

SUNY Upstate Department of Orthopedic Surgery

Research History

Bioelectricity and the Enhancement of Fracture Healing (1965 - 1985)

Faculty: RO Becker, DG Murray, DA Webster, BE Fredrickson, JA Spadaro, AA Marino

Some bone fractures do not heal or heal very slowly with prolonged pain and disability and require multiple surgeries. Some potential solutions to this problem grew out of early research on the small electrical currents associated with bone injuries and the reshaping process that is part of the healing and the skeleton's adaptation to changes in loading over time. Methods were developed first using implanted electrode wires and later non-invasive, non-surgical pulsing magnetic fields to enhance fracture healing in difficult cases and also to improve outcomes in spinal fusions. Extension of this work has led to alternative methods of treating bone infections following traumatic injury and also basic research to identify the mechanisms through which electromagnetic fields can influence bone cells and tissue growth and even the regeneration of missing structures. For his contributions, Robert O. Becker MD was awarded the Middleton Award in 1964 by the U.S. Veteran's Administration, the Nicholas Andry Award by the American Association of Bone and Joint Surgeons in 1979, and was twice nominated for the Nobel Prize.

The Body Electric, R.O. Becker, G. Selden, William Morrow Publisher, New York, 1985.

Generation of electric potentials by bone in response to mechanical stress. C.A.L. Bassett, R.O. Becker, Science 137: 1063-1064, 1962.

Stimulation of partial limb regeneration in rats. R.O. Becker, Nature 235: 109-111, 1972

Silver anode treatment of chronic osteomyelitis. D.A. Webster, J.A. Spadaro, R.O. Becker, S. Kramer, Clin. Orthop. Rel. Res. 161: 105-114, 1981.

The electrical control system regulating fracture healing in amphibians. R.O. Becker, D.G. Murray, Clin. Orthop. Rel. Res. 73: 169-198, 1970.

Development of a Total Knee Replacement (1972 - 1985)

Faculty: DG Murray, JA Shaw, JH Somerset

Many early total knee replacements experienced gross loosening of the components in part due to being implanted without rigorous laboratory testing. David Murray, MD came up with a new knee replacement design while on a trip to Mexico, which was in part based on the ball and socket joint of the hip. This was the first knee replacement design that included a tibial component consisting of a metal tray and stem with removable plastic (polyethylene) inserts. Dr. Murray started a research project between the Department of Orthopedic Surgery and the Department of Mechanical Engineering at Syracuse University to develop and test this new knee replacement design. Prototype implants were created, using the curvature of the inside of a tennis ball and these designs were tested for millions of cycles in a mechanical knee simulator. Only after additional successful testing was performed was the new design finalized and implanted into patients. The clinical success of the Variable Axis Knee was a remarkable improvement upon other early knee replacements. Current knee designs include many of its unique features.

Experience with the Variable Axis Knee Prosthesis. R. Rutledge, DA Webster, DG Murray, Clinical Orthopaedics and Related Research 205:146-52, 1986.

Total knee replacement with a Variable Axis Knee Prosthesis. DG Murray, Orthopedic Clinics of North America 13(1):155-72, 1982.

The Variable-Axis Knee Prosthesis. Two-year follow-up study. DG Murray, DA Webster, Journal of Bone and Joint Surgery (Am) 63(5): 687-94, 1981.

Knee Joint Simulator. JA Shaw, DG Murray, Clinical Orthopaedics and Related Research 94:15-23, 1973.

Anatomy and Biomechanics of the Ulnar Aspect of the Wrist (1978-2008)

Faculty: AK Palmer, WH Short, FW Werner

The ulnar aspect of the wrist has been referred to as the Low Back Pain of the upper extremity. Study of patients with ulnar wrist pain led to a need to understand the anatomy and biomechanics of this complex area. Cadaver anatomical studies led to biomechanical studies and the eventual naming of this complex area as the Triangular Fibrocartilage Complex (TFCC). This work received the Emanuel B. Kaplan award of the NY Hand Society in the late 70's. Clinical application of this work led to the introduction of the "Classification and Treatment of Afflictions of the TFCC". Funding for this work was received from the American Society for Surgery of the Hand and National Institutes of Health.

"The Triangular Fibrocartilage Complex of the Wrist: Anatomy and Function", by Andrew K. Palmer and Frederick W. Werner. Journal of Hand Surgery, Vol. 6, No. 2, pp. 153-162, 1981.

Triangular fibrocartilage complex lesions: a classification. Palmer AK. J Hand Surg Am. 1989 Jul;14(4):594-606. Review.

Biomechanics of the distal radioulnar joint. Palmer AK, Werner FW. Clin Orthop Relat Res. 1984 Jul-Aug;(187):26-35.

The stabilizing mechanism of the distal radioulnar joint during pronation and supination. Kihara H, Short WH, Werner FW, Fortino MD, Palmer AK. J Hand Surg Am. 1995 Nov;20(6):930-6.

A Wrist Joint Motion Simulator - how it helped define wrist biomechanics (1981-ongoing)

Faculty: Andrew K. Palmer, Frederick W. Werner, Walter H. Short, James H. Somerset

Beginning with the classic paper by Dobyns and Linscheid on Carpal Instability in 1972, there has been great interest in the intrinsic and extrinsic ligamentous anatomy of the wrist and clinical problems related to ligamentous disruption and resultant abnormal wrist biomechanics. Based on a clinical review of patients treated for carpal instability at the Mayo Clinic, we began to study carpal mechanics and carpal instability through anatomical and biomechanical studies. This work led to the development of the first wrist joint motion simulator in the United States. Under computer control, it pulls on up to 9 cadaver wrist and finger tendons to cause repeatable wrist motion. During wrist motion the tendon forces and the motion of specific carpal bones were measured. To visualize carpal bone motion in the intact wrist and after simulated injury using the wrist motion simulator, 3-dimensional images of each bone were computer animated using the experimental data as input. The simulator has been used to determine the consequences of torn wrist ligaments on the motion of the carpal bones, the loading in the forearm bones and to evaluate total wrist replacements. This novel approach has clearly demonstrated the importance of testing the wrist with dynamic motion and continues to be used today to study various surgical repairs or treatments of the injured or arthritic wrist. This work was funded by the Centers for Disease Control and National Institutes of Health.

"Wrist Joint Motion Simulator" by Frederick W. Werner, Andrew K. Palmer, James H. Somerset, Jason J. Tong, Douglas B. Gillison, Maria D. Fortino, and Walter H. Short. Journal of Orthopaedic Research 14:639-646, 1996.

"A Dynamic Biomechanical Study of Scaphoid Instability" by Walter H. Short, Frederick W. Werner, Maria D. Fortino, Andrew K. Palmer, Kenneth A. Mann. Journal of Hand Surgery 20A:986-999, 1995.

"Biomechanical Evaluation of Ligamentous Stabilizers of the Scaphoid and Lunate" by Walter H. Short, Frederick W. Werner, Jason K. Green, Shunji Masaoka. *Journal of Hand Surgery*. 27A:991-1002, 2002.

Biomechanics of the Treatment of Spinal Burst Fractures (1987 - 1993)

Faculty: BE Fredrickson, JC Bayley, WT Edwards, KA Mann, HA Yuan

Burst fractures of the spine are caused by high energy impacts, usually as a result from a fall from a height or sudden deceleration such as an automobile accident. Prior to the mid 1980s, these fractures were thought of as flexion/compression injuries because of the shape of the vertebrae after fracture. We performed impact experiments on isolated lumbar spine sections and found that axial impacts could produce fractures that were similar to what is found clinically. Further, we found that bone fragments that were displaced into the spinal canal could be deflected away from the spinal cord by distraction of the spine. Correction of the flexion deformity (kyphosis), by itself, did not adequately remove the bone fragment from the spinal canal. This line of research led to the 1992 Volvo Award for research led by Dr. Bruce Fredrickson. This work was funded by the Orthopedic Research and Education Foundation.

1992 Volvo Award in experimental studies. Vertebral burst fractures: An experimental, morphologic, and radiographic study. Fredrickson, B.E., Edwards, W.T., Rauschnig, W., Bayley, J.C., Yuan, H.A. *Spine* 17 (9), pp. 1012-1021, 1992

Reduction of the intracanal fragment in experimental burst fractures. Fredrickson, B.E., Mann, K.A., Yuan, H.A., Lubicky, J.P. *Spine* 13 (3), pp. 267-271, 1988

Conservative treatment of fractures of the thoracic and lumbar spine. Krompinger, W.J., Fredrickson, B.E., Mino, D.E., Yuan, H.A. 1986 *Orthopedic Clinics of North America* 17 (1), pp. 161-170

Biomechanical Assessment and Treatment of the Intervertebral Disc in the Lumbar Spine (1992-2010)

Faculty: HA Yuan, BE Fredrickson, NR Ordway, AH Fayyazi, MJ Allen, WT Edwards

Degeneration and herniation of the intervertebral disc can result in debilitating back and leg pain by altering the normal function of the spinal cord and nerve roots. When non-surgical treatments fail, spine surgery is used to relieve the pain. Surgical procedures either eliminate the motion at the diseased spine segments through use of a spinal fusion or retain the motion of the segment with an intervertebral disc replacement. We have been investigating the biomechanics of the normal and diseased lumbar spine as well as novel surgical approaches and implant technologies. We helped develop one of the earliest nucleus replacements and developed new methods to assess the function of this new class of implants. Our research has focused on how the spine adapts to these surgical procedures and/or new implant designs. One aspect of this research led to the 1997 Lyman Smith, MD Award for research by Nathaniel Ordway, PE.

Comparison of Cobb technique, quantitative motion analysis, and radiostereometric analysis in measurement of segmental range of motions following lumbar total disc arthroplasty. S-A Park, N.R. Ordway, A.H. Fayyazi, B.E. Fredrickson, H.A. Yuan. *Journal of Spinal Disorders and Techniques*, 22(8): 602-609, 2009.

Preclinical evaluation of a poly(vinyl alcohol) hydrogel implan as a replacement for the nucleus pulposus. M.J. Allen, J.E. Schoonmaker, T.W. Bauer, P.F. Williams, P.A. Higham, H.A. Yuan. *Spine* 29(5):515-523, 2004.

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Increasing neuroforaminal volume by anterior interbody distraction in degenerative lumbar spine. D. Chen, L.A. Fay, J. Lok, P. Yuan, W.T. Edwards, H.A. Yuan. Spine 20(1):74-79, 1995.

A historical cohort study of pedicle screw fixation in thoracic, lumbar, and sacral spinal fusions. H.A. Yuan, S.R. Garfin, C.A. Dickman, S.M. Mardjetko. Spine 19(20 Suppl):2279S-2296S, 1994.

Growth Plate Radiation Effects, Radioprotection, and Radiorecovery (1994 - 2010)

Faculty: TA Damron, JA Spadaro, BS Margulies, FM Middleton

When children receive radiotherapy for malignancy, their growth plates may be damaged, resulting in growth arrest, limb length discrepancy, and angular deformity. To date, no solution has been found for this problem, but researchers here have built a solid foundation for potentially clinically beneficial future interventions. In 1994, a drug developed during cold war years as a chemoradioprotectant at Walter Reed Medical Center, WR-2721 (Amifostine), was being investigated for its chemoprotectant effects; Upstate Medical University was the site for pharmacokinetic evaluation in this multi-institutional study sponsored by what was then the Pediatric Oncology Group. Conversations about potential orthopedic oncology uses of WR-2721 between pediatric oncologists Abdul Souid, MD and Ron Dubowy, MD and orthopedic oncologist Tim Damron, MD led to the suggestion of its potential as a radioprotectant drug for children with radiosensitive sarcomas. An animal experiment showed for the first time that radioprotection of growth plate cartilage could be accomplished successfully. Subsequent work led to demonstration of further success with various radioprotectant and even novel radiorecovery agents. Integral to this work was the ground-breaking technique of separating the layers of the growth plate for individual molecular analysis by means of laser capture microdissection. This technique, developed in our laboratory, has provided the basis for understanding of the complex molecular changes in the growth plate over time, between zones, and after the damaging effects of radiotherapy. This work was funded by the Children's Miracle Network, Orthopaedic Research and Education Foundation, and National Institutes of Health-National Cancer Institute.

Microarray analysis of proliferative and hypertrophic growth plate zones identifies differentiation markers and signal pathways Wang, Y., Middleton, F., Horton, J.A., Reichel, L., Farnum, C.E., Damron, T.A. 2004 Bone 35 (6), pp. 1273-1293

Sequential histomorphometric analysis of the growth plate following irradiation with and without radioprotection Damron, T.A., Margulies, B.S., Strauss, J.A., O'Hara, K., Spadaro, J.A., Farnum, C.E. 2003 Journal of Bone and Joint Surgery - A 85 (7), pp. 1302-1313

Amifostine before fractionated irradiation protects bone growth in rats better than fractionation alone Damron, T.A., Margulies, B., Biskup, D., Spadaro, J.A. 2001 International Journal of Radiation Oncology Biology Physics 50 (2), pp. 479-483

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Development and Maintenance of Skeletal Characteristics Associated with Gymnastic Loading During Growth. (1997-ongoing)

Faculty: TA Scerpella, JN Dowthwaite, JA Spadaro

Enhancement of bone mass and structure is an important strategy for the prevention of osteoporosis and fracture. Mechanical loading appears to increase bone acquisition during growth, yet the extent to which these benefits are maintained is unclear. Our ongoing research uses gymnastics as a model of pediatric mechanical loading, evaluating improvement of peak bone mass, structure, and strength and assessing maintenance of benefits to adulthood. The goal is to provide a foundation for the development of an adolescent exercise prescription to improve ultimate bone health.

Female gymnasts and non gymnasts were recruited at a baseline age of 7-12 years. Annual dual energy X-ray absorptiometry (DXA) scans of the forearm, hip, lumbar spine, and total body assess bone characteristics, complemented by contemporaneous peripheral quantitative computed tomography scans (added 2006). Other measurements include annual muscle strength tests, as well as semi-annual assessments of diet, physical activity, body size/composition and physical maturity. In 2008, NIAMS funded continued study of existing mature subjects, with the addition of 80 immature subjects for improved skeletal measures representing late childhood through early puberty. This work provides a unique longitudinal perspective of exposure to mechanical loading during growth; by 2013, mixed longitudinal data for over 150 girls will have characterized skeletal development and maintenance from age 7 through 29 years.

Initial results suggest that exposure to gymnastic loading during growth yields persistent skeletal benefits in indices of bone mass, size and theoretical strength. More conclusive longitudinal evidence will support development of more widely applicable modalities for skeletal enhancement. This research has led to several young investigator awards for Dr. Dowthwaite (International Bone and Mineral Society 2007, International Congress for Children's Bone Health 2007, American Society for Bone and Mineral Research 2007, International Sun Valley Workshop on Skeletal Biology 2008).

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Skeletal benefits of pre-menarcheal gymnastic activity are retained after activity cessation. Scerpella TA, Dowthwaite JN, Gero N, Kanaley JA, Ploutz-Snyder RJ. 2010. *Pediatric Exercise Science* 22(1): 21-33.

Distal radius geometry and skeletal strength indices after peri-pubertal artistic gymnastics. Dowthwaite JN, TA Scerpella. 2010. In press, *Osteoporosis International*, 2/10.

Breast Cancer and Bone (1997 - 2010)

Faculty: MJ Allen, TA Damron and KA Mann

One in eight women will develop breast cancer at some point in their life. The majority of women with advanced breast cancer develop secondary tumors (metastases) in their bones. Although these bone metastases are not usually life threatening, they cause significant pain, restrict the patient's ability to carry out activities of daily living, and weaken the bone to the point where spontaneous fractures (known as "pathological fractures") may occur. In 1995, Matthew Allen's mother, Kate, was diagnosed with an aggressive form of breast cancer that subsequently spread to bone. This personal experience led to the development of a research effort aimed at better understanding the interactions between breast cancer and bone with the goal developing improved therapies for patients with bone metastases. An animal model was developed that mimicked many of the key features of bone metastasis, including localized bone destruction and increased bone fragility. Treatment with radiation therapy was shown to be capable of killing tumor but incapable of preventing bone fragility. We developed a computer modeling approach to predict the risk of pathological in mouse bone, with the long-term goal of translating this into clinical use in patients with bone metastases. More recently we successfully used bisphosphonates (drugs that are widely used to treat osteoporosis in women) and anabolic agents (drugs that build new bone) to reduce the risk of pathological fracture in the mouse model. Additional work will be needed to more completely define the best drug dose and dosing schedule, but the use of combination treatments holds real promise as a means of reducing the risk of fracture and improving the quality of life for women diagnosed with advanced breast cancer.

This work was funded by the Orthopaedic Research and Education Foundation, the New York State Department of Health, the US Army Breast Cancer Research Program, the Carol M. Baldwin Breast Cancer Research Fund, and the Kate Allen Breast Cancer Fund, established in memory of Kate Allen (1935-2000).

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Investigations on the Cause of Loosening of Total Joint Replacements (1999 - 2010)

Faculty: MJ Allen, KA Mann, A Race, DC Ayers, MT Clarke

Joint replacements are a very successful procedure to restore function to diseased or fractured hips and knees. Despite their widespread use, a large number of second surgeries to replace loose joint replacements are performed. Research efforts have focused on determining why these joint replacements become loose, how surgical procedures can be modified to improve fixation, and studies of the biologic response using animal models and detailed studies of autopsy retrieved implants. We found that certain cements used to fix implants to bone result in defects at the implant interface. In addition, roughened stem surfaces, when cemented in place can result in defects at the same interfaces. More recent work has shown that joint replacements retrieved at autopsy have interfaces that are very different from those created in the lab, due to dramatic biologic changes to the bone. This finding has implications as to how these joint replacements function and could improve implant designs in the future to last longer. Another strategy investigated in our lab has been to study the effects of bone anti-resorptive drugs to prevent bone loss after implantation. This approach shows promise to help implants from becoming loose and also possibly reduce the need for surgery for those that do become loose. This work was funded by the Whitaker Foundation and National Institutes of Health.

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Micromechanics of postmortem-retrieved cement-bone interfaces. Miller MA, Eberhardt AW, Cleary RJ, Verdonchot N, Mann KA. 2010 *Journal of Orthopedic Research* 28(2): 170-177

The influence of surface roughness on stem-cement gaps. Race A, Miller MA, Ayers DC, Cleary RJ, Mann KA. 2002 *Journal of Bone and Joint Surgery - Series B* 84(8):1194-204

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