | 5.0% |
| OSTEOCHONDROPATHY NOS | $59,277 | 5.3% | 7 | 7.0% |
| CHONDROMALACIA | $49,253 | 4.4% | 7 | 7.0% |
| CHONDROMALACIA PATELLAE | $43,727 | 3.9% | 7 | 7.0% |
| INT DERANGEMENT KNEE NOS | $37,551 | 3.3% | 5 | 5.0% |
| JOINT DIS NOS-L/LEG | $34,614 | 3.1% | 4 | 4.0% |
| DERANGEMENT MENISCUS NEC | $33,385 | 3.0% | 2 | 2.0% |
| SPRAIN OF KNEE LEG NOS | $31,163 | 2.8% | 3 | 3.0% |

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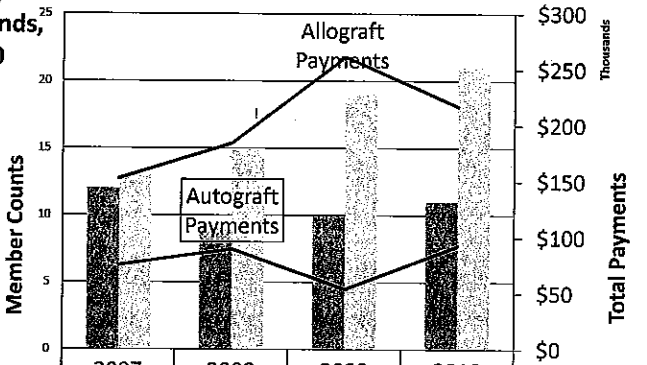
## Osteochondral Transplantation State Agency Utilization

**All Agency Allograft vs Autograft Trends, 2007-2010**




| | 2007 | 2008 | 2009 | 2010 |
|---|---|---|---|---|
| Autograft Count | 12 | 9 | 10 | 11 |
| Allograft Count | 13 | 15 | 19 | 21 |
| Autograft Payments | $75,477 | $89,775 | $54,144 | $92,538 |
| Allograft Payments | $152,893 | $184,509 | $261,637 | $217,226 |



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## Osteochondral Transplantation: Other Centers, Agencies and HTAs

**CMS** – No national coverage decision

**Private Payers** – Variable coverage policies – see tech assessment report



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## Osteochondral Transplantation: Risks & Benefits

**Risks**

Uncertain case selection criteria

No long-term outcomes data

**Benefits**

Some evidence of symptomatic and functional benefit in cases failing conservative management

Evidence of efficacy and effectiveness of osteochondral transplantation is low quality and shows variable outcomes





## Osteochondral Transplantation Summary

**State Agencies Summary View**

- Evolving technology with weak evidence base
- Long-term safety and efficacy uncertain
- Potential for overuse/misuse given lack of consensus on patient- and technique selection criteria

Osteochondral Transplantation

**State Agencies Recommendation**

- Cover, with conditions:
  - Only for knee (and possibly talus)
  - Age <50
  - Absence of arthritis diagnosis
  - Failure of conservative management



Washington State Health Care Authority

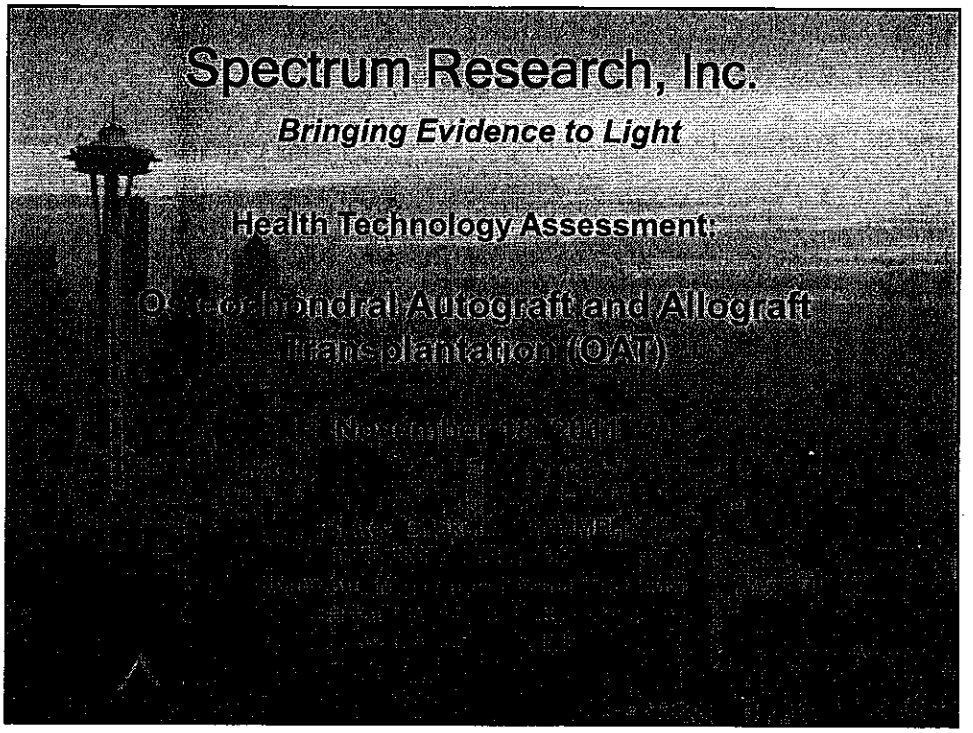
# Questions?

More Information:
http://www.hta.hca.wa.gov/oats.html

Dr. Steve Hammond, Medical Director
Department of Corrections
gshammond@doc1.wa.gov
Tel: 360-555-5555



Washington State Health Care Authority



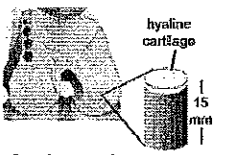

## Scope of Report

Critically summarize research on the efficacy, effectiveness and safety of osteochondral autograft and allograft transplantation (OAT/mosaicplasty) for the treatment of osteochondral defects

The report focuses on the highest quality evidence available based on systematic review of the literature

## Background

- Articular hyaline cartilage
  - Hard, white tissues composed of chondrocytes within an extracellular matrix of collagens, proteoglycans and noncollagenous proteins without intercellular connections
  - Facilitates smooth articulation of bearing surface of synovial joints; resistant to compressive forces
  - Avascular and without nerve supply
- Osteochondral unit
  - Articular surface and underlying cartilage, calcified cartilage, subchondral bone plate and subchondral trabecular bone
  - Vasculature and nerves from subchondral region extend into the calcified cartilage layer

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## Background

- Osteochondral defects
  - Knee arthroscopy series: Chondral lesions/articular cartilage pathology found in >60% of evaluations
  - Causes:
    - Trauma
    - Repetitive microtrauma
    - Osteochondritis dissecans
    - Chondromalacia patellae
  - Natural history, unknown; progression to arthritis suggested in several studies

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# Background

Assessment of Osteochondral defects

- Physical exam
- Diagnostic assessment
  - Plain radiographs: Rule out global OA; check alignment
  - MRI: biological information; size, location, thickness, depth, involvement of bone, meniscus and ligaments; accuracy versus arthroscopy (knee)
  - Diagnostic arthroscopy: structural aspects of the cartilage surface primarily; cannot evaluate bone
  - Combination of MRI and arthroscopy may be used

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SPECTRUM

# Defect Classification - Arthroscopy

| | |
|---|---|
| **Outerbridge Classification** | **Grading system for joint cartilage breakdown:**<br>• **Grade 0 - normal**<br>• **Grade I – cartilage with softening and swelling**<br>• **Grade II – a partial thickness defect with fissures on the surface that do not reach subchondral bone or exceed 1.5 cm in diameter**<br>• **Grade III – fissuring to level of subchondral bone in area with a diameter more >1.5 cm**<br>• **Grade IV – exposed subchondral bone** |
| **International Cartilage Repair Society (ICRS) Classification** | **Grading system for joint cartilage breakdown:**<br>• **Grade 0 – normal**<br>• **Grade 1 – nearly normal:**<br>o **A. Superficial lesions with soft indentation and/or**<br>o **B. Superficial fissures and cracks**<br>• **Grade 2 – abnormal: lesions extending down to <50% of cartilage depth**<br>• **Grade 3 – severely abnormal:**<br>o **A. Cartilage defects extending down >50% of cartilage depth**<br>o **B. As well as down to calcified layer**<br>o **C. Down to but not through the subchondral bone**<br>o **D. Down to but not through the subchondral bone with blisters included**<br>• **Grade 4 – severely abnormal: through the subchondral bone** |

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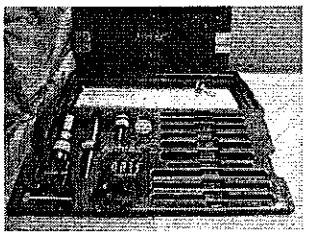
SPECTRUM

## Osteochondral autograft and allograft transplantation

http://www.kneejointsurgery.com/html/articular_cartilage/oats_mosaicplasty.htm



http://www.dotmed.com/listing/o-r-instruments/other/arthrex-oats-set/666863

- OAT, OCA mosaicplasty
- Focus: press-fit dowel, cylindrical or geometric plugs of bone and intact articular cartilage
- **Autograft/autologous** graft: non-weight bearing portion of the joint (knee)
- **Allograft:** fresh or cryopreserved tissue, usually cadaver – (FDA regulation as Human Cell or Tissue Product)
- Arthroscopic or open

SPECTRUM RESEARCH

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## Comparators used in included studies

- Microfracture
  - Following debridement, awl is used to create holes 3-4 mm apart
  - Blood/bone marrow create clot that release cartilage-building cells; repair tissue is mixture of hyaline and fibrocartilage
- Autologous chondrocyte implantation (ACI)
  - 1st procedure: chondrocytes removed arthroscopically from non-weight-bearing area
  - Cells grown *in vitro* for 6 weeks – 10-12 million cells
  - 2nd procedure: periosteal flap applied, injection of the dedifferentiated chondrocytes into defect

SPECTRUM RESEARCH

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## Key Questions

1. What is the case definition of a patient suitable for OATS/mosaicplasty surgery, and are there measures of reliability and validity for case identification?
2. What are the expected treatment outcomes of OATS/mosaicplasty, and are there validated instruments and scores to measure clinically meaningful improvement?
3. What is the evidence of efficacy and effectiveness of OATS/mosaicplasty (open or arthroscopic)?
4. What is the evidence of the safety of OATS surgery?
5. What is the evidence that OATS surgery has differential efficacy or safety issues in sub-populations?
6. What is the evidence of cost implications and cost-effectiveness for OATS/mosaicplasty?

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SPECTRUM RESEARCH

## Scope: Inclusion criteria

- **Population**
  - Persons with cartilage damage
- **Intervention**
  - Osteochondral autograft transplantation (OAT); Osteochondral allograft transplantation (OCA) using dowels, cylinders, plugs; mosaicplasty
- **Comparator**
  - Autologous chondrocyte implantation (ACI); Microfracture surgery
- **Study design**
  - Randomized controlled trials (RCTs),comparative studies with concurrent controls, full economic studies sought
- **Publication**
  - Full-length studies published in English in peer-reviewed journals, FDA reports (no meeting abstracts, proceedings)

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SPECTRUM RESEARCH

## Primary Outcomes (based on available literature)

Efficacy and Effectiveness

- Patient-reported and clinician-based outcomes measures

Safety

- Donor site morbidity (autograft)
- Complications, revision, additional procedures, mortality

Economic

- ICER or similar

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SPECTRUM RESEARCH

## Literature search and overall quality

- Electronic databases, HTA sites were searched using a systematic approach; bibliographic review was done
- Literature search: 332 unique potentially relevant citations, >160 were case series;
- Primary evidence (some studies used for multiple questions)
  - KQ 1: 3 reliability studies
  - KQ 2: 5 psychometric analyses of outcomes measures
  - KQ 3-5: (OAT/mosaicplasty with autograft) -5 RCTs (LoE IIb), 7 cohort studies (LoE III), 15 case series (> 30 patients, safety only)
  - KQ 3-5: (allograft) – 2 cohort studies (LoE III), 6 case series (>18 patients using press fit plugs)
  - KQ 6: No full economic studies were found

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SPECTRUM RESEARCH

## Key Question 1: Case definition, measures of validity and reliability

- No specific case definitions were found
- Treatment algorithms (knee):
  - lesion size and classification (thickness of defect) are used for treatment decision making after ligament and meniscus stability and patient activity determined
- Inclusion/exclusion criteria for RCTs (OAT/MOS):
  - Symptomatic, isolated, full-thickness (ICRS or Outerbridge grades 3 or 4) lesions
- Inclusion/exclusion criteria OCA (dowel) – case series:
  - Symptomatic lesions

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SPECTRUM

## Key Question 1: Case definition, measures of validity and reliability

Treatment algorithm for focal chondral lesions (adapted from Cole, 2009)

| | Femoral Condyle | | | |
|---|---|---|---|---|
| | Lesion size | | Lesion size | |
| | < 2-3 cm² | < 2-3 cm² | > 2-3 cm² | > 2-3 cm² |
| **DEMAND** | High | Low | High | Low |
| **First line treatment** | OAT | OAT | OCA | OAT (possible option)<br>OCA (best option) |
| **Second line treatment** | OCA is an option | | | |

| | Patellofemoral Joint | | | |
|---|---|---|---|---|
| | Lesion size | | Lesion size | |
| | < 2-3 cm² | < 2-3 cm² | > 2-3 cm² | > 2-3 cm² |
| **DEMAND** | High | Low | High | Low |
| **First line treatment** | Neither OAT nor OCA | OAT and OCA possible options | OCA | Neither OAT nor OCA |
| **Second line treatment** | OCA is an option | | | |

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SPECTRUM

**Key Question 1: Case definition, measures of validity and reliability**

## Overall SoE: very low

- No validation studies for primary lesion classification schemes (ICRS, Outerbridge); no studies of clinical decision making specific to OAT/OCA
- Overestimation of lesion size by arthroscopy compared with open evaluation was reported in one clinical study.
- Only one of two clinical studies evaluating the reliability of the ICRS grading system evaluated agreement beyond chance and the agreement was fair to slight.
- One study reported moderate agreement between surgeons in discriminating between Outerbridge grades 2 and 3.

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SPECTRUM RESEARCH

**Key Question 2: Treatment outcomes, validated measures and clinically meaningful improvement**

## Overall SoE: Very low

- Psychometric analyses: persons with osteochondral defects:
  - International Cartilage Repair Society (ICRS) cartilage repair assessment
  - Lysholm Knee Scoring Scale (LKSS)
  - Modified Cincinnati Knee Rating System (MCRS)
  - International Knee Documentation Committee subjective knee form (IKDC SKF)
  - Knee Injury Osteoarthritis Outcome Score (KOOS)
- None adequately tested for validity; reliability inadequate
- Responsiveness evaluated in one study (IKDC, MCRS)
- MCID: pre- to post-op improvement IKDC and MCRS.

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SPECTRUM RESEARCH

## Key Question 3: Efficacy OAT (Autograft) versus Microfracture Patient Reported Outcomes (LoE IIb RCTs)

ICRS (IKDC Subjective Knee Form)

| | Gudas (2005) - Athletes | | | Gudas (2009) - Children | | |
|---|---|---|---|---|---|---|
| | OAT (n = 28 ) | MF (n =29) | | OAT (n=25) | MF (n=22) | |
| | Mean ± SD | | P-value | Mean ± SD | | P-value |
| pre-op | 50.7 ± 4.05 | 50.8 ± 4.07 | NS | 51 | 51 | NS |
| | Mean Change Score (%) | | | Mean Change Score (%) | | |
| 12 mos | 35.2 (69.2) | 24.8 (48.8) | < 0.03 | 41 (80.4) | 35 (68.6) | NR |
| 24 mos | 37.3 (73.6) | 25.2 (47.6) | < 0.001 | 43 (84.3) | 24 (47.1) | NR |
| 36 mos | 38.3 (75.5) | 24.2 (47.6) | < 0.001 | 33 (64.7) | 13 (25.5) | < 0.001 |
| 48 mos | — | — | — | 32 (62.7) | 12 (23.5) | < 0.05 |

Population /lesion characteristics

| | | | |
|---|---|---|---|
| Size: 1 to 4 $cm^2$ | Age: 24.3 years | Size: 2 to 4 $cm^2$ | Age: 14.3 years |
| Number: Single | % Male: 61.4 | Number: Single | % Male: NR |
| Average number plugs: 4.3 | | Average number plugs: 4.7 | |

IKDC MCID = 16.7 point increase at one year post-surgery from pre-surgery levels

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SPECTRUM

## Key Question 3: Efficacy OAT (Autograft) versus Microfracture Clinician Based Outcomes (LoE IIb RCTs)

Hospital for Special Surgery Score

| | Gudas (2005)- Athletes | | |
|---|---|---|---|
| | OAT (n = 28 ) | MF (n =29) | |
| | Mean ± SD | | P value |
| pre-op | 77.9 ± 6.23 | 77.2 ± 8.12 | NS |
| | Mean Change Score (%) | | |
| 12 mos | 10.1 (13.0) | 5.8 (7.5) | < 0.05 |
| 24 mos | 13.1 (16.8) | 4.8 (7.5) | < 0.01 |
| 36 mos | 13.1 (16.9) | 3.4 (4.4) | < 0.01 |

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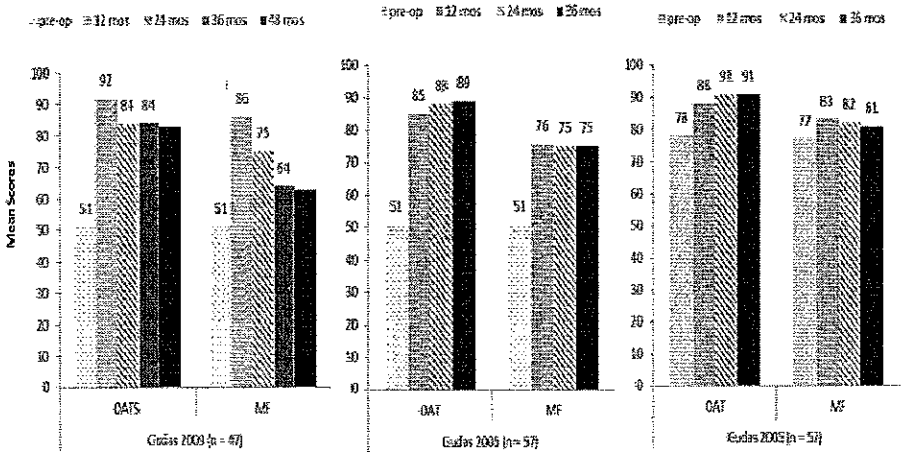
SPECTRUM

## Key Question 1: Efficacy OAT (Autograft) versus Microfracture

**ICRS (IKDC Subjective Form)** | **HSS Score)**




IKDC MCID = 16.7 point increase at one year post-surgery from pre-surgery levels

Excellent: 85-100
Good: 70-84
Fair: 60-69
Poor: <60

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## Key Question 3: Efficacy OAT (Autograft) versus ACI Patient Reported Outcomes (LoE IIb RCTs)

**Horas (2003) (45% had previous surgery)**

| | Lysholm Knee Scoring Scale (LKSS) | | | Tegner Activity Scale (TAS) | | |
|---|---|---|---|---|---|---|
| | OAT (n = 20 ) | ACI (n =20) | | OAT (n = 20 ) | ACI (n =20) | |
| | Mean ± SD | | P-value | Mean ± SD | | P-value |
| pre-op | 28.45 | 24.9 | NS | 1.6 | 1.6 | NS |
| | Mean Change Score (%) | | | Mean Change Score (%) | | |
| 3 mos | -0.5 (-1.8) | 2.65 (10.6) | NR | -0.05 (-3.1) | -0.05 (-3.1) | NS |
| 6 mos | 25 (87.9) | 20.85 (83.7) | ≤ 0.015 | 1.95 (121.9) | 1.35 (84.4) | NS |
| 12 mos | 39.8 (139.9) | 32.6 (130.9) | ≤ 0.001 | 3.4 (212.5) | 2.65 (165.6) | NS |
| 24 mos | 44.25 (155.5) | 41.85 (168.1) | ≤ 0.012 | 3.6 (225.0) | 3.5 (218.8) | NS |

No MCID found

Age 33.4 years old, 57.5% male
Single lesions; size 3.75 cm² (3.2 - 5.6); plugs NR

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## Key Question 3: Efficacy OAT (Autograft) versus ACI
## Patient Reported Outcomes (LoE IIb RCTs)

**Dozin (2005) (only 23/44 randomized were treated)**

**Based on modified LKSS - 12 months**

| | Mosaic (n = 22 ) | ACI (n =22) | P-value |
|---|---|---|---|
| | No. of cases (%) | | |
| Complete success | 15 (68.2) | 10 (45.5) | 0.12 |
| Partial success | 2 (9.1) | 5 (22.7) | |
| Failure | 0 (0) | 1 (4.5) | |
| Loss to follow-up | 5 (22.7) | 6 (27.2) | |

Age: 28.7 years
% male: 61.4%
Lesion: single
Size:1.93 ± 0.03 cm²
Number plugs: NR

**Bentley (2003) (94% had previous surgery)**

**Based on Modified Cincinnati Rating Scale - 12 months**

| | Mosaic (n = 42 ) | ACI (n = 58) | P value |
|---|---|---|---|
| | No. of cases (%) | | |
| Excellent | 9 (21.4) | 23 (39.7) | 0.02 |
| Good | 20 (47.6) | 28 (48.3) | |
| Fair | 6 (14.3) | 7(12.1) | |
| Poor | 7 (16.7) | 0 (0) | |

Age: 31.6 years
% male: 57%
Lesion: NR
Size:4.66 cm² (1-12.2 cm²)
Number plugs: NR

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## Key Question 3: Efficacy OAT (Autograft) versus ACI
## Clinician Based Outcomes (LoE IIb RCTs)

**Horas (2003)**

| | Meyers Score | | |
|---|---|---|---|
| | OAT (n = 20 ) | ACI (n =20) | |
| | Mean ± SD | | P-value |
| pre-op | 7.85 | 7.2 | NS |
| | Mean Change Score (%) | | |
| 3 mos | 0 (0) | 1.3 (18.1) | NS |
| 6 mos | 5.9 (75.2) | 4.85 (67.4) | NS |
| 12 mos | 8.05 (102.5) | 6.95 (96.5) | NS |
| 24 mos | 8.9 (113.4) | 8.7 (120.9) | NS |

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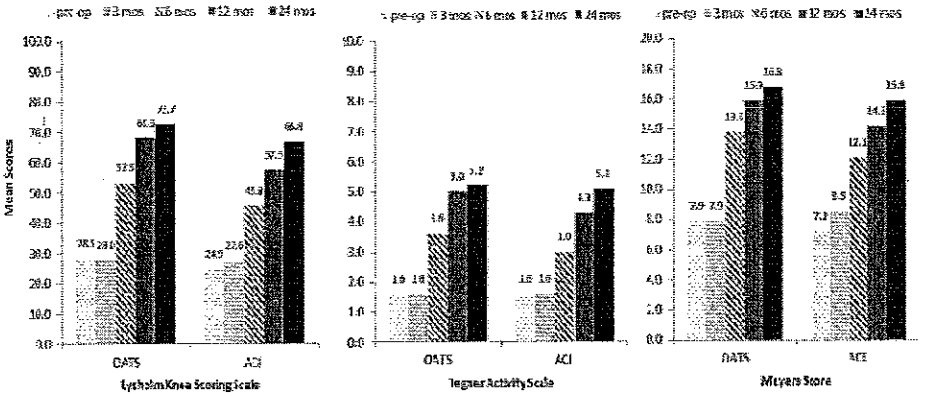
## Key Question 3: Efficacy OAT vs. ACI - Longevity of treatment

Horas (2003) N = 40; LoE IIb




Excellent: 95-100
Good: 84-94
Fair: 65-83
Poor: <65
No MCID

Range: 0-10
10 = competitive sport
0 = sick leave/disability

Excellent: 18
Good: 15-17
Fair: 12-14
Poor: <12

SPECTRUM RESEARCH

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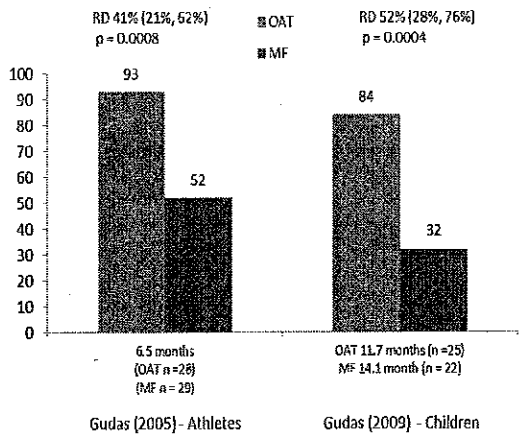
## Key Question 1: Efficacy OAT (Autograft) - Other Outcomes

Return to pre-injury activity




Children at 4.2 years: OAT 81% who achieved pre-injury level practicing at same level vs. 43% of MF

Other outcomes

No direct comparisons

- Open versus arthroscopic
- Allograft versus autograft
- Number of grafts/plugs
- Recovery time

SPECTRUM RESEARCH

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## Summary Key Question 3: OAT (Autograft)

- **OAT versus microfracture – Overall SoE - Low**
  - Two small (LoE IIb) RCTs; one in young athletes, one in children
  - OAT associated with better functional outcomes;overall appeared to be sustained to last follow-up; higher percentage of patients returned to pre-injury sporting activity versus microfrature recipients
- **OAT/mosaicplasty versus ACI – Overall SoE – Low**
  - Three LoE IIb RCTs; significant heterogeneity across studies
  - Two smallest RCTs: Possibly better function with OAT/mosaicplasty based on PROs; statistical significance reached only in one study (LKSS)
  - Largest RCT: 94% had prior intervention; significantly smaller percent of mosaicplasty versus ACI patients had excellent/good outcomes

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## Key Question 3: Effectiveness of Osteochondral allograft (OCA) using OAT-like procedure (dowel, cylindrical or geometric shaped plugs)

- No RCTs comparing OCA to other treatment options were found
- Two poor quality, small retrospective cohort studies (LoE III, total N =70, page 117)
  - One study: Tegner scores significantly improved for OCA compared with loose body removal and internal fixation
  - One study: SF-12 MCS significantly improved in those who had OCA with meniscal allograft compared with those receiving ACI with MA

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SPECTRUM

**Key Question 3: Effectiveness of Osteochondral allograft (OA) using OAT-like procedure (press fit dowel, cylindrical or geometric shaped plugs)**

- Six case series, LoE IV
- Three primarily used dowel, cylindrical or geometric plugs without hardware, three used other types as well (Table 26, page 121)
  - Improved function and quality of life following OCA were reported compared with pre-operative status
  - 91% graft survival rate at 5 years and 76% at both 10 and 15 years reported in one study (N = 65)

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SPECTRUM RESEARCH

**Summary Key Question 3: OCA (Allograft )**

- **Efficacy- No RCTs – no evidence**
- **Effectiveness – Overall SoE – Very Low**
  - Two small poor quality retrospective comparative studies (LoE) reported no differences in most functional measures; confounding by indication
  - Six case series suggest improved outcomes following OCA but in the absence of a comparison group, comparative effectiveness cannot be assessed.

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SPECTRUM RESEARCH

## Key Question 4: Safety – OAT Autograft

Donor site morbidity (DSM)

- Rates: 10% in 2 RCTs
- 6-17% across 3 case series of the knee, 2-9% in 2 studies of ankle, 3% in one study of both sites
- Additional 5 case series specifically examined DSM
  - Young male competitive athletes: no longer-term morbidity in 2 studies (N = 23 total, follow-up 12 - 65 months)
  - Two series (N = 123): LKSS scores suggest that 10.5% (n = 13) of patients experienced poor function (follow-up 25-124 months)
  - Largest series (N=112): number of grafts and size of plugs weren't related to LKSS or WOMAC scores

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SPECTRUM RESEARCH

## Key Question 4: Safety – OAT Autograft

Complication Rates: RCTs

| | Studies | OAT | MF | ACI |
|---|---|---|---|---|
| Reoperation/revision | 3 | 1% (1/53) | 33% (17/51) | 5% (1/20) |
| Evaluation arthroscopy | 2 | 24.5% (13/53) | 47% (24/51) | — |
| | 1 | 20% (4/20) | — | 25% (5/20) |
| Arthroscopic procedures | 2 | 8% (4/48) | 3% (1/29) | — |
| | 1 | 0% | — | 10% (2/20) |
| Donor site morbidity | 2 | 10% (5.48) | — | — |
| Joint stiffness | 2 | 13% (6/48) | 3% (1/29) | 15% (3/20) |
| Infection | 2 | 5.5% (4/73) | 0% | 0% |
| Hemarthrosis | 1 | 10% (2/10) | — | 0% |
| Joint swell/effusion | 2 | 6.6% (3/45) | 45% (10/22) | 15% (3/20) |
| Subchondral cyst | 1 | 8% (2/25 | 33% (7/21) | — |

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SPECTRUM RESEARCH

# Key Question 4: Safety – OAT Autograft

Complication Rates: Non-Randomized studies

| | Studies | N | OAT | Ranges |
|---|---|---|---|---|
| **Reoperation/revision** | 10 | 432 | 21.3% | 0% - 28% |
| **Diagnostic arthroscopy** | 7 | 1328 | 11.4% | 7% - 38% |
| **Arthroscopic debridement** | 2 | 27 | 14.8% | 13% - 16.6% |
| **Donor site morbidity** | 6 | 1360 | 8.8% | 2% -17% |
| **Infection** | 5 | 1366 | 0.9% | 0.4% - 3% |
| **Hemarthrosis** | 5 | 1275 | 5.8% | 2%-44.8% |
| **Joint swell/effusion** | 2 | 70 | 64.3% | 20%-76% |
| **Deep vein thrombosis** | 5 | 1235 | 0.6% | 0.4%-3% |
| **Osteoarthritis progression** | 3 | 98 | 29.6% | 0% -76% |
| **Edema/sclerosis -MRI** | 1 | 27 | 71.0% | |
| **Graft osteonecrosis** | 1 | 55 | 11.0% | |

No deaths reported

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SPECTRUM RESEARCH

# Key Question 4: Safety – Allograft (OCA)

| ALLOGRAFT complication rates: Non-Randomized Studies | | | |
|---|---|---|---|
| | Studies | N | OCA % (n) |
| Reoperation/revision | 7 | 191 | 12.5% (24) |
| Diagnostic arthroscopy | 1 | 23 | 4% (1) |
| Manipulation under anesthesia | 1 | 19 | 5% (1) |
| Infection | 1 | 23 | 4% (1) |
| Graft failure | 2 | 47 | 21% ( 10) |
| Subchondral cysts | 1 | 29 | 17% (5) |

No reports of disease transmission and no reported deaths

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SPECTRUM RESEARCH

**Key Question 4: Safety**
**Summary and Overall Strength of Evidence (SoE)**

## KQ #4: Safety OAT (autograft) – SoE Low

- No deaths reported in studies reviewed
- Infection, DVT, hemarthrosis rates <7%
- Donor site morbidity 10% (RCTs), 3%-17% ( case series)
- Revision rates: 1% for OAT vs. 33% for microfracture, 5% for ACI in RCTs; 21.3% (non-randomized)

## KQ #4: Safety OCA (allograft) – SoE Low

- Non-randomized studies only (primarily case series)
- No deaths or disease transmission reported
- Reoperation rate 12.5% (24/191), graft failure 10/47)

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SPECTRUM RESEARCH

**Key Question 5:**
**Differential outcomes for subpopulations**

Comparisons within RCTs (OAT with autograft)

- **Age**: athletes <30 years old had better outcomes for both OAT and microfracture (MF) (no data)
- **Defect size:** 1 study-comparable functional outcomes for OAT and MF; MF patients with defects > 2cm$^2$ had worse functional outcomes (no data)
- **Defect location** – medial femoral condyle: MF patients had worse outcomes vs. other locations but no association between location and outcomes for OAT patients; greater proportion of ACI patients had excellent/good result versus mosaicplasty recipients

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SPECTRUM RESEARCH

## Key Question 5: Subpopulations
## Summary and Overall Strength of Evidence (SoE)

### KQ #3: Differential efficacy, effectiveness or safety in special populations – SoE- Low

- RCTs - Limited data are provided to truly evaluate differential effectiveness or safety
- Indirect comparisons based on case series cannot provide evidence

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SPECTRUM RESEARCH

## Key Question 6: Cost-effectiveness
## Summary and Overall Strength of Evidence (SoE)

### KQ #6: Cost implications and cost-effectiveness: SoE - no evidence

- No full economic studies were identified

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SPECTRUM RESEARCH

## Observations and remaining questions

- There are substantial differences across studies with respect to patient populations, lesion sizes, comparators and outcomes measures making it difficult to draw overall conclusions.
- Indications for OAT versus mosiacplasty, autograft versus allograft appear to be based on case series primarily.
- The majority of studies are in populations less than 50 years old.
- The overall quality of the literature is poor, particularly with respect to evaluation of allograft.

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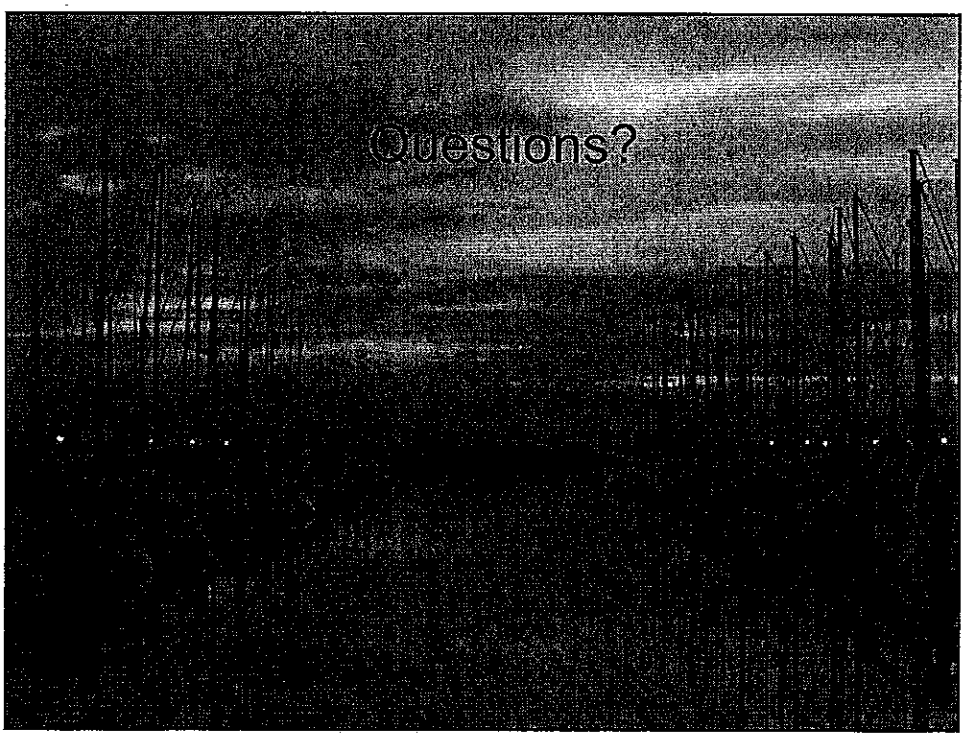

# HTCC Coverage and Reimbursement Determination Analytic Tool

HTA's goal is to achieve *better health care outcomes* for enrollees and beneficiaries of state programs by paying for proven health *technologies that work*.

To find best outcomes and value for the state and the patient, the HTA program focuses on these questions:

1. Is it safe?
2. Is it effective?
3. Does it provide value (improve health outcome)?

The principles HTCC uses to review evidence and make determinations are:

## Principle One: Determinations are Evidence based

HTCC requires scientific evidence that a health technology is safe, effective and cost-effective[1] as expressed by the following standards. [2]

- Persons will experience better health outcomes than if the health technology was not covered and that the benefits outweigh the harms.
- The HTCC emphasizes evidence that directly links the technology with health outcomes. Indirect evidence may be sufficient if it supports the principal links in the analytic framework.
- Although the HTCC acknowledges that subjective judgments do enter into the evaluation of evidence and the weighing of benefits and harms, its recommendations are not based largely on opinion.
- The HTCC is explicit about the scientific evidence relied upon for its determinations.

## Principle Two: Determinations result in health benefit

The outcomes critical to HTCC in making coverage and reimbursement determinations are health benefits and harms.[3]

- In considering potential benefits, the HTCC focuses on absolute reductions in the risk of outcomes that people can feel or care about.
- In considering potential harms, the HTCC examines harms of all types, including physical, psychological, and non-medical harms that may occur sooner or later as a result of the use of the technology.
- Where possible, the HTCC considers the feasibility of future widespread implementation of the technology in making recommendations.
- The HTCC generally takes a population perspective in weighing the magnitude of benefits against the magnitude of harms. In some situations, it may make a determination for a technology with a large potential benefit for a small proportion of the population.
- In assessing net benefits, the HTCC subjectively estimates the indicated population's value for each benefit and harm. When the HTCC judges that the balance of benefits and harms is likely to vary substantially within the population, coverage or reimbursement determinations may be more selective based on the variation.
- The HTCC considers the economic costs of the health technology in making determinations, but costs are the lowest priority.

[1] Based on Legislative mandate: See RCW 70.14.100(2).

[2] The principles and standards are based on USPSTF Principles at: http://www.ahrq.gov/clinic/ajpmsuppl/harris3.htm

[3] The principles and standards are based on USPSTF Principles at: http://www.ahrq.gov/clinic/ajpmsuppl/harris3.htm

## Using Evidence as the basis for a Coverage Decision

Arrive at the coverage decision by identifying for Safety, Effectiveness, and Cost whether (1) evidence is available, (2) the confidence in the evidence, and (3) applicability to decision.

### *1. Availability of Evidence:*

Committee members identify the factors, often referred to as outcomes of interest, that are at issue around safety, effectiveness, and cost. Those deemed key factors are ones that impact the question of whether the particular technology improves health outcomes. Committee members then identify whether and what evidence is available related to each of the key factors.

### *2. Sufficiency of the Evidence:*

Committee members discuss and assess the evidence available and its relevance to the key factors by discussion of the type, quality, and relevance of the evidence[4] using characteristics such as:

- Type of evidence as reported in the technology assessment or other evidence presented to committee (randomized trials, observational studies, case series, expert opinion);
- the amount of evidence (sparse to many number of evidence or events or individuals studied);
- consistency of evidence (results vary or largely similar);
- recency (timeliness of information);
- directness of evidence (link between technology and outcome);
- relevance of evidence (applicability to agency program and clients);
- bias (likelihood of conflict of interest or lack of safeguards).

Sufficiency or insufficiency of the evidence is a judgment of each clinical committee member and correlates closely to the GRADE confidence decision.

| Not Confident | Confident |
|---|---|
| Appreciable uncertainty exists. Further information is needed or further information is likely to change confidence. | Very certain of evidentiary support. Further information is unlikely to change confidence |

### *3. Factors for Consideration - Importance*

At the end of discussion at vote is taken on whether sufficient evidence exists regarding the technology's safety, effectiveness, and cost. The committee must weigh the degree of importance that each particular key factor and the evidence that supports it has to the policy and coverage decision. Valuing the level of importance is factor or outcome specific but most often include, for areas of safety, effectiveness, and cost:

- risk of event occurring;
- the degree of harm associated with risk;
- the number of risks; the burden of the condition;
- burden untreated or treated with alternatives;
- the importance of the outcome (e.g. treatment prevents death vs. relief of symptom);
- the degree of effect (e.g. relief of all, none, or some symptom, duration, etc.);
- value variation based on patient preference.

[4] Based on GRADE recommendation: http://www.gradeworkinggroup.org/FAQ/index.htm

## Medicare Coverage and Guidelines

| Organization | Date | Outcome | Evidence Base | Grade / Rating |
|---|---|---|---|---|
| CMS National Policy Decisions – WA HTA<br><br>Centers for Medicare and Medicaid Services<br><br>Page: 61 | | ▪ The Centers for Medicare and Medicaid Services have no published National coverage determinations (NCD) for osteochondral autograft/allograft transplantation (OATS) or mosaicplasty. | N/A | N/A |
| Guidelines – WA HTA<br>Page: 42<br><br>*American Academy of Orthopaedic Surgeons (AAOS)* | 2009 | *The treatment of glenohumeral joint osteoarthritis: guideline and evidence report (NGC: 007581)*<br><br>AAOS was unable to recommend for or against the use of osteoarticular allograft or autograft for the treatment of glenohumeral arthritis due to lack of studies of sufficient quality. | | |
| Guidelines – WA HTA<br>Page: 42<br><br>*Work Loss Data Institute* | 2008 | *Shoulder (acute & chronic)*<br><br>A summary provided by the NGC indicates that OATS was considered as a treatment for workers with occupational shoulder disorders and not recommended. This guideline is in the process of being updated. | | |
| Guidelines – WA HTA<br>Page: 42<br><br>*Work Loss Data Institute* | 2007 | *Knee & leg (acute & chronic)*<br><br>A summary provided by the NGC indicates that OATS and mosaicplasty were considered as treatments for workers with knee and leg ailments for relieving pain and improving function. OATS was recommended; mosaicplasty was not recommended. This guideline is in the process of being updated. | | |
| Guidelines – WA HTA<br>Page: 42<br><br>*National Institute for Health and Clinical Excellence (NICE)* | | The National Institute for Health and Clinical Excellence (NICE) provides guidance on health technologies and clinical practice for the National Health Service in England and Wales. A variety of keyword searches were performed, including *"osteochondral autograft transfer," "mosaicplasty," "OATS," "chondral OR osteochondral," "allograf" and "Osteochondritis Dissecans."* One guideline was found, *Mosaicplasty for knee cartilage defects 2006*, and is summarized as follows[69]:<br><br>• Current evidence suggests that there are no major safety concerns regarding the use of mosaicplasty for | | |

| Organization | Date | Outcome | Evidence Base | Grade / Rating |
|---|---|---|---|---|
| | | the treatment of knee cartilage defects; however, procedure-related and long-term complications are inadequately reported in studies.<br>• Some evidence exists for short-term efficacy, but data is inadequate regarding long-term efficacy. | | |

## HEALTH TECHNOLOGY EVIDENCE IDENTIFICATION

Discussion Document: What are the key factors and health outcomes and what evidence is there?

| | **Osteochondral Allograft / Autograft Transplantation (OATS)** |
|---|---|
| **Safety Outcomes** | **Safety Evidence** |
| Mortality | |
| Morbidity<br>▪ Rates of Donor Site Morbidity | |
| Surgical Complications | |
| Re-operations | |
| MRI Findings | |
| Progression of Osteoarthritis | |
| Rate of Graft Failure | |
| Disease Transmission from the Donor Tissue | |
| Other Adverse Events | |
| **Efficacy – Effectiveness Outcomes** | **Efficacy / Effectiveness Evidence** |
| Functional Outcomes | |
| Longevity of Treatment Effect | |
| Return to Work or Pre-injury Activity Levels | |
| Differential Results between Open and Arthroscopic Procedures or other factors | |
| Quality of Life | |
| Patient Satisfaction | |
| Other Patient Outcomes | |
| **Special Population / Considerations Outcomes** | **Special Population Evidence** |
| Defect Type | |

| | |
|---|---|
| Defect Location | |
| Sex | |
| Age | |
| Patients with no Prior Surgical Intervention | |
| Patient Selection | |
| Payer or Beneficiary Type | |
| **Cost** | **Cost Evidence** |
| Total Health Care Costs / Societal Costs | |
| Direct and indirect<br>- Short terms<br>- Over expected duration of use | |
| Cost Effectiveness | |

## Clinical Committee Evidence Votes

**First voting question**
The HTCC has reviewed and considered the technology assessment and information provided by the administrator, reports and/or testimony from an advisory group, and submissions or comments from the public. The committee has given greatest weight to the evidence it determined, based on objective factors, to be the most valid and reliable.

**Is there sufficient evidence under some or all situations that the technology is:**

| | **Unproven** (no) | **Equivalent** (yes) | **Less** (yes) | **More** (yes) |
|---|---|---|---|---|
| **Effective** | | | | |
| **Safe** | | | | |
| **Cost-effective** | | | | |

**Discussion**
Based on the evidence vote, the committee may be ready to take a vote on coverage or further discussion may be warranted to understand the differences of opinions or to discuss the implications of the vote on a final coverage decision.

- Evidence is insufficient to make a conclusion about whether the health technology is safe, efficacious, and cost-effective;
- Evidence is sufficient to conclude that the health technology is unsafe, ineffectual, or not cost-effective
- Evidence is sufficient to conclude that the health technology is safe, efficacious, and cost-effective for all indicated conditions;
- Evidence is sufficient to conclude that the health technology is safe, efficacious, and cost-effective for some conditions or in some situations

A straw vote may be taken to determine whether, and in what area, further discussion is necessary.

**Second vote**
Based on the evidence about the technologies' safety, efficacy, and cost-effectiveness, it is

_____Not Covered. _____ Covered Unconditionally. _____ Covered Under Certain Conditions.

**Discussion Item**

Is the determination consistent with identified Medicare decisions and expert guidelines, and if not, what evidence is relied upon.

## Clinical Committee Findings and Decisions

**Next Step: Cover or No Cover**
If not covered, or covered unconditionally, the Chair will instruct staff to write a proposed findings and decision document for review and final adoption at the following meeting.

**Next Step: Cover with Conditions**
If covered with conditions, the Committee will continue discussion.

1) Does the committee have enough information to identify conditions or criteria?
   - Refer to evidence identification document and discussion.
   - Chair will facilitate discussion, and if enough members agree, conditions and/or criteria will be identified and listed.
   - Chair will instruct staff to write a proposed findings and decision document for review and final adoption at next meeting.

2) If not enough or appropriate information, then Chair will facilitate a discussion on the following:
   - What are the known conditions/criteria and evidence state
   - What issues need to be addressed and evidence state

The chair will delegate investigation and return to group based on information and issues identified. Information known but not available or assembled can be gathered by staff ; additional clinical questions may need further research by evidence center or may need ad hoc advisory group; information on agency utilization, similar coverage decisions may need agency or other health plan input; information on current practice in community or beneficiary preference may need further public input. Delegation should include specific instructions on the task, assignment or issue; include a time frame; provide direction on membership or input if a group is to be convened.

***Efficacy Considerations:***

- What is the evidence that use of the technology results in more beneficial, important health outcomes? Consider:
  - Direct outcome or surrogate measure
  - Short term or long term effect
  - Magnitude of effect
  - Impact on pain, functional restoration, quality of life
  - Disease management
- What is the evidence confirming that use of the technology results in a more beneficial outcome, compared to no treatment or placebo treatment?
- What is the evidence confirming that use of the technology results in a more beneficial outcome, compared to alternative treatment?
- What is the evidence of the magnitude of the benefit or the incremental value
- Does the scientific evidence confirm that use of the technology can effectively replace other technologies or is this additive?
- For diagnostic tests, what is the evidence of a diagnostic tests' accuracy
  - Does the use of the technology more accurately identify both those with the condition being evaluated and those without the condition being evaluated?
- Does the use of the technology result in better sensitivity and better specificity?
- Is there a tradeoff in sensitivity and specificity that on balance the diagnostic technology is thought to be more accurate than current diagnostic testing?
- Does use of the test change treatment choices

***Safety***

- What is the evidence of the effect of using the technology on significant morbidity?
    - Frequent adverse effect on health, but unlikely to result in lasting harm or be life-threatening, or;
    - Adverse effect on health that can result in lasting harm or can be life-threatening.
- Other morbidity concerns
- Short term or direct complication versus long term complications
- What is the evidence of using the technology on mortality – does it result in fewer adverse non-fatal outcomes?

***Cost Impact***

- Do the cost analyses show that use of the new technology will result in costs that are greater, equivalent or lower than management without use of the technology?

***Overall***

- What is the evidence about alternatives and comparisons to the alternatives
- Does scientific evidence confirm that use of the technology results in better health outcomes than management without use of the technology?