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TITLE: Vitamin D Supplementation for Prevention of Post-Traumatic Osteoarthritis: Evaluation in Animal and Clinical Models

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Fort Detrick, Maryland 21702-5012

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**Vitamin D Supplementation for Prevention of Post-Traumatic Osteoarthritis: Evaluation in Animal and Clinical Models**

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Next page
Abstract

The goals of this translational study are to create an animal model of joint injury and evaluate the impact of Vitamin D in prevention and progression of PTOA. Concurrently, we will evaluate a clinical cohort of USMA cadets treated for ACL tear, with pre- and post-injury serum 25-hydroxy-Vitamin D levels and correlation with joint space narrowing and biomarkers of cartilage injury. If Vitamin D supplementation can prevent the onset of often rapid joint destruction that occurs with PTOA, this simple, safe, and inexpensive intervention could potentially translate to pre-emptive treatment for high-risk military occupations. In addition, Vitamin D could be used at the time of injury to possibly mitigate ongoing articular cartilage damage.
# Table of Contents

1. Introduction ................................. 4  
2. Keywords .................................. 4  
3. Overall Project Summary ................. 4  
4. Key Research Accomplishments .......... 12  
5. Conclusion ................................ 13  
7. Inventions, Patents and Licenses ......... 13  
8. Reportable Outcomes ...................... 13  
9. Other Achievements ....................... 13  
10. References ................................ 13  
11. Appendices ............................... 14
Introduction

The purpose of this study is to create an animal model of joint injury and evaluate the impact of Vitamin D supplementation in prevention and progression of post-traumatic osteoarthritis (PTOA). Concurrently, this funding supports an add-on study at the United States Military Academy, to evaluate a clinical cohort of USMA cadets treated for anterior cruciate ligament (ACL) tear, with pre- and post-injury serum 25-hydroxy-Vitamin D levels and correlation with joint space narrowing and biomarkers of cartilage injury. If Vitamin D supplementation can prevent the onset of often rapid joint destruction that occurs with PTOA, this simple and safe intervention could potentially translate to pre-emptive treatment in high-risk military occupations. In addition, Vitamin D could be used at the time of injury to possibly mitigate ongoing articular cartilage damage.

Keywords

Murine, post-traumatic osteoarthritis, military, ACL, knee, medial meniscus, femoral, tibial, 25-hydroxy-Vitamin D, supplementation

Overall Project Summary

This report represents the second annual summary of work for the 2015-16 year of funding for this project. Reporting will be organized by task as noted in the Statement of Work.

Specific Aim 1: to evaluate the impact of systemic Vitamin D supplementation on the initiation and development of surgically induced OA in a murine model

Objectives: Vitamin D Supplementation and Rodent Surgery
Imaging/Tissue Analysis of Surgical Model

Progress

- We have completed the all three rounds of animal experimentation with C57-BL6 mice fed to supplement with four levels of Vitamin D:
  - control (1.5 IU/kg - minimal Vitamin D)
  - 1500 IU/kg (normal dietary level of Vitamin D)
  - 5000 IU/kg
  - 10,000 IU/kg
- A total of 300 mice underwent surgical initiation of osteoarthritis using destabilization of the medial meniscus and MCL sectioning. Small subgroups were treated with anterior cruciate ligament (ACL) sectioning to evaluate the degree of osteoarthritis induction.
- We changed the timepoints to evaluate mice at 8, 12, 16, and 20 weeks as we noted minimal induction of osteoarthritis at 4 and 8 weeks.
- Initial testing using mouse Vitamin D ELISA confirmed graduated levels of Vitamin D in the sera of treated mice groups.
We then performed histology, faxitron Xray imaging, and selected micro-CT analysis of the murine knees.

A group of experienced animal histology investigators performed a blinded rating of the degree of osteoarthritis of the murine knee histology using the Glasson scale, for rounds 1 and 2 of murine experimentation.

**Results**

Using ELISA, we evaluated differential levels of circulating 25-hydroxy-Vitamin D in each of the 4 groups of mice fed different levels of Vitamin D over time, and noted initial increase in circulating 25-hydroxy-Vitamin D levels that differed by feeding dose, with metabolic equilibration over time. While high doses of Vitamin D have been previously shown to be well-tolerated in mice, the findings of metabolic equilibration over time have not been previously reported. In males, the dose-response from minimal to high levels was shown best at 2 and 4 weeks; we did not have data on females in this group at 2 weeks.

We also tested Vitamin-D binding protein (DBP), which binds Vitamin D metabolites in plasma up to a certain species-specific level. It has been shown that free Vitamin D metabolites are active, and thus once DBP binding is maximized, the free metabolite levels will increase. Our results showed the highest levels of DBP in the mice given minimal Vitamin D, with DBP decreasing as supplementation increased.
In analysis of the histology from round 2, performed by the same three blinded examiners for consistency, we noted improved consistency of arthritic change at the 8, 12,16, and 20 week timepoints. Histological analysis again showed some evidence in female mice of mitigation of post-traumatic osteoarthritis in the ACL group, as well as in females at 12 weeks, but no trends in male mice.

On the left, 20-week female with 0 Vitamin D supplementation with thinned cartilage and joint narrowing. On the right, female with 5000IU/kg supplementation, showing normal staining of the cartilage with less articular change. Note that in both, tibial squaring and osteophyte is visualized.
20 week histology samples from male mice with 5000 IU/kg Vitamin D. Note osteoarthritic changes on the left, with lesser changes on the right. Supplementation again seems to be more effective in female sex of mice.

- We completed the third round of murine surgery and murine sacrifice at 20 weeks just before the PI’s institutional move from the University of Connecticut to the University of Chicago, while micro-CT analysis began for the round 2 mice. Micro-CT analysis is ongoing for the 12, 16, and 20 week timepoints of round 2, with measurement of subchondral bone volume and osteophyte counts. Histological analysis and micro-CT of round 3 murine specimens is beginning.

**Faxitron imaging** showed progressive signs of osteoarthritis over time.

8, 12, and 16 week views with DMM (surgical) limb on left, sham surgery on right; all are of male mice with 1500 IU (normal) feed levels.
**Micro-CT analysis** has similarly shown signs of progressive osteoarthritis with aging in the murine model. Because micro-CT was to be performed in the 2\textsuperscript{nd} and 3\textsuperscript{rd} rounds, we only have completed data from the 2\textsuperscript{nd} round. The third round analysis is pending funding transfer to set up a subaward to complete the work.

Above, 12 week female murine knees with 1.5U/kg (minimal) Vitamin D supplementation. The right knee (above on left) is the operative knee with induced osteoarthritis, compared to the sham surgery left knee of the same mouse.

This is compared to a 12 week male murine knee image, with supplementation of 10,000 IU/kg Vitamin D. Note the lack of osteophyte formation on the operative right knee (above, left).
At 20 weeks, we begin to see more osteoarthritis in general. Below, left is a female fed 10,000 IU/kg of Vitamin D; in the middle, one fed 5,000 IU/kg. On the right, a female fed normal levels (1500 IU/kg Vitamin D).

The results of the micro-CT are suggestive, but not confirmatory, that there is some impact of increased Vitamin D supplementation, with fewer signs of joint degeneration seen on radiography and micro-CT. However, analysis will include pooled data from rounds 2 and 3 with measurement of osteophyte volume.

Histology analysis is ongoing, with the first two rounds showing promising data. A group of three experienced investigators rated histology slides in a blinded fashion using the Mankin scoring system for severity of murine joint osteoarthritis, with the findings of:

- Overall minimal induction of osteoarthritis in the earlier timepoints
- No correlation between Vitamin D supplementation and osteoarthritis in male or female mice at 4 or 8 weeks.
In female mice at 12 and 16 weeks, ratings showed decreased OA histologically on the tibial side at 12 weeks and on both the tibial and femoral sides at 16 weeks.

We did not observe this effect in male mice, as shown below:

In a subset of mice treated with ACL transection in combination with destabilization of the medial meniscus, we observed faster onset and more severe osteoarthritic changes. Note the near complete loss of cartilage on the left side of the knee, with fibrillation and displacement of the meniscus.
Evaluation of these mice showed a protective effect of Vitamin D supplementation, although all of these mice developed osteoarthritis at 8 weeks. However, there was a trend toward less severe involvement in the supraphysiologically dosed female mice, as shown below.

![ACL Transection at 8 weeks in female mice](chart)

**Accomplishments**

- Completed animal surgeries and round 2 of histology.
- Established reliable histology ratings techniques using Mankin scoring rubric.
- Showed early correlative findings of protective effect of Vitamin D using Faxitron Xray and micro-CT.
- We have some exciting potential evidence of Vitamin D mitigation of OA in female animals.

**Challenges**

- Transfer of grant funding from the University of Connecticut to the University of Chicago.

**Specific Aim 2: To evaluate the serum 25-hydroxy-Vitamin D status of military cadets before and after ACL injury and reconstruction and correlate these findings with biomarkers of articular cartilage injury as well as radiographic joint space narrowing**

**Objectives: Initiation of Add-on to Existing Study**

*Subject Enrollment/Specimen and Data Collection*

**Progress**

- We obtained Keller Army Hospital and UConn Institutional Review Board (IRB) approval in October 2014 to add-on to the existing study of ACL tears in United States
Military Academy (USMA) cadets and biomarkers for initiation of PTOA. Our IRB approval allows us to also measure 25-hydroxy-Vitamin D levels in pre-injury, at-injury, at-surgery, and post-surgical serum samples from USMA subjects.

- To date, study participation is as follows per Dr. Cameron (USMA PI):
  - 88 ACL injured cadets screened
  - 55 ACL injured cadets enrolled in study; this is on target for 90-100 cadets to be enrolled over three years.
  - Matched control subjects are also enrolled for each ACL injured case.
- We will not perform Vitamin D testing until we have reached target enrollment, both for reliability of testing (batched testing is much more comparable) and budget costs.

Results/Accomplishments reporting is deferred pending further enrollment for this segment of the study.

Problems/Changes

- With the change in institution and delay in funding transfer, completion of histology and rating for round 3 of animal surgery is not finished.
- Immunohistochemistry of murine knees, similarly, has not begun pending funding.
- It is anticipated that a no-cost extension may be necessary.

Key Research Accomplishments

- The main accomplishment is the preliminary finding of a correlation between increased Vitamin D supplementation and decreased OA histologically in the murine model. It is interesting to note that this was only seen in females, implying a possible sex-differential effect. Van Grootheest et al showed in a recent epidemiological study in the Netherlands that circulating Vitamin D levels were higher in women than men, particularly in the group under 35 years. In contrast, Rabenberg et al showed no sex differences in 25-hydroxy-Vitamin D levels in an adult census study. In our second round of the animal study, this appeared to be a consistent effect.

Conclusion

This combined animal and clinical study is making progress in both focus areas. We have successfully induced post-traumatic osteoarthritis in murine knees, and have demonstrated that we can effectively supplement mice with dietary Vitamin D in varying doses. Additionally, we have obtained some interesting preliminary evidence that Vitamin D in supraphysiologic doses mitigates the degree of PTOA in female animals. We are analyzing data from micro-CT, further histology, and X-ray, and will be starting immunohistochemical work shortly, pending finalization of grant funding transfer to the University of Chicago.
Our add-on to the clinical study has been successful thus far and enrollment continues. Over half of subjects have been enrolled. Data from these subjects will be available for analysis once we perform batched serum Vitamin D testing, at the end of enrollment.

Publications, Abstracts, and Presentations - Nothing to report

Inventions, Patents, and Licenses – Nothing to report

Reportable Outcomes – Nothing to report

Other Achievements - Nothing to report

References

6. Rabenberg M, Scheidt-Nave C, Busch MA, Rieckmann N, Hintzpeter B, Mensink GB. Vitamin D status among adults in Germany--results from the German Health Interview and Examination Survey for Adults (DEGS1). BMC Public Health 2015;15:641.

Appendix

- PI CV

- Relevant clinical research from PI – recent publication about Vitamin D and bone turnover levels in patients with distal radius fractures
CURRICULUM VITAE
Jennifer Moriatis Wolf, MD

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EDUCATION

1987-1991 University of Maryland
College Park, MD
B.A., magna cum laude with General Honors

1991-1996 University of Pennsylvania School of Medicine
Philadelphia, PA
M.D., May 21, 1996

POST-DOCTORAL EDUCATION

1996-1997 Brown University Department of Surgery - Internship
Providence, RI
Director: Kirby I. Bland, MD

1997-2001 Brown University Department of Orthopaedic Surgery - Residency
Providence, RI
Director: Michael G. Ehrlich, MD

2001-2002 Brown University Division of Orthopaedic Trauma, Department of Orthopaedics – Orthopaedic Trauma Fellowship
Providence, RI
Director: Peter G. Trafton, MD

2002-2003 Mayo Clinic Division of Hand Surgery, Department of Orthopaedics – Hand Surgery Fellowship
Rochester, MN
Director: Robert D. Beckenbaugh, MD/Richard A. Berger, MD, PhD

CERTIFICATION

2005/2013 Board Certified (Diplomate) - American Board of Orthopaedic Surgery (Chicago, Illinois)

2006/2013 Certificate of Added Qualification (Hand Surgery) - American Board of Orthopaedic Surgery (Chicago, Illinois)
LICENSURE
Licenses active in Connecticut, Colorado, Minnesota, Illinois and Georgia

ACADEMIC APPOINTMENTS

2003 – 2009  Assistant Professor, Department of Orthopaedic Surgery
University of Colorado Health Sciences Center

2009-2010  Associate Professor, Department of Orthopaedic Surgery
University of Colorado-Denver

2010-2015  Associate Professor, Department of Orthopaedic Surgery
University of Connecticut

2015-2016  Professor, Department of Orthopaedic Surgery
University of Connecticut

2016-present  Professor, Department of Orthopaedic Surgery
The University of Chicago

TEACHING/EDUCATIONAL APPOINTMENTS

University of Colorado School of Medicine
Co-Director, Musculoskeletal Block (required 3rd-year course) (2007-2010)
Director, Orthopaedic Medical Student Courses/Sub-Internships (2007-2010)

University of Connecticut School of Medicine
Curriculum Reform Clinical Education Committee (2015-2016)
Medical School Admissions Committee (2014-2016)
Instructor, Musculoskeletal Block (2010-present)

The University of Chicago
Program Director, Hand Surgery Fellowship (2016-present)

HOSPITAL APPOINTMENTS

2003-2010  University of Colorado Hospital
2004-2010  Denver Veterans Administration Medical Center
2004-2010  Denver Health Medical Center
2004-2010  The Children’s Hospital of Denver
2005-2010  Rose Hospital (Denver)
2010-2016  John Dempsey Hospital
2014-2016  Connecticut Children’s Medical Center
2016-present  The University of Chicago Hospital

AWARDS & HONORS

2014  Connecticut Technology Council Women of Innovation Award
2013  American British Canadian Traveling Fellowship – American Orthopaedic Association
2010  Sterling Bunnell Traveling Fellowship – American Society for Surgery of the Hand
2008  Clinician Scientist Award – Orthopaedic Research and Education Foundation
2008  Leadership Fellows Program – American Academy of Orthopaedic Surgeons
2006  American Society for Surgery of the Hand – Young Member Leadership Program
2006  Alexandra Kirkley Traveling Fellowship - Ruth Jackson Orthopaedic Society
2005  United States Bone and Joint Decade Young Investigator
2001  Haffenerfer Award for Resident Research
1996  William G. Munn Memorial Prize for Promise in Orthopaedics
1995  Alpha Omega Alpha Medical Honor Society
1990  Phi Beta Kappa
1987  Chancellor’s Scholar  (full four-year college merit scholarship)

PROFESSIONAL SOCIETY MEMBERSHIP

American Society for Surgery of the Hand (Active Member, 2007 - present)
American Academy of Orthopaedic Surgeons (Fellow, 2007 – present)
American Orthopaedic Association (Member, 2012-present)
American Association of Hand Surgeons (Member, 2003-present)
Orthopaedic Leadership Institute (2010-present)
Ruth Jackson Orthopaedic Society (2002-present)
Rocky Mountain Hand Surgery Society (2003-present)
Connecticut Orthopaedic Society (2010-present)
New England Orthopaedic Society (2015-present)

JOURNAL REVIEW

Deputy Editor-in-Chief, Journal of Hand Surgery (2016-present)
Associate Editor, Scientific – Journal of Hand Surgery (2009-present)
Associate Editor, Hand and Microsurgery, Journal of Bone and Joint Surgery Reviews (2013-present)
Editorial Board, Orthopedics (2003-2016)
Web Updates Editor, Skeletal Trauma (2008-2016)
Expert Contributor, British Medical Journal Best Practice website (2014-present)

Consultant Reviewer
  Journal of Bone and Joint Surgery – British (2009-present)
  Clinical Orthopaedics and Related Research (2007-present)
  Orthopedics (2003-present)
  Hand (2010-present)
  British Journal of Sports Medicine (2013-present)
  International Journal of Sports Medicine (2012-present)
  BMC Musculoskel Disorders (2014-present)

**COMMITTEES/SERVICE**

**American Society for Surgery of the Hand**
- Council Member-at-Large (2014-2017)
- Program Co-Chair, Annual Meeting (2014)
- Annual Meeting Committee (Co-Chair, 2016-2018)
- Publications and Products Committee (2015-2016)
- Membership Application Task Force (2015)
- Commercial Support Committee (2012-2015)
- Touching Hands Project (2012-2015)
- Bunnell Traveling Fellowship Committee (2010-2013; Chair, 2013-2014)
- Products and Publications Committee (2005-2011)
- Annual Meeting Scientific Displays Committee (Member, 2006-2015; Chair, 2009-2012)
- Mentoring Task Force (2006)
- Resident Education Committee (2007-2010)
- Crucial Elements of Hand Surgery Committee (2007-2008)
- Courses and Meetings Advisory Committee (2007-2010)
- Young Members Steering Committee (Member, 2008-2010; Chair 2010-2011)
- Diversity Committee (2008-2011)
- Membership Task Force (2009)

**American Foundation for Surgery of the Hand**
- Board Member-at-Large (2012-2014)
- Complus Manus Committee (2012-2014)
- Nominating Committee (2012-2013)
- Touching Hands Project (2012-2013)

**American Academy of Orthopaedic Surgeons**
- Chair, Residents, Fellows, and Candidate Members Subcommittee (2008-2011)
- Chair, Residents, Fellows, and Candidate Members Subcommittee (2006-2009)
- Co-Editor, Residents’ Monthly E-Newsletter (2007-2009)
- Co-Chair, Leadership Development Endowment Fund Meeting Committee (2010-2012)

**American Board of Orthopaedic Surgeons/National Board of Medical Examiners**
- Joint Committee for CAQ Question-Writing Task Force (2011-2015)

**Orthopaedic Research and Education Foundation**
- Grant Reviewer (2010-present)

**Ruth Jackson Orthopaedic Society Governing Board**
- President (2014-2015)
- Vice-President (2013-2014)
- Secretary (2011-2013)
Chair, Nominating Committee (2015)

Orthopaedic Leadership Institute
   Inaugural Meeting Program Coordinator (2011)

American Association of Hand Surgery
   Research Committee (2008-2011)

Board of Directors, Rocky Mountain Hand Surgery Society (2008-2011)
   Secretary/Treasurer (2008-2009)
   Vice President (2009-2010)

New England Hand Society (2011-present)

Department of Orthopaedic Surgery, University of Connecticut
   Research Committee (2011-present, Chair 2012-present)
   Admissions Committee member (2010-present)
   OR Lean Committee (2014-15)

Colorado Multiple Institutions Review Board (IRB) reviewer, 2004-2008

Faculty Advisor, Orthopaedic Student Interest Group, University of Colorado School of Medicine, 2008-2010

Department of Orthopaedics, University of Colorado
   Finance Committee member, 2006-2010
   Academic Council member, 2007-2010
   Curriculum Committee member, 2006-2010

University of Colorado Hospital Trauma Committee member, 2004-2010

Active Women’s Health Initiative, University of Colorado Hospital, 2004-2010

PEER-REVIEWED PUBLICATIONS


NON-PEER REVIEWED PUBLICATIONS


ELECTRONIC MEDIA


TEXTBOOK CHAPTERS


TEXTBOOKS


RESEARCH SUPPORT

PEER-REVIEWED

CURRENT

1. Wolf (PI) 9/1/14-5/1/16 $20,000 3% effort
   American Foundation for Surgery of the Hand
   Conditional Deletion of Relaxin Receptor in Ligament: In Vivo Model
   We will create a transgenic mouse with inducible deletion of relaxin receptor at the level of tendon and ligament using a cross of relaxin null and scleraxis-Cre mice.

2. Wolf (PI) 10/7/14-10/6/17 $750,000 10% effort
   Department of Defense/Congressionally Directed Medical Research Program
   Supplementation of Vitamin D in Prevention of Post-Traumatic Osteoarthritis: Animal and Clinical Models
   This project will study the impact of oral Vitamin D in prevention of surgically induced arthritis in a murine model, as well as evaluate Vitamin D levels in military cadets prior to and after ACL injury.

3. Wolf (PI) 7/1/14-6/30/15 $50,000 5% effort
   Orthopaedic Research and Education Foundation/Goldberg Arthritis Grant
   Animal Model of Vitamin D Supplementation for Prevention of Osteoarthritis
   This project evaluates the potentially preventive impact of Vitamin D oral supplementation on the initiation and development of surgically induced osteoarthritis in mice.
   Awarded but declined due to overlap with DOD/CDMRP grant above.

COMPLETED

1. Chung (PI) 06/01/2011-05/30/2016 $22,500 3% effort
   NIH/NIAMS RO1. WRIST Study Group
   A clinical trial for the surgical treatment of elderly distal radius fractures
   This multicenter randomized trial compares 3 different methods of fixation in surgically treated distal radius fractures in elderly patients.
   Role: Co-investigator, PI on subcontract
2. Wolf (PI) 9/14/13-09/13/15 $20,000 3% effort
American Foundation for Surgery of the Hand
Impact of local and systemic relaxin in a murine osteoarthritis model
This study uses a murine model to examine the impact of locally and systemically delivered relaxin on the development of surgically induced osteoarthritis.

3. Rozental (PI) 05/01/2012-04/30/2013 $45,000 3% effort
Orthopaedic Research and Education Foundation/RJOS/DePuy
Markers of bone turnover and Vitamin D in patients with distal radius fractures
This study expands the smaller pilot study to evaluate biomarkers of bone turnover and 25-hydroxy-Vitamin D in patients with distal radius fractures, compared to controls.
Role: Co-Investigator

3. Wolf (co-PI) 09/01/11-08/31/12 $20,000 3% effort
American Foundation for Surgery of the Hand
25-Hydroxy-Vitamin D and bone turnover marker levels in patients with distal radius fractures
This study will evaluate Vitamin D and biomarkers of bone turnover in patients with wrist fractures and controls.
Role: co-PI

4. Wolf (PI) 08/20/10-06/01/11 $20,000 3% effort
University of Connecticut GCRC/CICATS Pilots and Feasibility Funds-2010
Correlation of serum relaxin with joint mobility and ligament injury and analysis for gender differences
This study will correlate serum relaxin with a prospective injury database in military cadets.
Role: PI

5. Wolf (PI) 09/01/08-08/31/10 $20,000 3% effort
American Foundation for Surgery of the Hand
Effect of relaxin on gender differences in laxity and arthritis of the thumb base
This study will evaluate hormonal effects on gender differences in thumb laxity and osteoarthritis.
Role: PI

6. Wolf (PI) 07/01/08-06/30/11 $300,000 15% effort
Orthopaedic Research and Education Foundation Clinician-Scientist Award
Does relaxin mediate gender differences in joint laxity and osteoarthritis of the thumb carpo-metacarpal joint?
This study’s goal is to correlate serum relaxin levels and joint laxity in normal subjects as well as to evaluate this relationship in patients with surgically treated thumb CMC osteoarthritis.
Role: PI

7. Wolf (PI) 10/01/06-09/30/08 $20,000 3% effort
American Foundation for Surgery of the Hand
A prospective, randomized, controlled trial of autologous blood injection vs. corticosteroid injection for the treatment of lateral epicondylitis.
This is a prospective, blinded, multicenter trial to evaluate the efficacy of autologous blood injection for lateral epicondylitis.
Role: PI

8. Dawson (PI)  2/01/08-1/31/09  $1000  2% effort
   **Southwest Orthopaedic Trauma Association**
   Incidence of scaphoid fractures in a young, active population.
   This study uses a military database of healthcare visits coded by ICD-9 to calculate the incidence of scaphoid fracture in a young, active population as well as analyze potential demographic risk factors for this injury.
   Role: Co-investigator

9. Sobky (PI)  07/01/04-06/30/05  $5,000
   **Department of Orthopaedics, University of Colorado Health Sciences Center**
   Comparison of bending strength and load to failure of multiple volar plates.
   This was a biomechanical study of the strength and stiffness of multiple plates used for fixation in distal radius fractures.
   Role: Co-investigator

10. Wolf (PI)  07/01/94-06/30/95  $20,000
    **American Heart Association**
    Sequencing of bone morphogenetic proteins and effects on human osteoblast-like cells.
    This was a project to evaluate the effect of BMP-2 and BMP-4 on osteoblasts in culture.
    Role: PI

**NON-PEER-REVIEWED**

1. Wolf (PI)  01/01/04-04/01/06  $20,000
   **Orthologic, Inc., Phoenix, Arizona**
   A double-blind, randomized, placebo-controlled Phase III study to evaluate the efficacy and safety of Chrysalin on the rate of healing in distal radius fractures.
   This was a multicenter trial of an injectable substance with the goal to increase healing in distal radius fractures.
   Role: PI

**INVITED PRESENTATIONS and LECTURES (National/International)**


2. Trapeziometacarpal Arthritis and Other Degenerative Arthropathies of the Hand: *Evidence-Based Treatment*. Instructional Course Lecture, ASSH Annual Meeting, September 2007, Seattle, WA.


28. Acute and Chronic Scapholunate Ligament Injury. Invited Speaker, Department of Orthopaedic Surgery, Landspitalinn Hospital/University of Iceland, June 8, 2011, Reykjavik, Iceland.


53. Ulnar Collateral and Radial Collateral Ligament Repair and Reconstruction. AAOS Complex Wrist and Hand Trauma Course, April 15, 2016, Rosemont, Illinois.

54. Radial Tunnel Syndrome. AAOS Complex Wrist and Hand Trauma Course, April 15, 2016, Rosemont, Illinois.

**NATIONAL/INTERNATIONAL PRESENTATIONS**

1. Wolf JM; Gannon FH; Shore EM; Bilker W; Zasloff MA; Kaplan FS: The prevalence, natural history, and pathogenesis of limb swelling in patients who have fibrodysplasia ossificans progressiva. Adult Bone and Mineral Working Group, American Society for Bone and Mineral Research Annual Meeting; September 10, 1995, Baltimore, Maryland. (podium)


5. Wyman JJ; Greisberg J; Wolf JM; Zou L; Terek R: “The effects of gadodiamide on proteoglycan production, cell proliferation, and apoptosis in chondrocytes.” Symposium
of the International Cartilage Repair Society, June 16, 2000, Göteborg, Sweden. (podium)


34. Wolf JM, Scott F, Williams AE, Delaronde S, King KB. Serum Relaxin is Correlated with Relaxin Receptors and MMP-1 in the Anterior Oblique Ligament. 2012 World Congress on Osteoarthritis, Barcelona, Spain, April 26-29, 2012. (poster)


41. Rohde RS, Wolf JM, Adams JE. Where are the Women in Orthopaedic Surgery? Special Interest Poster, American Orthopaedic Association Annual Meeting, Providence, Rhode Island, June 24-27, 2015. (poster)


COURSE FACULTY


15. Co-Chair, Interactive Case Reviews, American Society for Surgery of the Hand, October 2013, San Francisco, California.


17. Program Co-Chair, Annual Meeting, American Society for Surgery of the Hand, September 2014, Boston, Massachusetts.


20. Faculty, 2nd Annual Course on Wrist Arthroscopy and Arthoplasty, October 10-12, Arezzo, Italy.


25. Co-Chair, Interactive Case Reviews, ASSH Annual Meeting: Thumb CMC Arthritis. October 2016, Austin, Texas.


REGIONAL/LOCAL PRESENTATIONS


3. Osteoporosis and Orthopaedics. Sargent School of Physical Therapy, Boston University, November 6, 2001, Boston, Massachusetts.

4. Foot and Ankle Injuries. Sargent School of Physical Therapy, Boston University, November 13, 2001, Boston, Massachusetts.


PERSONAL
Married to Douglas S. Wolf
2 children
Hobbies: rowing, hiking, running
Volunteer physician at overnight camp (2006-present)
Medical Director, Ramah Rockies Summer Camp (2009-10)
The purpose of this study is to evaluate the impact of Vitamin D in prevention and progression of post-traumatic osteoarthritis (PTOA). The animal portion of this study involves surgical induction of osteoarthritis in mice, with supplementation of varying levels of Vitamin D, and evaluation using histology and micro-CT. The clinical portion is an add-on study at the United States Military Academy, evaluating a clinical cohort of USMA cadets treated for anterior cruciate ligament (ACL) tear, with pre- and post-injury serum 25-hydroxy-Vitamin D levels and correlation with joint space narrowing and biomarkers of cartilage injury. Findings from the animal model show preliminary evidence that Vitamin D supplementation may decrease OA in female animals, with less severe micro-CT imaging and histologic changes in animals given supraphysiologic doses of oral Vitamin D. Micro-computed tomography analysis is ongoing and immunohistochemistry is pending. In the clinical portion, we have enrolled 55/100 (55%) of the required patients for the clinical study, but will evaluate serum 25-hydroxy-Vitamin D once the entire cohort is enrolled. Our findings provide preliminary support for the concept that Vitamin D supplementation could prevent the onset of often rapid joint destruction that occurs with PTOA, with important implications for high-risk military occupations.