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Foreword

At 4 PM on Monday, April 26, 1937 a lone Heinkel 51 bomber, the town square, the Julian Hotel and the rail station of Guernica in Basque Spain. This event is the most remembered event of the Spanish Civil War between the Republicans and the Nationalists. The Republican government of Spain had granted autonomy to the Basques. Guernica was the capital city of the independent republic and a symbol of freedom. To teach the Republicans a lesson, the Spanish Nationalist commander, General Emilio Mola, under orders of fascist Francisco Franco, invited the Condor Legion of the German Luftwaffe to use the small city for incendiary bomb target practice. The bombing prompted Picasso to begin painting his greatest masterpiece... "Guernica"... a prophetic vision of the Second World War.

The gored and speared horse recalls the Spanish Republic, the bull (Franco) lording over the bereaved, shrieking woman with her dead child, all of which contrast with the symbols of peace: the broken sword, the solitary flower, and the dove. "Guernica" is now an international icon for peace and the most important work of art of the twentieth century.

Picasso’s war casualties, with their protruding tongues, rolling eyes, splayed toes and necks arched in spasms, are similar to those persons presenting today to emergency rooms seeking our help. Like the central figure at the top of the painting who extends a lamp, we seek to shed light and warmth to those in need. The figure to the lower right, like our students and residents, is drawn to this lamp. The newsprint across the horse’s body recalls the importance of publishing findings so that others may share in the benefit from clinical and basic research. You may see other connections between the depiction of tragedy and our efforts to offset its effects. As Picasso himself said, “It isn’t up to the painter to define the symbols. Otherwise it would be better if he wrote them out in so many words! The public who look at the picture must interpret the symbols as they understand them.” If you want to see Picasso’s masterpiece in person, you must visit the Museo Nacional Centro de Arte Reina Sofia in Madrid to which museum it was moved from New York’s Museum of Modern Art only after the death of Franco.

Investigating and treating injuries, arthritis, tumors and degenerative conditions of the musculoskeletal system is the domain of the orthopaedic specialist. Whether working in the lab or in the operating room, specialists focus their energy and scholarship on a sharply defined problem, much as a magnifying glass focuses the energy of the sun on a single spot on a piece of paper. When I first heard former Academy President Jim Strickland speak on the power of specialization using the story of his father, the shooter, as a metaphor, I could not resist asking him if I could reproduce his lecture. We are honored to have Jim’s and his sister Jill’s permission to share this story of specialization with you here.

In this issue of our Research Report we include many examples of the power of specialization – the resident honing interest toward a subspecialty, the fellow securing the skills to succeed in academic orthopaedics, and the faculty member making substantial contributions in a highly specialized domain to the knowledge which forms the basis on which Orthopaedics and Sports Medicine is based. These contributions range from the genetics of musculoskeletal tumors, through the biology of connective tissues, the influence of hormones and mechanical loading on bone and ligaments, sports-related conditions, the management of fractures so that disability is minimized, and finally to the way information can be developed by knowledge-building communities and shared the world round.

One of the sentinel events for our Department this year was the completion of the Lynn T. Staheli Endowed Chair for Pediatric Orthopaedics. Dr. Staheli was the first full-time faculty member at Children’s Hospital – a true specialist. He remains one of the quintessential observers of the growth and development of the child, reassuring countless parents that most “flat” feet and “bowed” legs in children are completely normal. This endowed chair, established through the generosity of many and under the guidance of Dr. Lana Staheli, will be a permanent source of academic venture capital for the faculty at Children’s, providing resources essential to exploring better treatment for childhood deformities, injuries, and tumors.

The type of support that made the Staheli Chair possible is essential to the growth and development of our Department. In times when resources from patient care, the State of Washington, and the federal government are on the wane, our growing excellence is increasingly dependent on endowed support from you our friends, patients, industrial partners and alumni. We are succeeding, thanks to you.

U.S. News and World Report lists both our services at Harborview and at University of Washington Medical Center, in the top ten programs in the United States (http://www.usnews.com/usnews/ncsu/health/hospital/specorth.htm). The National Institutes of Health lists our Department in the top four of all orthopaedic departments in terms of NIH grants awarded for excellence of research (http://silk.nih.gov/public/cb222oz@www.rank01medrkn.htm). Combined with the fact that we are the only academic orthopaedic program for 25% of the landmass of the U.S. (the states of Washington, Wyoming, Montana, Alaska and Idaho) and host to one of the most outstanding residency and fellowship programs, ours is a special team indeed.

To all of you who generously support excellence in care, teaching, and research at the University of Washington Department of Orthopaedics and Sports Medicine, thank you!

Best wishes,

F. L. Matsen III, M.D.
Residency Alumnus, 1975
My Dad The Shooter - A Case For Specialization

JAMES W. STRICKLAND, M.D.

My dad could really shoot the basketball. He developed his skills in the small town of Owensville Indiana (pop. 450) where growing boys had little else to do but play basketball. Dad’s father was an old time country doctor who was frequently called away to tend to the sick, make house calls or deliver babies. As a result dad had alot of time alone and he spent it like many rural Indiana boys did; shooting baskets. He spent countless solitary hours in his back yard on a wide dirt patch where the grass had been worn away by the constant impact of basketballs and tennis shoes. At the back of the patch was a basketball goal not unlike thousands of others which could be seen throughout the Indiana countryside and from which numerous wonderful Hoosier players have been spawned over the years. The goal, which his father had erected for him, consisted of a wooden backboard with a black metal rim and a ragged grey net firmly anchored in the ground with concrete. Dad’s unchanging routine consisted of monotonously dribbling a worn leather ball out to a variety of positions well away from the goal; he would then turn, square himself with the basket and shoot the classic two-handed set shot that would become his trade mark. He would then follow the ball to the basket, retrieve it and shoot again. This sequence would be repeated time after time until my grandmother would call him in or it became too dark for him to continue. These private shooting practices were a year around ritual. Occasionally he would be joined by other boys and they would go to another goal around town or the high school gymnasium where they would play pick-up games. But, for the most part, it was a lonely self discipline and it produced a very good shooter.

For a small town, the Owensville boys basketball team was pretty competitive and dad was easily their best player. He was big boned, about six feet tall by his junior year and he quickly learned to use his height and weight to his advantage. He possessed an innate understanding of the game, was an intense competitor and, above all, he became a deadly shooter from almost any position on the court. From 1924 until 1926 Owensville won a lot of games. They beat the big Evansville teams on a regular basis, won their sectional tournament two out of three years and almost never lost in the confines of their own gym; which, incidentally, is believed to have had the first glass backboards in the state of Indiana. The gym also had a well localized dead spot on the basketball floor and the members of the team learned to entice opposing players to dribble over the spot during crucial moments of a game. When the ball failed to return to the dribbler’s hand the anticipating defensive player would scoop it up and proceed unmolested for a basket.

From Owensville, dad went 100 miles northeast to Indiana University where he played for Everett Dean and with Indiana legend Branch McCracken. He led the team in scoring his junior years and was selected as Indiana’s second All-American (third team, College Humor Magazine) in 1929. As a Senior, his playing time was restricted to a half of each game by a physician who thought he detected a heart murmur. Throughout his collegiate career dad’s shooting ability was the predominante feature of his game. It was described in at least one national sports publication as the classic, perfect form, underhanded set shot.

After college, dad went to New York City where he played for five years at what was then the mecca of U.S. amateur sports, the New York Athletic Club. During those years he taught and coached underprivileged boys at a church and played professional basketball in upstate New York under the name Strickleivitch in order to make some money and preserve his amateur status. When mother, announced that I was on the way in 1935, dad decided that they should return home to Indianapolis to settle down and raise a family. Dad would not play organized basketball again, but that shot; that glorious shot, became famous in every neighborhood we ever lived in.

No basketball player today, at any level, shoots the ball the way players did back then. I truly believe, that dad’s form was absolutely textbook for the two-handed shot. He was a big man for that time at six feet one and he weighed 210 pounds. His hands were fairly large but he could barely palm the laced leather basketballs of his period. Perhaps the key to the shot was the way he positioned his hands on the ball. His fingers were spread to maximum separation and placed on each side of the ball with his thumbs pointed straight upward and his fingers aligned directly out from his body. The shot was started just above the waist and about six inches out from his body with the wrists straight ahead. He would initiate the shot by pulling his arms back slightly at the shoulder and rotating his hands so that his fingers were pointing downward and his thumbs were pointing out towards the basket. This motion was quickly reversed as his arms thrust forward at the shoulder and his wrists snapped upward. His hands were well past their original position with his thumbs pointed towards his body at the time of release. This rolling movement resulted in a tremendous amount of backspin; more, I believe, than most players today achieve with their one-handed shots. The trajectory and direction of dad’s shot was rarely inaccurate and he would only miss if the ball was a bit long or short. Even then, the softness of the semi-underhanded delivery and the reversed spin that he created would often hold the ball to the rim where, after a bounce or two, it would almost always fall through. He could hit that shot with deadly accuracy from five to thirty feet from the basket with only slight variation in his basic form. Free throws were almost automatic and, after heretired from active competition, he could stand at any free-throw line and hit shot after shot with the ball rarely touching the rim.

From 1941 until 1946, dad was the Indiana Director of the Office of Price Administration (OPA) and was subsequently asked to run for Governor.
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two-hander. After that, we could usually
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memory tells me must have been about
move out to the back fence which my
consecutive free-throws, he would
go anywhere from twenty to forty or more
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they would award you a free pass

The big event of many sessions
and we would play until dark.
activity. Guys (and some girls)
the center of neighborhood
years that dusty court became
house and for the next six
and grass field behind our
backboard and goal in a dirt
personally erected a post,
back yard until I ask for one at
push me into basketball and
past.

Dad was very careful not to
push me into basketball and
we didn’t have a goal in our
back yard until I ask for one at age nine. He and some friends
personally erected a post, backboard and goal in a dirt
and grass field behind our
house and for the next six
years that dusty court became
the center of neighborhood
activity. Guys (and some girls)
of all ages would come over
after school and on weekends
and we would play until dark.
The big event of many sessions
would occur whenever we
could get dad out to the court to put
on one of his remarkable shooting
exhibitions. After he would make
anywherefrom twenty to forty or more
consecutive free-throws, he would
move out to the back fence which my
memory tells me must have been about
forty feet from the basket. It would
usually take him several shots to get the
range following which he would
invariably sink his patented
two-hander. After that, we would usually
coax him to go over the fence and into
the alley where he would take a position
up to sixty feet from the basket. Several
of us would relay the ball to him and
sooner or later he would put it through.
Sometimes, when it was getting dark,
you couldn’t even see where he was
shooting from, the ball would just come
flying through the, sky and rip through
the nets. A great cheer would erupt and
dad would emerge from the alley, climb
the fence and call it quits having
astonished all my neighborhood
buddies and left his son with incredible
pride.

During the forties and early fifties,
there was a recreational area not too far
from our home called Little America.
It had a golf driving range, miniature
golf, archery, badminton and a number
of other diversions. Most important to
our family were the two basketball goals
which they had located near their
entrance. For a quarter you could get
five free-throws and, if you made all
they would award you a free pass

the management of the recreation park
to any activity on the premises. Several
nights a week, my sister, brother and I
would warm dad up in the back yard,
drive to Little America and, within ten
minutes we would have all the free
prizes, second and third rows, culminating in
a brand new Hutch leather basketball
on the top row. For twenty-five cents you got
three shots and, if you hit them all, you had the option
of quitting and taking a prize
from the lowest row or
Receivings twomore shots in
an effort to move to the
second row of prizes and so
on. It would take twelve
straight baskets to win the
ball, which, I deeply coveted.
I couldn’t wait to get dad to
the fair. After all I’d seen him
make more than twelve shots
in a row on numerous
occasions. There was no
question in my mind that he
could do it.

I described the situation
to dad at dinner that night
and we struck a deal that I
would back him and when
(not if) he won, the
basketball would be mine. On the
following day, we warmed up for a
while on our goal in the back yard
and headed for the fair. I brought along a
grand total of fifty cents to finance dad’s
efforts realizing that there was an
outside chance that he might miss a
shot on his first try. That he might miss
twice was unthinkable. In my mind that
beautiful Hutch ball was already my
prize.

At the fair, I grabbed dad’s hand
and pulled him directly to the
predetermined concession. Dad looked
the game over and immediately
recognized many problems that had
gone totally unnoticed by my young,
simplistic mind. The shot was not a
typical free-throw. The goals (there
were two) were at least twelve feet high,
the rims were much smaller than regulation and they were tilted asymmetrically. The ball return was facilitated by netting which extended from the underside of the backboards to a rail at the shooting platform. That rail was high enough that the shot had to be taken from at least eighteen feet away from the basket. Finally the balls were rubber, worn smooth and very warped. The two balls which were in use at the concession were dissimilar in weight and configuration and the sleazy guy who was running the game alternately interchanged the balls to each shooter to keep him from becoming familiar with any single ball. In short, the game was very heavily stacked against the shooter. The possibility of anyone, at any level, hitting three straight, let alone twelve in a row, was remote.

Prior to dad's chance to shoot, we watched four or five other fruitless contestants pay their money, miss all their shots, complain about the unfair conditions and leave. Finally, dad's time came and, after I proudly stepped up and paid the entry fee of twenty-five cents, he stepped up on the platform. For a short time he moved the ball around between his large hands looking for the best way to hold the warped orb. He then took several practice throws without releasing the ball and found that he would have to stand back a little farther to shoot his low-release shot. He lifted the ball above his head and shrugged his shoulders to remove any tension. Finally, he was ready.

I watched with confident expectation as the familiar rolling motion sent the first shot toward the high, tilted basket. It rattled around the rim and, aided by the strong backspin, dropped through. The next two shots were perfect and, when asked if we wanted to accept a prize from the lowest row or go on, there was never a hesitation. The next three shots went through without touching the rim. Same decision. Shot seven was perfect and, then, much to my disbelief and horror, he missed. Dad turned and looked at me with an expression of disappointment. "Sorry Chum," he said.

"Hey pop," I replied "don't worry about it. I've got another twenty-five cents." With that, I gave the sleazy proprietor my last quarter, patted my dad on the back and returned to my spot behind the platform. By then there was quite a crowd around the concession; much to the delight of the ball man who was quite certain that his expensive top prize was safe. In retrospect the crowd, which would cheer his every shot, must have added considerably to the already formidable pressure on dad.

Again he began his machinery-like shooting motion. Three, six, nine in a row. At each level I simply nodded to the man that dad wished to keep on shooting. Ten, eleven: As I remember it they were all perfect. The eleventh basket brought a tremendous cheer from the now considerable gallery. Then, there was a hush. The concession man dropped the ball at dad's feet in an effort to break his concentration. Dad picked it up without changing expressions, looked for the best place to place his hands, took a deep breath and sent it on its way. The only sound was that of the ball settling in the center of the nets. There was a tumultuous cheer by those behind us. The concession man conceded that it was the only ball he'd lost that year.

I don't think I appreciated how great my dad's state fair performance was for many years. He's gone now and it remains as a treasured memory. My dad could really shoot the basketball!
Visiting Lecturers

This year at our annual LeCocq Lecture on January 24 and 25, we were most honored to have one of our fellow alumnus as our lecturer - Dr. Robert Winquist. Dr. Winquist was one of our Department of Orthopaedics and Sports Medicine’s graduating residents in 1974 and after a six month fellowship in Switzerland and Germany, he joined the faculty of the Department of Orthopaedics as an Assistant Professor and later was promoted to Associate Professor. He currently is a Clinical Professor of Orthopaedics Surgery at the University of Washington and practices at Swedish Hospital and Medical Center where he has been the Chief of Orthopaedics. Dr. Winquist’s work in the field of traumatology is well known and he is well sought after to be a visiting professor at many of the universities throughout the world. Thus, it was a special treat to have him accept our invitation to be this year’s LeCocq Lecturer. The faculty, residents, and community physicians were treated to 3 innovating lectures from Dr. Winquist: “Intramedullary Nailing of the Femur,” “Design Implant: A Toy Story,” and “Intramedullary Nailing of the Tibia.”

Robert A. Winquist, M.D.

This year at our annual Residents’ Research Days on May 16 and 17, we were honored to have Dr. Joseph Buckwalter, Professor and Head of the Department of Orthopaedic Surgery at the University of Iowa Hospitals and Clinics, return to be our OREF Hark Lecturer. Dr. Buckwalter was our OREF Hark Lecturer in 1992 and due to the overwhelming response from the residents to have him back, we were delighted when he accepted our invitation to return this year. Dr. Buckwalter earned his bachelor’s degree in psychology in 1969 and a master’s degree in pathology in 1972. He earned his medical degree in 1974 and completed his orthopaedic residency at the University of Iowa Hospitals and Clinics. Ever since he has served as a faculty member at the University of Iowa Hospitals and Clinics with the exception of serving as a Visiting Professor at the University of Bern in Switzerland in 1991. During the 2 days of lectures, the faculty, residents, and community physicians were treated to 3 lectures from Dr. Buckwalter: “Aging and Osteoarthritis,” “Ankle Osteoarthritis - Unique Characteristics and Treatment,” and “Orthopaedics in 2020.” In addition to Dr. Buckwalter’s lectures, the R3’s and the R4’s presented the progress of their research, while the R5’s presented the completion of their research projects.

Joseph Buckwalter, M.D.
Dr. Lynn Staheli is one of the pioneers who established the current Pediatric Orthopedic Society in 1975 and is a past president of the society. He founded the Journal of Pediatric Orthopedics 22 years ago and remains an active co-editor. An author of 85 original articles, 10 book chapters, and 8 books, Lynn continues to contribute to the scientific foundation of pediatric orthopedics and to disseminate that information to the world through his writings and lectures. He produces his books through desktop publishing to keep costs down so that the books can be purchased in developing countries. As a guest speaker in more than 25 countries, he is aware of the financial challenge that those physicians face in affording our very expensive books. As well, Dr. Staheli has just been awarded the Distinguished Achievement Award for a lifetime of excellent work in pediatric orthopaedics by the Pediatric Orthopaedic Society of North America.

Most clinical research in orthopedics involves the demonstration that one operation is more effective or safer than another, or that surgery is more effective than nonoperative treatment. Lynn has published the results of such research, many of which have become landmark studies. He developed the “Staheli” shelf acetabular augmentation procedure that has become an international standard in the surgical armamentarium for hip dysplasia. But his most significant contributions have been those that have shown that no surgery and, in fact, no treatment are better than surgery or sham treatment in certain conditions. Among those landmark studies are ones demonstrating that flatfeet are a normal foot shape in children, that toeing in and toeing out are normal limb alignments in children, and that most children develop an arch and change their in-toeing and out-toeing through normal growth and development. As a function of this extensive body of work, he is the ultimate child advocate, using research and teaching to provide evidence-based care to his patients and to train others to do the same. He’s not done. He has more questions to answer, more “right answers” to question, and more information to disseminate. Congratulations to Lynn and to all those who generously made this Chiar possible.
Is the Absence of an Ipsilateral Fibular Fracture Predictive of Tibial Pilon Fracture Severity?

DAVID P. BAREI, M.D., F.R.C.S.(C), SEAN E. NORK, M.D., CARLO BELLABARBA, M.D., and BRUCE J. SANGEORZAN, M.D.

The management of tibial pilon fractures remains controversial and challenging. Axial loading, particularly from motor vehicle collisions or falls from significant heights, is a common mechanism of injury. Principles of operative treatment include reconstruction of the distal tibial articular surface followed by restoration of mechanical axes. Anatomic reduction of the articular surface along with stable fixation allowing early motion has been shown to be the most important predictor of satisfactory outcome, and should be prioritized. The ability to obtain anatomic reduction with stable fixation, however, decreases with increasing comminution of the articular surface.

Fibular fractures are commonly associated with tibial pilon injuries, particularly those caused by shearing-type mechanisms. Other fracture patterns, however, do not demonstrate this associated feature. The absence of an ipsilateral fibular fracture in patients with tibial pilon injuries may predict a more severe injury pattern to the tibial plafond. Presumably, the injurious energy is completely absorbed by the tibial plafond resulting in more severe epiphyseal and metaphyseal injury, precluding accurate reduction and worse outcomes. Further, the deleterious effects of mechanical impact at the chondrocyte level may also lead to joint degeneration despite an accurate reduction. The purpose of this study is to evaluate the difference in the radiographic severity of tibial plafond injuries with fibular fractures as compared to those without fibular fractures.

**Materials and Methods**

Between January 1997 and February 2000, 20 consecutive tibial pilon injuries without associated fibular fractures were retrospectively identified using a prospectively gathered trauma database. Over the same period, an age and gender matched cohort of 20 tibial pilon injuries with fibular fractures were randomly selected. A computer-based image editing software program was used to digitize and conceal the fibula on the initial anteroposterior (AP) and lateral radiographs of all 40 injuries. Care was taken to completely eliminate any fibular fracture, and associated fibular malalignment, on both the AP and lateral views. Every effort was made to minimize concealment of the tibial plafond while maximizing the concealment of the fibula. Radiographs were then independently rank ordered (1 = least severe, 40 = most severe) by three orthopaedic traumatologists according to the severity of tibial plafond injury. Observers ranked all fractures taking into consideration all the radiographic factors they believe are important in the assessment of tibial pilon fracture severity. The observers were not given any specific guidelines regarding ranking, but relied on their significant clinical experience in managing these fractures. Injuries were also classified according to AO/OTA guidelines, which assigns fractures an alpha-numeric code according to body region and fracture location. Fractures affecting the metaphyseal and epiphyseal portions are divided into A, B, or C-type groupings, indicating an extra-articular fracture, partial articular fracture, or complete articular fracture, respectively. The premise is that increasing comminution results in a worse fracture pattern, and ultimately a worse prognosis.

**Results**

Inter-observer agreement was assessed using the weighted Kappa statistic (κ = 0.6). Mean rank scores for pilon injuries with fibula fractures was 24.4 while those without fibula fractures was 16.7 (T-test = 0.02). Rank order was repeated for only AO/OTA C-type pilon injuries and demonstrated a mean of 10.3 for those with fibular fractures and 8.7 for those without fibular fracture (T-test = 0.5). Mean rank order for AO/OTA B-type injuries was 11.1 whereas the mean rank order for C-type injuries was 24.5 (T-test = 0.001). The proportion of fibular fractures in B-type versus C-type pilon injuries was assessed using the Chi-square statistic (p = 0.006).

**Discussion**

Operative treatment of tibial pilon fractures is controversial. Evidence suggests that increasing comminution leads to a worse result for a variety of reasons. Identifying factors that are associated with a given outcome aid in clinical decision making. It has been theorized that the absence of fibular fractures in association with ipsilateral tibial pilon injuries may be associated with a poor outcome. Two different potential scenarios are suggested: the first is that the injurious energy is of lower magnitude and is insufficient to injure the fibula, or conversely, the energy is significant but is completely absorbed by the tibial plafond. To evaluate this theory, we used the rank order technique with experienced traumatologists blinded to the presence or absence of a fibular injury, who then independently assessed the radiographic severity of the tibial pilon fracture. The kappa statistic demonstrated satisfactory correlation, consistent with other published material on interobserver reliability of the AO/OTA fracture classification system. This study demonstrates that, overall, tibial pilon injuries with fibular fractures are more severe than those without fibular fractures. Complete articular (C-type) injuries, with or without fibular fractures, are equally severe. Supporting the OTA classification, C-type injuries were consistently ranked as significantly more severe than B-type injuries. The presence of a fibular fracture was more frequently associated with C-type injury than B-type. This data suggests that the presence of an intact fibula in a tibial pilon injury, but is predictive of a less severe, B-type, injury.
RECOMMENDED READING


Intramedullary Nailing of Fractures of the Proximal One-Quarter Tibia

SEAN E. NORK, M.D., DAVID P. BAREI, M.D., F.R.C.S.(C), JASON L. SCHRICK, B.S., SARAH K. HOLT, B.S., and BRUCE J. SANGEORZAN, M.D.

T
reatment of proximal tibial metaphyseal fractures remains problematic. Techniques include external fixation, plate fixation, and intramedullary nailing. Intramedullary nailing of proximal third tibial fractures has been associated with malalignment, nonunion, and the need for revision fixation. Previous reports suggest malalignment of 58% to 84% of patients. The purpose of this paper is to report the technique and results of intramedullary nailing of tibial fractures involving the proximal 25%.

MATERIALS AND METHODS

Over a 36 months period, 456 patients with fractures of the tibial shaft (OTA type 42) or proximal tibial metaphysis (OTA type 41A2 and A3) were treated operatively at a level one trauma center. Forty-two of these fractures involved or extended into the proximal 25% of the tibia. These fractures were treated with plates and two fractures were treated with external fixation based on the preference of the attending orthopaedic surgeon. The remaining thirty-seven fractures in thirty-five patients were treated primarily with intramedullary nailing of their proximal quarter tibial fractures and formed the study group. Thirteen fractures were open. There were 28 male and 7 female patients, ranging in age from 19 to 73 years (mean 42 years). All radiographs were evaluated by two orthopaedic traumatologists and the following variables were measured: total tibial length, proximal extent of the fracture, fracture classification, healing, preoperative, postoperative, and final alignment and reduction in two planes. An angular malreduction was defined as greater than 5 degrees in any plane. Three fractures had proximal intraarticular extensions. Twenty-two fractures had segmental comminution.

All patients were treated withreamed intramedullary nailing with the patient positioned supine and the knee flexed over a radiolucent wedge pillow. Techniques employed to facilitate maintenance of reduction included intraoperative use of a femoral distractor, a proximal and lateral starting point, and percutaneous clamp placement. In order to improve control of the proximal segment in difficult fracture patterns, thirteen patients underwent plate application in addition to intramedullary nailing. In three cases, these plate were removed intraoperatively after nail passage while in the other ten, the plates were left in place. Lag screw fixation was used to augment the fixation in an additional three patients.

RESULTS

These fractures extended proximally to an average of 17% of the tibial length (range, 4% to 25%). The average distance from the proximal articular surface of the fracture was 67.8 mm (range, 17 mm to 102 mm). The average tibial length was 397 mm (range, 353 mm to 449 mm). Angulation was within five degrees in all planes in 36 of 37 fractures (97.3%). One patient had an angular malreduction of seven degrees of varus. Postoperative angulation (average varus 0.4, valgus 0.3, flexion 0.2, recurvatum 0.2 degrees) as well as the final angulation (average varus 0.4, valgus 0.4, flexion 0.3, recurvatum 0.3 degrees) were acceptable. No secondary procedures were required to achieve union.

DISCUSSION

Intramedullary nailing offers an attractive alternative with proximal metaphyseal tibial fractures. Early reports reflected a poor understanding of tibial anatomy and the behavior of the proximal segment. This resulted in a high incidence of valgus and flexion malalignment with associated posterior translation of the distal segment. Recommendations have included avoidance of medullary implants in proximal third tibial fractures despite the biomechanical advantages of this technique.

These procedures were performed by orthopaedic traumatologists experienced with medullary nailing and knowledgeable about the pitfalls with proximal tibial fractures. The need for additional techniques to accomplish placement of a medullary device in a reduced fracture was quite common. A proximal and lateral starting point helps ensure placement of the nail accurately down the medullary canal. The most common adjuvant technique in our patients was temporary or permanent short plate fixations (35%) placed extraperiotostically to control the proximal fracture with nail passage. These plates can be placed through a separate posteromedial or anterolateral incision in closed fractures, and care should be taken to avoid further soft tissue stripping from the bone. In open fractures, the traumatic laceration can be incorporated into a surgical exposure that extends the skin incision yet doesn't further disrupt the osseous soft tissue attachments of the tibia. Loss of reduction did not occur and healing progressed despite additional fixations. Complications were uncommon.

In our series of patients, the articular extension was addressed prior to intramedullary nailing of the tibia. This was performed to prevent additional displacement and to assist in reduction of the proximal fragment. Loss of reduction of the articular segment was not seen with nail insertions. Strategic placement of periarticular lag screws may help prevent this potential complication. Articular fractures healed without loss of reduction in our series.

CONCLUSIONS

Despite the reported experience of others with a substantial incidence of malalignment, our experience reveals that in experienced hands, intramedullary nailing of proximal tibial fractures is a safe and effective technique. Alignment can be well maintained despite the short segment of the proximal tibia. Simple articular fractures and extensions are not a
Figure 1: AP and lateral radiographs of a classic proximal quarter tibial fracture with segmental comminution (AO/OTA type 41A3) in a patient who was struck by an automobile. This injury was open and associated with a compartmental syndrome.

Figure 2: Post operative radiographs after intramedullary nailing. The open wounds were used intraoperatively to allow for fracture reduction during reaming and nail passage.

Figure 3: Post operative radiographs of a proximal quarter tibial fracture (AO/OTA type 42A) treated with short plate fixation and reamed intramedullary nailing.
contraindication to intramedullary fixation. Short plate fixations to maintain this difficult reduction, either temporary or permanent, were effective and not associated with complications.

**Recommended Reading**


Complications Associated With Internal Fixation of Comminuted, Bicondylar Tibial Plateau Fractures


Complex bicondylar tibial plateau fractures are high-energy injuries that often occur in polytraumatized patients. Articular depression, sagittal and coronal plane condylar separation, and detachment of the metaphysis from the diaphysis are defining fracture characteristics. Marked swelling, abrasions, compartmental syndrome, and open wounds commonly occur. Treatment goals include accurate articular reconstruction, restoration of knee stability, reestablishment of condylar width, maintenance of the normal mechanical axis, and stable fixation. Treatment techniques include isolated lateral plating, small wire external fixation with or without limited internal fixation, lateral plating combined with medial external fixation, and double plating. Unfortunately, medial and lateral plating, particularly through a single anterior incision, has been associated with high wound complications and deep sepsis. Double plating through separate medial and lateral incisions may minimize anteromedial soft tissue dissection and decrease significant wound complications. The purpose of this study is to report the complications and infection rate associated with double plating complex tibial plateau fractures stabilized through two incisions.

Materials and Methods

Over a 79-month period, all patients sustaining an intra-articular fracture of the proximal tibia were collected from a prospectively designed orthopaedic database and reviewed retrospectively. This search identified 308 patients with 319 bicondylar tibial plateau fractures. Ten fractures were misclassified, leaving 309 fractures eligible for review. One hundred and seventy-eight fractures had simple articular involvement (AO/OTA type 41-C1 and 41-C2) and were excluded. Thirteen fractures were treated with primary amputation, five were treated non-operatively, two were treated with staged arthroplasty, 13 fractures were excluded for various reasons, and 8 fractures with insufficient data for review were also excluded. The remaining 90 patients sustained 90 complex tibial plateau fractures (AO/OTA type 41-C3) and formed the study group. All 90 patients were treated with plate fixation through two operative approaches. The use of a single midline anterior surgical approach was abandoned prior to the study period.

There were 57 male and 33 female patients with a mean age of 44.03 years (range, 21 to 88 years). Twelve fractures were open (13.3%) and classified as type II (1 patient), type IIIA (8 patients), type IIIB (2 patients), and type IIIC (1 patient). Compartmental syndrome was diagnosed and treated with fasciotomies in 12 patients (13.3%). Temporary anterior spanning external fixation was performed in 45 patients (50%) secondary to the severity of the local soft tissue injury or associated life-threatening injuries. The average interval from injury to definitive surgical treatment was 8.98 days (range, 0 - 40 days).

Technique

Medial column fixation through a posteromedial approach is typically performed first. The incision is placed approximately one centimeter posterior to the postero-medial edge of the tibial metaphysis, then parallels the sartorius and pes tendons proximally. Subperiosteal dissection is limited to the fracture edges and anticipated plate position. Disruption of the soft tissues on the anteromedial aspect of the tibia is avoided. The postero-medial plateau and metaphyseal fracture components are reduced, provisionally held, and stabilized with a postero-medial plate.

Lateral column fixation is performed using a standard anterolateral approach. A longitudinal skin incision is made one centimeter lateral to the tibial crest curving laterally over Gerdy’s tubercle and extending proximally in a longitudinal fashion to the lateral femoral epicondyle. The iliotibial band is incised in line with the skin incision and mobilized from Gerdy’s tubercle. A sub-mensal arthrotomy is performed followed by provisional articular and metaphyseal reconstruction. Subchondral defects are bone grafted. Buttress plate fixation of the lateral column is performed with the proximal screws strategically placed to support articular comminution. Supervised knee motion is started when the incisions are secure. Patients remain non-weightbearing for a minimum of twelve weeks.

Results

Non-septic complications included one nonunion at the proximal tibial metaphysis requiring bone grafting and revision plating. Thirteen patients, exclusive of those with infections, required delayed (greater than six months from injury) implant removal for relief of local symptoms. Two of these patients also underwent resection of heterotopic ossification to improve knee motion. Six patients required a knee manipulation for extension contracture, and one patient underwent tendo-Achilles lengthening for an equinus contracture. Seventeen patients incurred significant deep venous thromboses (DVT). No patient was diagnosed with pulmonary embolism. There were no deaths.

Septic Complications

Deep wound infections occurred in seven patients (7.78%), two of which were associated with septic arthritis. Two of the seven infections occurred in patients who sustained open injuries. One patient declined surgical or medical management of his infection. The remaining six patients had clinical resolution after an average of 4 additional procedures (range 1 to 7 procedures) combined with antibiotic therapy.

Two patients sustained vascular injuries and were treated with vascular reconstruction and prophylactic fasciotomy. The presence of an open injury, compartmental syndrome, the
use of temporary spanning external fixation, or surgical timing was not found to be associated with the occurrence of sepsis with statistical significance.

Superficial wound complications occurred in eight patients (8.9%). One patient required debridement of the lateral operative site seven days after fixation for persistent serous wound drainage. The remaining patients were managed successfully with local wound care. One person required surgical debridement for bone graft donor site sepsis.

DISCUSSION

Management goals for tibial plateau fractures include re-establishment of articular congruity, restoration of anatomic and mechanical axes, and stable fixation to allow early knee range of motion while maintaining fracture reduction. Extensive dissection through the injured soft tissue envelope to achieve reduction and apply stabilizing implants may significantly increase post-operative infection rates, hindering long-term successful outcome. Deep wound infection rates in patients treated with double plating have been reported to be as high as 87.5%. Recently, Veri et al., reported a matched cohort series comparing internal fixation with ring fixator methods for high-grade tibial plateau fractures. These authors found 44% of the fractures treated with open methods had an infection requiring intravenous antibiotics and/or operative debridement as compared to 12% in the ring fixator group. The high complication rate reported with open reduction and plate fixation in complex tibial plateau fractures has prompted recommendations for alternative methods of reduction and stabilization. Combined limited internal fixation with external fixation, hybrid external fixation, and small wire external fixation offer presumed decreased wound sepsis rates by minimizing further soft tissue injury. Marsh reported on 21 bicondylar tibial plateau fractures managed with limited internal fixation and medial half-pin external fixation, with septic arthritis occurring in two patients (9.5%). Other studies of bicondylar tibial plateau fractures treated with hybrid external fixation report infections in 12 to 13% of patients.

The ability to obtain an accurate reduction with indirect means is difficult and radiographic confirmation may be misleading. Furthermore, ligamentotaxis techniques are unable to reduce depressed articular segments that do not have soft tissue attachments. Direct articular surface visualization with open techniques, therefore, may allow the fractures to be more precisely reduced. The posteromedial and anterolateral incisions allow direct reduction and stabilization of their respectively displaced articular surfaces. A plate and screw construct that buttresses the split fracture components while providing a "raft" of screws to support elevated articular segments is preferred. These surgical approaches are intended to minimize injury to the tenuous soft tissue envelope on the anteromedial aspect of the proximal tibia. This area often sustains severe injury at the time of the fracture, and an extensive midline anterior approach may further jeopardize its viability.

Deep wound infections occurred in 7 of the 90 patients that formed this study group (7.78%). Two of these patients also had septic involvement of the knee joint (2.2%). Because of the low incidence of infection, no consistent co-factors could be singled out as risk factors with statistical significance. Clinical resolution was obtained in the six patients who agreed to surgical and medical management. This report reviews the wound complication rates associated with medial and lateral plating using a two incision approach in a homogeneous population of high-energy tibial plateau fractures. Accordingly, these injuries can be successfully treated with the double plating technique described. The deep infection rate of 7.78% remains significant with this procedure, but responds well to surgical and medical management, and is similar to those rates reported in studies advocating indirect reduction and external fixation methods. The deep infection rate using the two-incision approach is also substantially lower than previous studies reporting results of open reduction and plate fixation.

Figure 1: Injury radiographs and CT scans of a 44 year old male after a high energy accident. The sagittal CT is centered at the medial plateau and demonstrates the coronal fracture line with separation of the posteromedial plateau.
Recommended Reading


Figure 2: Postoperative radiographs demonstrating reconstruction of the articular surface.
Surgical Treatment of Displaced Femoral Head Fractures

SEAN E. NORK, M.D., TIMOTHY B. RAPP, M.D., AND M. L. CHIP ROUTT, JR., M.D.

Femoral head fractures are uncommon injuries associated with hip dislocations and fracture dislocations. Optimal treatment of femoral head fractures remains poorly defined. Closed management techniques have been associated with poor clinical results, mostly symptomatic posttraumatic arthritis of the hip joint. Surgical treatment may be beneficial, especially in fractures that involve the weight-bearing area of the femoral head. Complications are related to both the injury and surgical treatment of femoral head fractures and include aseptic necrosis, heterotopic ossification, malreduction, fixation failure, and posttraumatic arthritis. The purpose of this study is to evaluate the operative treatment of displaced femoral head fractures using an anterior surgical exposure and management protocol.

MATERIALS AND METHODS

Over a five-year period, 21 patients with displaced femoral head fractures were treated surgically at our institution and retrospectively reviewed. All of the patients had posterior hip dislocations.

There were 15 male and 6 female patients, ranging in age from 18 to 58 years (mean 30.9 years). The mechanisms of injury were automobile accidents in sixteen patients, motorcycle accidents in three, all terrain vehicle accident in one, and a fall while snow skiing in another. The left hip was injured in eleven patients. The patients’ average ISS was 16.8 (range, 9 – 50).

Associated injuries included six patients with traumatic brain injuries, three with spinal injuries, and ten with other orthopaedic injuries requiring operative intervention. One patient had an ipsilateral sciatic nerve palsy. Preoperative patient evaluations included standard resuscitations, physical examinations, urgent attempted closed reductions of the dislocated hip, and pelvic anteroposterior and oblique plain radiographs, and two-dimensional pelvic computed tomography (CT) scans.

The fractures were classified by location according to Pipkin. The fractures were supraacetabular in 12 patients, and infraacetabular in 9 patients. There were seven Pipkin type 1 fractures, twelve type 2 fractures, two type 3 fractures, and zero type 4 fractures. Eight patients had peripheral posterior wall acetabular injuries, but none required surgical treatment. Fracture comminution and impaction were noted on the preoperative pelvic computed tomography scans in 19 patients (90.5%). Intraarticular debris was identified on the scans in 16 patients (76.2%). The displaced femoral head fragment remained in the acetabulum in 17 patients, and was extruded in the other 4 patients.

Our indications for operative treatment were radiographic: (1) fragment displacement greater than 3 millimeters, (2) hip joint debris, (3) nonconcentric reduction of the hip joint, and clinical: (4) obstructed passive range of hip motion under anesthesia, and (5) hip joint instability.

Surgical Treatment Protocol

Each patient was treated according to a uniform management scheme. After complete resuscitation and evaluation of the patient, operative timing depended on the patient’s overall medical condition and specific injury pattern. Two patients with associated femoral neck fractures and another with an irreducible fracture-dislocation required emergent operative intervention.

In the 19 patients without an associated femoral neck fracture, the fractures were exposed using a modification of the Smith Peterson anterior surgical approach. Fracture reductions were accomplished after surgical anterior dislocations of the hips.

Postoperatively, intravenous cephalosporin antibiotics were administered until the drains were discontinued according to their outputs. Postoperative duplex vascular evaluations screened for venous thrombosis of the lower extremities and were documented. Immediate postoperative pelvic plain radiographs and CT scans were obtained. Ectopic bone prophylaxis was not used.

No orthoses were used. In all patients, hip flexion was restricted to less than 60 degrees for 6 weeks after surgery. If their overall condition allowed, protected partial weight bearing of the injured hip was progressed over 12 weeks after surgery. Postoperative clinical and radiographic examinations occurred at the six and twelve-week intervals, and annually thereafter.

RESULTS

Nineteen patients were available for follow-up averaging 27.3 months postoperatively (range, 8 – 78 months). Two patients had uncomplicated early radiographic and clinical follow-up limited to three months.

Eleven patients were treated with reduction and internal fixation. In the eleven patients treated with internal fixation, the fracture was supraacetabular in nine patients, and infraacetabular in two patients. Severe fracture comminution prevented accurate reduction and stable fracture fixation in the other ten patients. As opposed to the fixation group, in these ten patients treated with fragment excision the femoral head fracture was supraacetabular in three patients and infraacetabular in seven patients.

Fixation consisted of 1.5 mm and 2.0 mm cortical lag screws. A total of 29 screws was used. The number of screws per patient ranged from two to five (mean, 2.6), depending on the number and size of the femoral head fragments. Since the majority of the fragment preparation was accomplished prior to anterior surgical hip dislocation, the average inoperative anterior dislocation time for joint debridement and internal fixation was only 12.2 minutes (range 10 - 26 minutes). Of these eleven fixation patients, ten had anatomical reductions. In the remaining patient, the clinical articular fragment reduction appeared accurate, however the postoperative computed tomography scan revealed areas of missing cancellous bone between the
Figure 1: (A) The plain pelvic anteroposterior radiograph in this 27 year old male patient reveals his right hip fracture-dislocation. The femoral head fracture fragment remains within the joint. The displaced peripheral posterior wall fracture is seen superolaterally. The femoral neck is not fractured. (B) Using intravenous sedation and muscle relaxation, closed manipulative reduction of the hip was atraumatic and successful. This pelvic computed tomography (CT) scan axial image demonstrates the peripheral posterior wall acetabular fracture and the congruent location of the femoral head within the acetabular dome. (C) This CT axial image reveals the displacement and location of the femoral head fracture fragment. (D) On the day after injury, the hip joint was irrigated and the femoral head fracture was accurately reduced through an anterior surgical exposure. Stable fixation was achieved with two minifragment intraosseous lag screws. The hip was stable after femoral head fracture reduction and fixation. (E) One year later, he remains asymptomatic. He returned to playing competitive soccer. According to these oblique plain pelvic radiographs, the femoral head fracture has healed without aseptic necrosis. Class I ectopic bone formation is seen in the region of the rectus femoris tendon repair. The posterior wall fracture healed uneventfully. His hip joint spaces are symmetrical.
fracture fragments due to comminution. The peripheral fracture contact was excellent yet the cancellous surfaces had gap according to the scan. This situation was not visible clinically intraoperatively. He had early loss of reduction and fixation failure. He developed symptomatic posttraumatic hip arthritides and required total hip arthroplasty 36 months after his injury.

After fixation or excision, all 21 patients had intraoperative hip stability to passive range of motion. This included the eight patients with peripheral minimally displaced posterior wall acetabular fractures. None of these eight patients therefore required reduction and fixation of their small acetabular fractures in order to achieve intraoperative hip stability.

The postoperative plain radiographs and CT scans revealed concentric hip reductions in all 21 patients. There were no screw related errors. Each of the 29 screws was subchondral and intraosseous in location. No patient had residual loose debris according to these CT scans.

Ten patients in the fixation group demonstrated uneventful fracture union. The other had early fixation failure and posttraumatic arthritides. Femoral head fracture fragment necrosis did not occur in the eleven patients treated with fixation. Similarly, aseptic necrosis of the femoral head did not occur in either treatment group. All eight associated posterior wall injuries healed uneventfully both clinically and radiographically. None of the patients demonstrated subsequent hip joint instability.

Heterotopic ossification developed in 19 patients (90.5%) with a mean Brooker Class of 1.6. In the patients treated with internal fixation, heterotopic ossification was Class 0 in two, Class I in four, Class II in three, Class III in one, and Class IV in one (average Brooker Class, 1.7). In the patients treated with fragment excision, heterotopic ossification was Class 0 in two, Class I in three, Class II in four, Class III in one, and Class IV in one (average Brooker Class, 1.5). The two patients with Class IV ectopic bone had functional compromise and opted for excision at five and fourteen months.

**Discussion**

The indications for open reduction and internal fixation of femoral head fractures remain controversial. Accurate reduction of suprafoveal femoral head fragments is necessary to help restore the normal peripheral loading characteristics and to decrease the peak articular cartilage stresses in the hip. In our series, postoperatively we planned to fix each fracture, however two distinct management patterns occurred. In the fixation group of eleven patients, nine had suprafoveal fractures. The other two had large infrafoveal fracture fragments which allowed stable fixation. Conversely, in the excision group of ten patients, only three had suprafoveal fractures. These were severely comminuted preventing accurate open reduction and stable fixation. Surprisingly, in these three patients with suprafoveal fractures, their excisions did not cause hip instability nor has early posttraumatic arthritides developed.

Femoral head fractures may be associated with displaced posterior wall acetabular fractures. Eight patients in our series had small peripheral posterior wall avulsion fractures noted on the injury pelvic CT scan. Interestingly, after surgical treatment of the femoral head fractures in these eight patients, hip stability was noted and they did not require a separate acetabular operation. Similarly, hip abduction orthoses were not used postoperatively in any patients and subsequent hip instability did not occur.

Several authors advocate that the anterior hip surgical exposure facilitates reduction of irreducible hip fracture-dislocations, identification of the anteromedial femoral head fracture, access to the acetabulum for removal of loose osteochondral debris, and accurate reduction of the femoral head fracture. Our results using a modified anterior surgical exposure support their findings. The anterior hip approach was modified in this series to include only the distal portion of the standard Smith-Peterson surgical exposure. Elevation of the origin of the tensor fascia muscle was avoided, possibly reducing hip abduction and flexion weakness and ectopic bone formation. Similarly, the anterior hip capsulotomy in our series was fashioned to diminish the chance of capsular vascular injury. In order to accurately reduce the femoral head fracture, all of the fragments were removed from the injury field. Even those fragments with the ligamentum teres still intact were removed from the acetabulum by incising their ligamentum and residual soft tissue attachments. The fragments were then prepared for reduction and fixation on the operating nurse's sterile field. Anterior surgical dislocation of the proximal femur into the wound allowed accurate reduction and fixation, or excision of the femoral head fracture fragments. Two patients with associated femoral neck fractures and associated infrafoveal femoral head fractures had Watson-Jones exposures without anterior hip surgical dislocation. As a result in both patients, the femoral head fracture fragments were able to be excised.

Aseptic necrosis is a potential complication in any traumatic hip joint injury. In posterior hip dislocations without an associated fracture, the incidence of aseptic necrosis has been reported from 10 to 21.8%. The combination of traumatic posterior hip fracture-dislocation, anterior surgical exposure of the hip joint with anterior capsulotomy, removal of the femoral head fracture fragment from the acetabulum for preparation, and surgical dislocation of the hip were not associated with aseptic necrosis of the fragment fracture or femoral head in our patients.

Few fixation options are available for femoral head fractures because of the fracture fragment size and location. The implants should be located beneath the articular cartilage surface, yet provide sufficient fixation to prevent early failure. In our patients, fixation was achieved with small implants (1.5 mm and 2.0 mm cortical lag screws) selected according to the fragment size. Multiple points of fixation (average 2.6 per patient) with countersunk screws allowed for symmetrical compression and stable fixation.

In our series, no difference was seen in the severity of heterotopic ossification in patients treated with excision or open reduction. While ectopic bone was commonly encountered (81%), clinically significant bone formation requiring excision was seen in only two patients, both of whom had closed head injuries. Given this and other series incidences of ectopic bone, we advocate routine prophylaxis for these patients.
**Conclusions**

Femoral head fractures are associated with posterior hip dislocations, yet are uncommon injuries. The displaced fracture fragment is located anteromedially and involves a variable amount of the weight bearing surfaces. Their successful management remains controversial. In our series of 21 operatively treated patients using a modified anterior surgical exposure, eleven had open reduction and internal fixation of their femoral head fractures. Comminution of the fracture fragments precluded internal fixation in the remaining ten patients. Operative management of these fractures allowed for anatomic restoration of the articular surface in over 90% of the patients. These fractures are frequently comminuted and associated with intrarticular osteochondral debris. Accurate reduction of femoral head fractures is possible in patients without severe comminution, using an anterior surgical exposure. It is unnecessary to elevate the tensor fascia lata from the outer ilium for exposure. The obturator oblique radiograph best demonstrates the injury. Stable fixation can be accomplished with minifragment, subchondral, intrasosseous screws. Ectopic bone formation is common, yet rarely symptomatic requiring excision. Despite being avascular, these femoral head fragments healed, and aseptic necrosis of the femoral head did not occur.

**Recommended Reading**


Wound Healing in Open, Displaced Calcaneal Fractures

Stephen K. Benirschke, M.D., Patricia Ann Kramer, Ph.D., and Sean E. Nork, M.D.

Recent reports in the orthopaedic literature have indicated that a substantial number of complications occur following open reduction and internal fixation (ORIF) of calcaneal fractures, even when a lateral approach is used. In one report that included 63 feet, 12 feet (19%) developed deep dehiscences requiring inpatient care. Another report of 190 patients treated with ORIF via a lateral approach found that 40 (21%) developed wound complications that required surgical intervention. Wound healing complications in open calcaneal fractures is much more of a pervasive problem than in closed fractures. In one study of 43 open calcaneal fractures treated over an 8 year study period, the overall infection rate was 37% and osteomyelitis developed in 19% of all fractures. The infection rate for O1 fractures was 22%, for O2 38%, for O3A 77%, and for O3B 7%. 46% of O3B fractures was 22%, for O2 38%, for O3A fractures. The infection rate for O1 osteomyelitis developed in 19% of all fractures, was increased by broadening the time frame. The radiographs and wound of a representative patient with an O3A fracture are shown in Figure 1.

Fracture classification and soft tissue status.

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Table 1: Fracture classification and soft tissue status.

METHODS AND MATERIALS

Two groups were retrospectively reviewed: all displaced calcaneal fracture patients treated by the senior author from June 1994 to December 1998 and those with open fractures from 1989 to 1998. The first group, which includes 252 fractures in 218 patients, was established to investigate fracture repair and outcome. The sample size of the open group, which includes 37 patients with 39 open fractures, was increased by broadening the time frame. The radiographs and wound of a representative patient with an O3A fracture are shown in Figure 1. Fracture classification and soft tissue status for both groups are given in Table 1. A lateral approach was used for all ORIF procedures; all incisions were closed with a two layer approach, using inverted mattress sutures in the deep layer and a horizontal modification of the Allgöwer-Donati suture in the superficial layer. Cefazolin was administered perioperatively.

Wound healing complications were established by review of patient records and follow-up contact. Patients requiring treatment beyond oral antibiotics were classified as having wound healing complications. The radiographs and wound from a representative patient with a wound healing problem is shown in Figure 2. Symptoms included persistent serous discharge, erythema, diffuse cellulitis, and other evidence of infection. Treatments for patients with wound healing problems included course(s) of intravenous antibiotics, irrigation and debridement (I&D), and hardware removal. No methicillin resistant Staphylococcus were encountered. All patients with wound healing complications went on to heal their incisions and their calcaneal fractures.

RESULTS

Six feet (of 252, 2.4%) with closed fractures and two feet (of 39, 5.1%) with open fractures experienced wound healing problems that required intervention beyond oral antibiotics and that were directly associated with their open calcaneal fracture. The wound healing complication rate for O1 fractures was 0%, for O2 7%, for O3A 6%, and for O3B 0%. All feet that became infected eventually healed their wounds and fractures. Seven total infections were found: 6 (5 closed and 1 open) in the all fractures 1994-98 group and an additional one in the open fractures 1989-98 group. The details are presented below.

The first patient required I&D of a hematoma 14 days after the initial surgery. This relatively aggressive treatment was indicated because the patient had concurrent bilateral tibial fractures, was positive for hepatitis B and C, and had a recent history of intravenous drug abuse and needle sharing. After I&D, he exhibited a typical progression of healing. Another non-diabetic, non-smoking and compliant patient experienced persistent drainage from the apex of his lateral incision, developed erythema at four months, and required hospitalization to administer IV antibiotics. Cultures showed polymicrobial growth. The drainage resolved after the IV antibiotic course and the incision was healed by 7 months post surgery.

The next patient, a diabetic with bilateral fractures, was referred from out of town and, consequently, received most of his care in an outside facility. At the time of discharge from the initial...
ORIF, his incisions appeared to be in excellent condition. On follow up here at six weeks and four months after surgery, his right foot was, however, not completely healed in the apex of the surgical incision. He was treated with antibiotics for *Staphylococcus* sp. and experienced drainage and intermittent cellulitic symptoms until his hardware was removed nine months after surgery. This incision healed uneventfully.

The next patient experienced persistent drainage from his incision that required IV antibiotics on two occasions; wound cultures grew *Staphylococcus epidermidis*. This patient had significant compliance problems and refused to consistently take his oral antibiotics or to quit smoking and was lost to follow up for several months. He also had hepatitis C for which he refused treatment. He reappeared at one year after his initial surgery and was noted to be cellulltic over the lateral aspect of the incision with a draining wound. His hardware was removed and he healed without further intervention.

Another patient presented for initial treatment with a full thickness eschar on his heel of uncertain etiology and required ORIF for a second metatarsal fracture in addition to the calcaneal fracture. His surgical incisions initially appeared to heal well, but ultimately became infected with *Staphylococcus aureus*. He developed a deep infection and required two episodes of I&D with IV antibiotics. His hardware was removed at ten months from the initial surgery and his foot healed without further complications. He eventually required a subtalar fusion to resolve chronic pain from subtalar arthritis, which developed due to the devastating nature of the initial injury, and healed uneventfully from this surgery.

In an interesting case, a non-smoking, compliant patient with bilateral, medially open fractures (O2, O3A) healed by primary intention, but began to spontaneously drain 10 months after surgery from the lateral aspect of his left heel (O2), ultimately developing a deep infection. The hardware in his left foot was removed one year post surgery; cultures showed coagulase negative *Staphylococcus epidermidis* and *Enterobacter cloacae*. This incision healed uneventfully. The right foot (O3A) never developed wound healing problems.

The final patient, a compliant non-diabetic smoker, had a medially open right calcaneus fracture (O3A) as well as closed left tibia-fibula and pelvic fractures. He never healed his calcaneal incision, developing a deep infection (*Staphylococcus aureus*) and requiring several courses of IV antibiotics. Hardware removal at one year after reconstruction did not stop the drainage. Finally, I&D, curettage and placement of antibiotic beads (12 methylene blue beads impregnated with tobramycin) at 2 years 3 months after initial surgery resolved the

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**Figure 1:** Patient with an O3A fracture. A) Lateral radiograph of injury; B) Open wound; C) Lateral radiograph of initial reduction; D) Lateral radiograph of reduction at 5 years.
infection and he went on complete healing.

**DISCUSSION**

Open wounds concurrent with calcaneal fractures are much more problematic than closed injuries because of the increased risk of infection. Nonetheless, meticulous and diligent care of the soft tissue can remove much of the risk of infection in these patients, as it does in patients with closed injuries. Although the data presented here indicate that open calcaneal fractures are associated with higher rates of complication than closed fractures (2.4%), the overall rate of 5.1% should not be taken as a contraindication to open reduction and internal fixation as the preferred method of treatment for this type of injury. In all feet that experienced difficulties, the infections were treatable with I&D, antibiotics, and hardware removal. All patients healed their wounds. In no case was calcaneectomy or amputation required.

Although calcaneal fractures associated with open foot wounds present a substantial challenge, meticulous soft tissue management allows these cases to be treated with the same techniques as closed fractures. Open reduction and internal fixation via the extensile lateral approach is the appropriate surgical technique because it can restore calcaneal anatomy after substantial disruption and soft tissue trauma without exposing the patient to undue risk of complications. Surgical skill and patient compliance remain critical to success. As with closed calcaneal fractures and other fractures of the weight-bearing system, anatomic reduction, stable internal fixation, atraumatic surgical technique, and early mobilization is the treatment regime of choice.

**RECOMMENDED READING**


Cervical spine whiplash injuries remain a common, expensive, and poorly understood health problem. The National Highway Traffic Safety Administration (NHTSA) reports that an average of 805,581 whiplash injuries occurred annually in the United States between 1988 and 1996, with an annual estimated cost for treatment of $5.2 billion dollars. According to the Insurance Institute for Highway Safety (IIHS), only 5% of 1995 model vehicles had a head restraint which allowed positioning above the top of the occupant's head and closer than about 3 inches from the back of the head. We have developed a research program to help prevent whiplash injuries by studying the mechanical deformations of the head and neck during a whiplash injury event and finding ways to diminish these forces. Our research has included studying cases of whiplash injuries, conducting studies with human volunteers, developing computer models to simulate the impact, and studying tissue level changes in experiments using human cadaveric spine specimens. One goal of this research is to develop a head restraint with improved geometry and the ability to absorb energy from contact with the head during impact. This approach could reduce spinal forces and the potential for whiplash injury.

**METHODS**

**Development of a modified head restraint**

A total of 432 actual low speed (under 7 mph) rear impacts were studied. Victims were primarily female, (70%), with an average age of 37 years, a height of 64 inches, and weight of 145 lbs. Separate observations of 719 drivers showed that 26% had the head restraint set below ear level, and 42% had a gap of greater than about 3 inches between the back of the head and the restraint, either resulting from a kyphotic posture, or because the seat was inclined backwards. Impact testing of seats demonstrated considerable variation in the stiffness of the head restraint and its ability to absorb the energy of contact with the head. These observations prompted the development of a modified head restraint, shown in Figure 1, which was higher and stiffer than existing devices. A pneumatic cushion (not an airbag) could be inflated to accommodate the shape of the occupant's torso, spine, and head, and a discharge valve on the cushion allowed air to escape from the bag, absorbing impact with the head.

The response of human volunteers

A representative vehicle seat was mounted on a 6 wheeled frame, Figure 2. With IRB approval, 28 subjects were tested. Each subject was seated in the sled and restrained with lap and shoulder belts. A light plastic headband was secured on the subject's head containing accelerometers measuring X (forward-backward) and Z (upward-downward) accelerations at approximately the level of each ear. The subject first underwent a rear end impact sitting upright against the modified head restraint with the air cushion inflated to the subject's comfort level. Then the modified head restraint was replaced with the standard head restraint. The impact was equivalent to about a 4-5 mph rear-end collision. All subjects underwent the two sequential impacts without incident. Subsequent symptoms consisting of some minor neck stiffness later that day or the next were reported by three subjects. All symptoms resolved rapidly. With the standard head restraint, Figure 2, the subject's chest was initially thrust forward while her head was falling backward toward the head restraint. Then her head was thrust forward as the chest motion stopped. With the modified head restraint, the subject's head and torso were in nearly simultaneous contact with the seat and head restraint and the maximum difference in horizontal position...
Figure 2: Test subject on sled with headband and chest plate containing accelerometers. Upper, modified head restraint, lower, the same subject with the standard head restraint. Note gap between head and head restraint in lower sequence (Time of images, from left to right: impact, 0 msec, 33 msec, 66 msec, 132 msec).

Figure 3: Computer model animation showing responses similar to volunteers and, in third frame forward thrust of torso with the head level causing anterior shearing of the cervical spine.

Figure 4: Cadaveric cervical spine responses from left, at 1, 88, 144, and 228 msec. Note lower to middle cervical spine extension at 144 msec and flexion at 228 msec.
between the head (at the center of gravity) and the sternum was reduced from about 48 mm to 20 mm. Measurements indicated lower peak accelerations and less variation in subject responses with the modified head restraint.

Computer modeling

MADYMO (Mathematical Dynamic Modeling, TNO Automotive, Delft Netherlands) is used in the automotive industry for design of safety devices. It simulated the motion of the occupant modeled as rigid bodies (the bones) connected by joints, with properties well defined by cadaveric testing. The seat was modeled as a finite element object based on mechanical testing of the seat frame and cushion. Using this approach allowed the internal forces in the cervical spine to be determined since the model included individual vertebrae and their connecting soft tissues. Responses at impact speeds much higher than tolerable by volunteers were studied. Also, various properties of the seat were altered and the response of the occupant determined.

The response of the model in terms of acceleration of the head and chest fell well within the responses measured in the volunteer studies described above. As shown in Figure 3, with a head restraint that reaches the top of the occupant’s head and an initial gap of about 4 inches, the major force acting is shear, that is, a horizontal force across the spinal vertebrae. With the head initially upright and momentarily stationary, while the torso is thrust forward by its contact with the seatback, an anterior shear or horizontal force acts on the cervical spine. Later, as the torso is stopped by the shoulder strap and the head is thrust forward by its contact with the head restraint, a secondary shear force develops. Reducing the head-to-restraint distance did not significantly alter these forces. It did prevent extension of the cervical spine and head, but instead created greater flexion during the forward rebound of the head. Making the seat and head restraint softer decreased the magnitude of the primary shear force and reduced the head rebound from the restraint by absorbing energy, thereby decreasing the secondary shear force.

Cadaveric Studies

In order to gain insight into the detailed deformations of cervical spine tissues, a series of 11 cadaveric cervicothoracic specimens with an instrumented artificial skull was tested. Each specimen was mounted onto a platform, replacing the seat, on the same cart used for human volunteer testing. The same head restraint was used and the impactor was adjusted so that the acceleration at vertebra T1 (about top of sternum level) was similar to that recorded by volunteers. High speed video was used to film the positions of markers on the lateral masses and the vertebral bodies and measurements were made of the contact pressures in the facet joints and around the nerve roots. The effect of the modified head restraint was studied.

Figure 4 showed formation of a partial “S” curvature, specifically extension of the lower cervical spine, which seemed to be most prominent when the head motion was stopped by the head restraint. Following rebound from the head restraint the spine was subjected to both anterior shear and tensile forces as the head moved forward of the lower spine. Reproducible pressure pulses occurred at the facet joints, first at levels C7-T1, and were maximum after peak acceleration of the chest but before peak acceleration of the head occurred. Pressure measurements in the facets showed pinching (a high pressure point in the joint instead of a uniform contact), in about 70% of tests, with C4-5 and C5-6 having the greatest likelihood of pinching. The modified head restraint reduced head acceleration and resulting spinal shear forces by about 30%.

Conclusion

In a rear-end vehicle impact, even when the occupant’s head is positioned close to the head restraint, significant forces can be developed in the cervical spine with resulting intervertebral displacements and tissue pressures and deformations. These forces are a primary anterior shear, due to the torso being thrust under the stationary head by its contact with the seat, and a secondary force from the head being thrust forward by its contact with the head restraint as the torso motion stops. The basic method for reducing spinal forces and intersegmental displacements is to soften the torso-to-seat and head-to-restraint contact, and importantly, use the head restraint to absorb the energy of these impacts.

Recommended Reading


Tencer AF, Mirza SK, Cummings, P, Do whiplash victims with neck pain differ from those with neck pain and other symptoms? Proceedings of the Association for the Advancement of Automotive Medicine, Sept, 2001.


Recent reports have highlighted the important relationship between residual intra-articular displacement and the long-term outcome of distal radius fractures. There appears to be a general consensus that accelerated development of arthritis and worsened severity of degenerative changes is associated with residual step-off displacements greater than 1 to 2 millimeters. Therefore, to improve clinical outcome after intra-articular fracture of the distal radius, many reports in the literature strongly advocate surgical reduction of fragments with articular incongruities greater than 1 to 2 millimeters. In each of these studies, the intra-articular step-off and gap displacements were measured in millimeters using plain radiographs.

Definitive standards for describing and quantifying articular surface incongruity do not exist. Kreder et al. in 1996 attempted to standardize the technique for measuring intra-articular displacement of distal radius fractures. Sixteen observers examined six radiographs of healed intra-articular distal radius fractures and found that, "... even experienced clinicians did not readily agree on the size of step and gap deformity." Specifically, they found that two experienced observers chosen at random to measure step-off and gap displacement would differ by 3 millimeters or more at least 10% of the time, while the same observer making repeat measurements would be expected to differ by 2 millimeters at least 10% of the time. Singer also demonstrated significant interobserver variability in the measurement of intra-articular distal radius fracture fragment displacement using plain radiographs. To date, the accurate and reliable measurement of intra-articular fracture displacements of less than 2 millimeters from plain radiographs has not been established.

The purpose of this study was to determine the accuracy and reproducibility of measured step-off and gap displacements involving the articular surface of the distal radius. Our hypothesis was that step-off and gap displacements of 2 millimeters or less would show poor accuracy and reproducibility for both intra- and inter-observer measurements. This study differs from others in that by using cadaver specimens, we have created a gold standard for the fracture displacements. Earlier studies, lacking such a gold standard, were limited to comparisons among observers and could not comment on the accuracy of measurement. Further, our cadaver model mimics intra-articular fracture in the acute setting. As Kreder et al. acknowledge, "It may well be that some parameters (such as step and gap deformity) are more readily quantified in the acute setting, since fracture lines have not been obscured by the healing process." Finally, by computing tolerance limits, we attempt to define a reliable threshold for the accuracy and reliability of plain film radiography in the setting of intra-articular distal radius fractures. Such information has value to the clinician in the decision-making process regarding the use of CT imaging.

**Methods**

A Melone three-part fracture was created in cadaver forearms to generate a total of 12 combinations of step and gap displacement (Figure 1). The range of step deformity was 3.5mm (0.5 min, 4.0 max) and the range of gap deformity was 3.9mm (0.1 min, 4.0 max). The radiographs were examined by 22 physicians (divided into three groups based on skill level: Group 1: six R1 and R2 level orthopaedic surgery residents; Group 2: four R4 senior orthopaedic surgery residents on the Hand service, five Hand Fellows; Group 3: six experienced Attending hand surgeons and one musculoskeletal radiologist) in a blinded, randomized fashion using a standardized technique. Twice each physician (range 3 weeks to 2 months) measured the step and gap displacements.

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<td>Tolerance (mm)</td>
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Table 1: Results for inter- and intra-observer measurements (see Methods for explanation). * Landis & Koch agreement criteria: <0.20 slight; 0.21-.40 fair; 0.41-.60 moderate; 0.61-.80 substantial; >0.80 almost perfect.
3 months) measured each radiograph to the nearest 0.1mm using Mitutoyo calipers.

**STATISTICAL ANALYSIS**

Agreement among raters was quantified using the intraclass correlation coefficient (ICC) for continuous data and the k-statistic for categorical data (x< 2mm, x> 2mm). Tolerance limits were calculated to describe the value x for which 95% of all measurements will be within ± x 90% of the time. The accuracy of raters was determined by calculating the accuracy of measurement, mean and standard deviation for each observer.

**RESULTS**

Table 1 shows the overall results for this study. For all data in this study, there were no statistically significant differences based upon skill level. The overall average observation was accurate to within .62 ± .53 millimeters (95% C.I.: .59 to .65). Radiographs in which the beam was parallel to the plane of fracture had an observer accuracy of .58 ± .47 millimeters. For radiographs of specimens number two, four and six, which did not have the x-ray beam parallel to the plane of fracture, observer accuracy decreased to .72 ± .70 millimeters (p < .01). Mathematically, this represents a statistically significant difference in accuracy and reproducibility based on the quality of radiograph.

**CONCLUSION**

The results of this study suggest that for intra-articular fractures of the distal radius, observers using plain radiographs, independent of skill level, may accurately measure step-off and gap displacements to within .62 millimeters with substantial to almost perfect agreement. Importantly, the quality of the radiograph proved to be a critical determinant of the ability of an observer to accurately and reliably measure step and gap displacement. These results should aid in the interpretation of outcome studies of intra-articular distal radius fractures based on plain radiography.

**RECOMMENDED READING**


Genomic Sequences and Expression of the RNA Splicing Factors TASR-1 and TASR-2

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Genes are transcribed into protein by a complex of enzymes named RNA polymerase II (Pol II). Before being exported from the nucleus to the cytoplasm as mature messenger RNAs (mRNA), pre-messenger RNA transcripts undergo extensive modification including splicing. Splicing, simply put, allows different portions of a gene to be assembled in several different ways, thus increasing the complexity of proteins without increasing the number of genes. The selection of alternative splicing pathways represents an important step in eukaryotic gene expression. For example, alternative splicing controls sex determination in fruit flies and alternative splicing of type II collagen appears to play important roles in development of the skeleton and osteoarthritis. Aberrant RNA splicing is also commonly observed in leukemia and solid tumors and probably exerts its effects by altering the expression of cell-cycle proteins.

The so-called ‘SR’ splicing factors contain multiple serine (S) and arginine (R) amino acids and play a critical role in RNA splicing. Individual SR proteins show specificity toward different pre-mRNAs and may display unique roles in cell growth and development. Our studies suggest that TLS and EWS, proteins implicated in the genesis of leukemia and sarcomas, may function as adapter molecules that recruit specific SR proteins to RNA Pol II, thus coupling gene transcription to RNA splicing. We have identified and studied two new SR proteins, TLS-associated SR protein-1 and TLS-associated protein-2 (TASR-1 and TASR-2), that bind to normal Ewing’s sarcoma protein (EWS) and TLS ("translocated in liposarcoma").

EWS and TLS are involved in translocations that are very likely to be the critical steps in the development of Ewing’s sarcoma, liposarcomas, chondrosarcomas, as well as other rarer sarcomas. A fusion protein resulting from a translocation may have different biochemical and functional properties than the two component proteins from which it is derived. For myxoid liposarcoma and Ewing’s sarcoma, the corresponding fusion proteins are TLS/CHOP and EWS/Fli-1, respectively. Unlike normal EWS and TLS, these fusion proteins are unable to bind to either TASR-1 or -2 and we have demonstrated that this results in dysregulation of RNA splicing. Disruption of EWS and TLS-mediated splicing pathways by fusion proteins may lead to degradation of unprocessed pre-mRNA or the generation of alternatively spliced products, with potentially profound affects on gene expression in Ewing’s and liposarcoma cells.

Little is known about the structure and function of TASR proteins. TASR-1 and -2 share identical N-terminal domains and differ in their C-terminal regions; however it is not clear whether the two proteins are encoded by separate genes or are the products of alternative splicing of the same primary transcript. The purpose of this study was to first determine whether TASR-1 and -2 are encoded by two different genes. Depending upon this result, we wanted to obtain the DNA sequence for one or both genes. Finally, we studied expression patterns of these proteins to identify any tissue specificity.

METHODS

TASR proteins are evolutionally conserved, to the degree that mouse and human TASR have identical protein sequences. In an attempt to identify mouse and human genomic sequences for TASR-1 and TASR-2, specific DNA primers were designed based upon their cDNA sequences and polymerase chain reaction (PCR) was performed with these primers. The DNAs corresponding to human TASR-1 and TASR-2 genes were amplified using HeLa cell genomic DNA as the template. The DNAs corresponding to mouse TASR-1 and TASR-2 genes were amplified using L-cell genomic DNA as the template. After separation on agarose gel, both mouse and human genomic DNAs were purified and sequenced.

To determine the level of expression of the TASR proteins in different cell lines, Western Blotting was performed using lysates from two Ewing’s cell lines (SK-N-MC & SK-ES) as well as HeLa cells. TASR-1 is highly expressed in

Figure 1: Structure of the TASR gene, schematic of splicing and polyadenylation. (a), The approximate location of each exon within the TASR transcription unit is depicted as an open box and numbered below. While TASR-2 mRNA is generated by transcription from exon I through exon VI, TASR-1 mRNA does not retain any sequence from exon VI but instead contains sequence from exon VII. Bold line represents the promoter region and arrows indicate the approximate locations of polyadenylation signals.
Ewing’s cell lines; SK-ES cells have higher expression than SK-N-MC and both have higher levels of expression than HeLa cells. Northern blotting was performed to examine the expression of TASR proteins in different tissues. TASR mRNAs were found to be ubiquitously expressed and are most abundant in testis.

RESULTS AND DISCUSSION

Sequencing analysis of mouse and human genomic DNAs revealed that TASR-1 and 2 are in fact encoded by a single gene in each species and are the result of alternative splicing. Even though TASR-1 and TASR-2 share the same sequence in the 5’ untranslated region and in the region encoding the N-terminal domain, these two genes diverge in regions encoding the C-terminal domain and the 3’ untranslated region. Several polyadenylation sites are observed in both TASR-1 and 2 genomic sequences, resulting in the generation of multiple mRNA transcripts encoding each TASR protein. The range of expression of the splicing and polyadenylation variants of the TASR gene in human tissue may reflect their essential roles in the proper control of cell growth and differentiation.

It also appears that pseudogenes are present within the human and mouse genomic sequences for both TASR-1 and 2. Pseudogenes in essence are nonfunctional stretches of complementary DNA, or “retroposons”, that have been introduced into the genome by reverse transcriptions. This is significant because it demonstrates that the TASR proteins are evolutionarily ancient and that they are critical molecules in the normal physiology of mammalian cells. This is confirmed by the Northern blot results which showed that the TASR proteins are ubiquitously expressed.

The expression of TASR 1 was found to be highly expressed in Ewing’s sarcoma cell lines versus HeLa cells. This may represent a compensatory response by the Ewing’s cells to the EWS/Fli-1-mediated disruption of the normal interaction between TASR proteins and EWS. These splicing proteins appear to play an important role in the development of a variety of sarcomas. Understanding the structure of TASR-1 and TASR-2 is an important step towards developing targeted therapies for these devastating diseases.
molecular treatments for these devastating cancers.

**Recommended Reading:**


Cancers arise when genetic changes, such as chromosomal translocations and point mutations, enable cells to escape the control mechanisms that usually serve to limit cell division to periods of growth or normal replenishment of cells. A better understanding of the specific pathways that lead from a genetic change to a cancerous cell may yield targets for molecular treatments.

Ewing’s sarcoma is a malignant neoplasm of bone and soft tissue. A chromosomal translocation, t(11;22) that fuses two distinct genes is associated with a large percentage (85%) of Ewing’s tumors. The translocation results in the Ewing’s sarcoma protein (EWS) being fused to the DNA binding domain of the ETS transcription factor Fli-1 (Figure 1). These fusion proteins retain the N-terminal portion of normal EWS (WT-EWS) while the fusion partner Fli-1 replaces the C-terminal portion of WT-EWS. The N-terminal portion of normal EWS has been found to bind the largest subunit of the RNA polymerase II (Pol II) complex, an enzyme necessary for transcription of genes from DNA to messenger RNA (mRNA). The C-terminal domain of normal EWS recruits proteins referred to as serine-arginine (SR) splicing factors that function in splicing of pre-mRNA to mRNA. The EWS/Fli-1 fusion protein retains the ability to bind RNA Pol II. However, EWS/Fli-1 cannot recruit SR proteins due to the replacement of its C-terminal domain by the Fli-1 fusion partner.

The EWS/Fli-1 fusion protein was originally believed to induce cellular transformation through improper activation of Fli-1 target genes. However, new evidence indicates that the EWS/Fli-1 fusion protein may interfere with adapter functions of normal-EWS. In an adenovirus E1A splicing model, EWS/Fli-1 has been shown to alter splicing of exogenous pre-mRNA when compared to ‘normal’ splicing patterns mediated by WT-EWS. This study was designed to test the effects of inhibiting expression of EWS/Fli-1 on patterns of splicing of molecules implicated in the development of sarcomas.

**RESULTS**

Using the Ewing’s sarcoma cell line SK-N-MC as a model system, a series of transfections were performed to integrate a “doxycycline-off” antisense EWS/Fli-1 construct into the genome of the Ewing’s cells. In this system, sense EWS/Fli-1 is expressed in the presence of doxycycline but upon withdrawal of doxycycline the antisense EWS/Fli-1 construct is expressed. Antisense EWS/Fli-1 then inhibits expression of the ‘normal’ EWS/Fli-1 sarcoma protein.

In our genetically engineered Ewing’s sarcoma cells, induction of antisense EWS/Fli-1 was monitored through the co-expression of green fluorescent protein (GFP) that could be visualized using laser light (Figure 2). RT-PCR analysis of EWS/Fli-1 mRNA and Western blotting of the EWS/Fli-1 fusion protein were used to monitor EWS/Fli-1 expression in induced and non-induced Ewing’s sarcoma cells.

The inducible expression of EWS/Fli-1 antisense RNA proved to be effective in reducing the quantity of EWS/Fli-1 fusion protein to an negligible level after withdrawal of doxycycline from the culture medium. Comparison of cellular growth rates indicated that antisense expression correlated with a decrease in the proliferation of Ewing’s sarcoma cells (Figure 3). In addition, RT-PCR analysis showed that down-regulation of EWS/Fli-1 leads to changes in mRNA splicing patterns for the cell surface marker CD44 and the tumor suppressor Bin-1.

**DISCUSSION**

The EWS/Fli-1 fusion protein is the hallmark of Ewing’s tumors, yet little is
known about its functional effects on cells. This study explored the possibility that the fusion protein could promote tumorigenesis by interfering with mRNA splicing in Ewing's cells. Aberrant splicing of pre-mRNA is a poorly understood but common feature of human tumors. Because alternative splicing can lead to the expression of nonfunctional proteins or proteins with altered activity, this process might have important implications as a general mechanism for the initiation of tumor development.

Our results showed that the EWS/Fli-1 fusion protein was successfully down-regulated by the expression of antisense EWS/Fli-1 RNA in Ewing's cells. This inducible system permits us to study genetically identical cells that differ only in the presence or absence of the EWS/Fli-1 fusion protein. As appropriate control constructs are also used, any changes in splicing patterns in these cells should therefore be attributable to the effect of the fusion protein itself.

Alternatively spliced forms of CD44 and Bin-1, proteins important in cell growth and differentiation, were identified by comparison of splicing patterns before and after the EWS/Fli-1 fusion protein was down-regulated. CD44 splice variants have been associated with increased invasiveness and loss of contact inhibition in tumor cells. Alternatively spliced forms of Bin-1 no longer possess the ability to interact with the protein myc, resulting in the inability of myc to function as a tumor suppressor. Our findings indicate that aberrant splicing of pre-mRNA, as mediated by the EWS/Fli-1 fusion protein, may explain the myriad changes in gene expression that transform a benign mesenchymal cell into a malignant sarcoma.

**Recommended Reading**


Using a Freeze Fixation Technique and Histological Crimp Analysis for Mapping the Strain in Functionally Loaded Ligaments

RICHARD BOORMAN, M.D., M.SC., TONY NORMAN, B.S.E., FREDERICK A. MATSEN III, M.D., AND JOHN CLARK, M.D., PH.D.

In a non-loaded state, type I collagen fibrils in tendons and ligaments assume a sinusoidal wave shape that disappears with modest tensile loads (Gathercole and Keller, 1991). This “crimp” is visible by polarized light microscopy because collagen fibrils are aligned in uniform register. A better understanding of how ligaments distribute load may yield critical information on how they fail with injury and disease. Yet the response of crimp to load has, by necessity, been studied primarily in subunits of tendons and ligaments small enough to transilluminate and not under functional loading conditions. Freeze-substitution fixation of tissues plunge-frozen under load permits conventional polarized light and electron microscopy examination of collagen fibers preserved in a loaded state. This study examines whether the distribution of strain can be mapped in loaded ligaments frozen in situ and fixed by freeze-substitution. In a second line of investigation crimping behavior of partially sectioned, loaded ligaments preserved by freeze-fixation was used to determine whether ligaments are composed of independent bundles of interconnected fibrils. We hypothesized that (A) the crimping pattern of patellar ligaments under polarized light would progressively extinguish with increasing loads, and (B) that fibrils within a loaded “functional band” would not recoil into a uniformly un-crimped state unless the entire band is transected.

METHODS AND MATERIALS

Hind-limbs of 11 mature New Zealand white rabbits sacrificed according to the ethical guidelines of the local animal care committee were harvested, and the soft tissues dissected leaving the femur- intact stifle joint- and tibia and extensor mechanism completely intact. The joint was fixed on to a frame while flexed at 90°, and a simulated isometric quadriceps pull was applied by means of a wire passed through the patella, thus functionally loading the patellar ligament. Specimens were loaded at 9N (n=3), 18N (n=3), 36N (n=3), 67N (n=3), 100N (n=1), and 220N (n=1). After 30 seconds a loaded joint was immersed in isopentane cooled to -165°C with liquid nitrogen. These knees and 2 unloaded control specimens were then fixed by freeze-substitution in methanol/acetone solutions of acrolein (-80°C for 4 days) and glutaraldehyde (-20°C for a further 4 days). Once brought to room temperature, the patellar ligaments were prepared for histological examination by paraffin embedding, 10μm sectioning in the mid-sagittal plane and staining with Masson's trichrome. The specimens were analyzed under polarized light microscopy, and the crimp pattern was analyzed by an observer blinded to the loading history. Based upon the relative amount of un-crimped tissue a speculation was recorded by the blinded observer as to whether no load, minimal load (9N), moderate load (18 and 36N), or high load (>67N) was applied.

Collagen Fiber Interaction

Three specimens had a "deep" transverse scalpel cut made through the anterior band of the patellar ligament at the mid-point. Three specimens had a "superficial" cut partially through the anterior band. All these specimens were loaded at 150N. Two uncut controls were similarly loaded at 150N. Specimens were prepared for polarized light microscopy and scanning electron microscopy.

RESULTS

Unloaded ligaments displayed a consistent, regular pattern of crimp along the entire length of the specimens (Figure 1). The specimens loaded at 9 Newtons were virtually indistinguishable from the unloaded specimens, with the exception of one specimen which had some uncrimping near the insertions. The specimens loaded at 18N had a band of uncrimping in the central 1/3 of the ligament.

The specimens loaded at 36 N had an increased area of un-crimping but crimping was still evident in the deep and superficial fibers of the ligaments.
Collagen Fiber Interaction

Loading the uncut ligaments at 150N resulted in complete un-crimping of the ligament. “Deep” section through the anterior 1/3 of the patellar ligament resulted in a crimping of the cut fibers which was visible to the full depth of the incision, and which was visible from insertion to insertion (Figure 5). The uncut fibers immediately deep to the incision were loaded and completely un-crimped (Figure 5). The cut fibers at the deepest point of the incision were retracted to approximately the same distance as the superficial fibers. Superficial section, partially through the superficial band of the patellar ligament, resulted in a localized retraction and crimping of fibers near the cut site (Figure 6). However, the cut fibers remained uncrimped along the majority of the length of the ligament. A triangular shaped lesion was visible on SEM, as the cut fibers adjacent to the loaded fibers were not as retracted, nor as crimped as the superficial cut fibers (Figure 7).

DISCUSSION

This study shows that freeze-fixation can preserve ligament collagen in an un-crimped state, and thus loaded fibers can be distinguished from non-loaded fibers in which a crimp remains. Using this technique, the rabbit patellar ligament showed a consistent pattern of strain dispersion with increasing load. Under these loading conditions, the central 1/3 of the ligament un-crimped at lower applied loads than the deep and superficial regions. The crimp in the entire specimen was extinguished at approximately 67N which, based upon ligament cross-sectional estimates, correlates closely with the previously reported toe-region of the stress strain curve of the rabbit patellar ligament (approx 4.5 MPa) (Woo et al, 1993). The strength of this technique is that it enables investigators to examine entire ligaments or tendons preserved in a functionally loaded state using various forms of microscopy, including the potential use of high
This study also confirms that the patellar ligament is composed of independent parallel units. When transected, the anterior third of the ligament remains fully crimped even when the intact ligament is under sufficient tension to completely ablate crimp. This condition would not occur in the face of any functional crossover between cut and uncut segments. It also strongly implies that mechanical coupling between collagen fibrils does exist within the anterior band, since partial section of that segment does not cause full recoil of the transected part. Collagen fiber recruitment is thought to be important to how ligaments resist elongation under load. This evidence for lateral support between collagen fibers further advances our understanding of the functional ultrastructure of normal ligaments.

**Recommended Reading**


Woo et al., *J. Orthop Res.*, 1993
Arthritis of the shoulder can substantially compromise a patient's general health status (Matsen et al, 2000). The goal of an arthroplasty is to improve not only the function of the joint, but also the patient's overall health and well being. Health-related quality of life, self-assessment questionnaires have been used to document these results (Hozak et al, 1997). The Medical Outcomes Study Short-Form 36 (SF-36) questionnaire is particularly useful in this regard and has been used extensively in various patient groups (Ware, 1993). This questionnaire has been tested for validity and reliability, and population control results are published.

Total shoulder arthroplasty (TSA) is the procedure of choice for managing patients with advanced glenohumeral osteoarthritis, however the degree to which shoulder arthroplasty improves the longer-term quality of life remains undefined. Furthermore, the relative effectiveness of shoulder arthroplasty in comparison to other common surgical interventions is unknown.

The purpose of this study was (1) to evaluate the impact of TSA on the SF-36 in patients with glenohumeral osteoarthritis several years after surgery, (2) to compare the SF-36 scores for patients before and after TSA to those from a control population, and (3) to compare the results of TSA to the results of other effective orthopaedic and cardiac surgical procedures.

**Methods and Materials**

One hundred and thirteen patients with primary glenohumeral osteoarthritis were treated with primary total shoulder arthroplasty (TSA) by an individual surgeon (FAM) between January 1, 1993 and December 31, 1997. All patients completed the SF-36 before surgery, and at 6-month intervals post-operatively. Eighty-five patients were men and twenty-seven were women. Thirteen patients (12%) underwent bilateral total shoulder arthroplasties during that time. For these thirteen patients only the information related to the first operated shoulder was included in the analysis. A total of ninety-one patients had followup SF-36 data collected during the 30-60 month time frame after surgery. The mean of the 6 monthly interval scores for each dimension, reported in the 30-60 month time window, for each patient, was used as the post-operative score for statistical comparison.

Postoperative values for SF-36 dimensions were compared with preoperative values by using a paired t-test. Further, patients' SF-36 scores were compared by paired t-test to those of age- and gender-matched general population controls reported in the literature. All analyses were performed using SPSS 10.0 for Windows.

A Medline search was performed to find articles that report SF-36 results both pre-operatively and post-operatively, and at least one year following total hip replacement and coronary artery bypass procedures. The average score weighted by sample size for each dimension from all studies that met our inclusion criteria were then calculated for both the THA patients and the CABG patients. These weighted average scores were compared to the TSA data from this study.

**Results**

The average age of the patients in the study group was 64 years (S.D. = 10 years), 62 years (S.D. = 10 years) among the seventy-two men and 73 years (S.D. = 7 years) among the nineteen women (p < .01). The ninety-one patients for whom 30-60 month followup data were available were not significantly different from the 22 patients for whom data in this time window were not available with respect to age, gender, or preoperative health status. Patients improved statistically significantly in the following SF-36 dimensions: physical role function (p<0.01), comfort(p<0.01), social function (p<0.01), and mental health (p<0.05). Preoperatively, patients scored poorer than population controls on all but two SF-36 dimensions (mental health and...
general health perception). These differences were statistically significant. After the surgery, although the amount of difference was much smaller, the scores for patients were still lower than population controls for most SF-36 dimensions (Figure 1). Preoperatively, TSA patients scored higher than THA patients on all SF-36 dimensions. Postoperatively, there was little difference between the TSA and the THA patients (Figure 2). Similarly, the TSA patients scored higher than the CABG patients in all SF-36 dimensions preoperatively. After surgery, the TSA patients scored better or equal to the CABG patients (Figure 3).

**Discussion**

The patients in this study experienced significant improvements in their health-related quality of life following TSA for glenohumeral osteoarthritis. These improvements in multiple dimensions of the SF-36 were durable, since these gains were documented between 30 and 60 months postoperatively. This study also documents the diminished quality of life of individuals coming to surgery for glenohumeral osteoarthritis. In six out of eight SF-36 dimensions, the preoperative SF-36 scores for these patients was significantly lower than that of age- and gender-matched population controls. These scores improved after surgery, but did not reach the levels found in the control population (Radosevich et al, 1994).

As increasing attention is focused on health care costs, the value of surgical intervention to the patient and the relative value of these procedures need to be well documented. In this spirit, we compared the changes in patient health status following TSA to the previously reported changes in quality of life following total hip arthroplasty, which is considered to be a very effective procedure. We observed that the SF-36 scores for patients with arthritis of the hip were lower than those of patients with shoulder arthrosis. Postoperatively, both reconstructive procedures (total shoulder and total hip) demonstrated a similar effectiveness in improving quality of life.

We also compared our results to another chronic medical condition which affects patients of a similar age, and for which the surgical solution is generally believed to be very effective: coronary artery bypass graft surgery. Patients with shoulder osteoarthritis appeared to score generally lower on the comfort score than those patients with chronic angina. In the other six health-related quality of life dimensions however, the patients with glenohumeral osteoarthritis tended not to score as low as the chronic angina patients did preoperatively. Postoperatively however, the total shoulder patients, and the CABG patients were brought up to similar levels for all eight SF-36 dimensions.

In conclusion, this study has shown that total shoulder arthroplasty can improve the quality of life in patients with glenohumeral osteoarthritis several years after surgery. Postoperative SF-36 scores were lower than the control population, but they were similar to those previously reported for other effective orthopaedic and cardiac procedures.
RECOMMENDED READING


Ware JE, Jr. SF-36 Health Survey: Manual and Interpretation Guide. The Health Institute, New England Medical Center, Boston, MA, 1993.
Efficient bone mass in the elderly arises due to degradation of the normal balance between bone resorption (i.e., removal) and bone formation (i.e., new bone growth) typical in the young adult. Current pharmaceutical strategies to counteract bone loss are highly successful in blocking the elevated resorption associated with menopause. However, options for enhancing bone formation as a means of increasing bone mass are extremely limited. Given our rapidly aging population, the current inability to safely and effectively build bone mass consigns millions to a fate of elevated fracture risk for a substantial portion of their lives.

Exercise represents one of the few potential means of building bone mass. To date, however, exercise regimens have proven only minimally successful in building bone mass. The elderly, in particular, are unable to consistently comply with the high-impact, strenuous loading events (such as jumping and vigorous running) typically associated with even minimal bone accretion. One objective of our group has been to develop low magnitude loading regimens that are highly stimulatory for bone formation. Based on data from our group and others, it appears that fluid flow within the tissue underlies bone mechanotransduction. We therefore hypothesized that inserting a non-loaded rest pause between each loading cycle (which would increase fluid flow within bone) would enhance the osteogenic potential of a low magnitude, locomotion-like mechanical loading regimen. To examine this hypothesis, we contrasted the ability of low magnitude loading regimens with and without a 10-s rest interval inserted between each load cycle to induce bone formation.

**METHODS**

Eighteen adolescent female C57Bl/6j mice (10 wk) underwent external loading of the right tibia using the non-invasive murine tibia loading device. Mice were randomly assigned to three groups: 1) low magnitude (low; n=6), 2) low magnitude, rest-inserted (rest-inserted, n=6), and 3) high magnitude (high, n=6). The low magnitude group underwent 100 cycles of a 0.25 N peak load, 1 Hz, 0.01/s strain rate trapezoidal waveform for 5 consecutive days (roughly equivalent to walking). The low magnitude rest-inserted group underwent a 10 cycle/d regime with a 10 s pause inserted between each load cycle. Peak load and peak strain rate were equivalent to the low magnitude group. The high magnitude group underwent a 100 cycle/d, 1 Hz regime with the peak load and strain rate doubled compared to the low magnitude group (roughly equivalent to vigorous running). The overall daily external loading period for the mice in all groups was therefore 100 s. All animals were allowed 23 d of additional cage activity following the 5 day loading regimen to facilitate consolidation of new bone. Bone formation was assessed via dynamic histomorphometry.

**RESULTS**

Consistent with normal long bone growth, the young mice examined in this study exhibited active osteoblast activity on both endocortical and periosteal surfaces at the initiation of the study. Periosteal bone formation rate was significantly elevated by both high magnitude (p=0.01; 3.7-fold vs paired contralateral tibia) and rest-inserted loading (p=0.01; 2.3-fold vs paired contralateral tibia; Figures 1, 2). While high magnitude and rest-inserted loading were more stimulatory for osteoblasts than low magnitude loading, no statistical differences were observed between high magnitude and rest-inserted loading with any assessed bone formation parameter. As compared to intact bones, both high magnitude (p=0.05) and rest-inserted (p=0.03) loading induced small, but significant increases in cortical area (5.1 and 6.2%, respectively).

**DISCUSSION**

Using the non-invasive murine tibia loading model, we found that low magnitude, rest-inserted loading significantly enhanced periosteal bone formation in growing mice. Surprisingly, the bone formation elicited by 10 cycles of rest-inserted loading was statistically comparable to that induced by a standard locomotion-like waveform 10-fold greater in cycle magnitude rest-inserted group underwent a 10 cycle/d regime with a 10 s pause inserted between each load cycle. Peak load and peak strain rate were equivalent to the low magnitude group. The high magnitude group underwent a 100 cycle/d, 1 Hz regime with the peak load and strain rate doubled compared to the low magnitude group (roughly equivalent to vigorous running).
number and 2-fold greater in load magnitude. To our knowledge, this represents the first report of enhanced bone formation induced by a reduced mechanical stimulus.

While rest-inserted loading remains to be optimized, it represents a departure from previous modalities of repetitively loading bone tissue. In general, in vivo and in vitro investigations have established the paradigm that the greater the mechanical stimulus, the greater the response elicited from bone cells or bone tissue. Here, we found that 10 cycles of rest inserted loading substantially enhanced bone formation compared to 100 cycles of an identical magnitude repetitive protocol. Surprisingly, the amount bone formation was not significantly different than that achieved with a group exposed to twice the load magnitude and rate and ten times the number of load cycles. The ability of rest-inserted loading to induce more (or equivalent) bone formation with less actual loading of bone directly challenges the concept that high magnitude, high impact loading is required to build bone mass.

In this context, the broad relevance of these data lie with their potential to substantially extend the skeletal benefits of mild exercise. The ability to induce bone formation in growing or mature skeletons via low magnitude, non-impact loading would make bone building exercise accessible to all ages while minimizing injury risk. A number of possibilities might be readily explored to implement rest-inserted loading. Tai Chi, which has already been suggested to enhance balance in the elderly, might be modified such that postures between movements are deliberately held for longer periods of time. Similarly, small hand weights might be held in fixed positions between each repetition to enhance bone mass in the upper extremities. With such ease of implementation, rest-inserted waveforms might also serve to beneficially modify the locomotion related loading that has proven to be of limited effectiveness in inhibiting space induced bone loss.

**RECOMMENDED READING**


Evidence that FGF-18 is a Growth Factor for Mature Human Articular Chondrocytes

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Articular cartilages are specialized connective tissues that dissipate loads as the bearing surfaces in joints. Cartilage cells, the chondrocytes, synthesize a complex extracellular matrix containing collagens, proteoglycans, and noncollagenous proteins. Type II collagen, the predominant collagen of cartilage is polymerized into a network and is responsible for the tensile strength of cartilage.

Trauma and disease of the synovial joint can cause structural damage to the articular cartilage. Changes include age-related fibrillation, cartilage degeneration due to osteoarthritis, and focal chondral and osteochondral defects. In most other tissues, such lesions would be rapidly repaired. Adult articular cartilage, however, has only a very limited capacity to heal. Efforts to stimulate cartilage healing have focussed on two general areas: surgical procedures, designed to stimulate the endogenous repair response, and biological repair, designed to stimulate chondrocyte proliferation and/or matrix production by the application of peptide growth factors or by cell transplantation.

The fibroblast growth factors (FGF's) play roles in tissue repair, embryonic development, and growth in animals. FGF-18, a novel member of the FGF family has been shown to stimulate hepatocytes and intestinal cells to proliferate. As part of a screen for factors that regulate angiogenesis, we expressed Fgf18 by adenovirus-mediated gene transfer in the pinnae of nude mice. Although an angiogenic response was not observed, a surprising phenotype developed: compared to pinnae that received null adenovirus, those that received adenovirus-expressing Fgf18 became visibly thicker. The increase in thickness was largely due to an Fgf18-mediated increase in chondrocyte proliferation, type-II collagen synthesis, and extracellular matrix production.

These interesting observations prompted us to investigate if Fgf18 was expressed by articular chondrocytes and examine the effects of highly purified FGF-18 protein on articular chondrocytes in vivo and vitro. Our results suggest that Fgf18 may play a role in the biology of normal cartilage.

METHODS

Cell and tissue culture

Full thickness adult human cartilage, and chondrocytes (high density monolayer or micromass) isolated from talus joints (Northwest Tissue Center, Seattle) were maintained in serum free culture (DMEM) in the presence or absence of 100ng/ml recombinant FGF-18 protein. Cell numbers from monolayer cultures were determined weekly with the aid of a Neubauer haemocytometer. Cell layer collagen from monolayer or micromass cultures was solubilized by pepsin digestion and the a1(II)chains were identified by western blotting after SDS-PAGE.

Histochemistry and Immunohistochemistry

Micromass cultures were fixed, embedded in paraffin, sectioned and stained with safranin O, H&E and immunostained with type II collagen antibody and proliferating cell nuclear antigen (PCNA) antibody.

RESULTS AND DISCUSSION

In situ hybridizations revealed that Fgf18 mRNA and mRNA for two of its receptors, Fgfr3-(IIIc) and Fgfr2-(IIIc), were localized within chondrocytes of human talus articular cartilage.

Incubation of primary cultures of adult human talus articular chondrocytes with FGF-18 protein increased the proliferation of these cells (Figure 1).

Western blot analysis of collagen deposited in the extracellular matrix showed an increase in type II collagen accumulation within one week after culture in the presence of FGF18 (Figure 2).

In high-density micromass cultures, (Figure 3) the thickness of the cell layer, cell numbers, staining of chondrocyte nuclei with antibodies to proliferating cell nuclear antigen (PCNA) (Figure 3, panels B, D) and type II collagen accumulation in the extracellular matrix (Figure 3, panels A, C) were increased by incubation with media containing 100ng FGF-18/ml for 4 weeks. Increased PCNA staining was also seen in the nuclei of chondrocytes from explant cultures treated with FGF-18 (data not shown).

These data imply that FGF-18 can act as a trophic factor for adult human articular chondrocytes in primary cell
culture and in explants. In addition, these data show that the differentiation state of the chondrocytes, as determined by type II collagen, was maintained by FGF-18 under these conditions. The expression of Fgf18 and its receptors by chondrocytes in cartilage suggests that Fgf18 may play an autocrine role in the biology of normal articular cartilage and could potentially be useful in stimulating chondrocytes to proliferate and promote repair of damaged cartilages.

**RECOMMENDED READING**


Figure 2: Western blot showing type II collagen deposition.

Figure 3: Immunohistochemical staining of 4 week micromass cultures of human adult talus chondrocytes. Panels A, B, untreated; Panels C, D, FGF-18 treated. Magnification 40X.

A Newly Identified Site of Cross-Linking Between Collagens IX and II: Insights On Molecular Assembly In Cartilage

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The collagenous framework of articular cartilage matures from a covalently cross-linked heteropolymer of types II, IX and XI collagens (Figure 1). Type IX collagen is a quantitatively minor component of the adult tissue but it has an important role in the assembly and function of the matrix. In cartilage, type IX collagen molecules are bound to the surface of type II collagen fibrils and to each other via lysine-derived cross-links. Mutations in type IX collagen genes can cause multiple epiphyseal dysplasia in which the cartilage collagen fibrils appear abnormal and show evidence of a deficiency in intermolecular cross-linking of type IX collagen. The type IX collagen molecule is a heterotrimer of α1(IX), α2(IX), and α3(IX) chains. Each chain contains three relatively short triple helical domains (COL1-3) and four noncollagenous domains (NC1-4). The three chains are linked intramolecularly by disulfide bonds in the NC1 and NC3 domains.

When analyzing the pepsin-solubilized type II collagen from bovine and human cartilages on SDS-PAGE by Western blotting, we consistently observed a minor fraction of type II collagen in a disulfide-bonded complex. By further characterization of the protein, we revealed a previously unrecognized and prominent intermolecular cross-linking site between collagen types II and IX.

MATERIALS AND METHODS

Slices of fetal human and fetal bovine epiphyseal cartilage were extracted at 4°C in 4M guanidine HCl for 24 h to remove non-cross-linked matrix proteins and proteoglycans. The washed residues were minced and digested with pepsin and salt fractionated into types II, IX and XI collagens. Type II collagen was resolved on a BioRad A5m agarose molecular sieve column. Protein fractions were assayed by SDS-PAGE and transblotted to PVDF membrane for either Western blot analysis or amino-terminal protein microsequencing. CNBr digestion was carried out in 70% formic acid at room temperature for 24 hr. Peptides containing the α1(IX)NC1 sequence were purified by a mAb 2B4 affinity column, followed by reverse-phase HPLC on a C8 column. Purified peptides were analyzed by Western blotting with a mAb 284. For amino-terminal sequence analysis, protein bands were transblotted to PVDF membrane and analyzed and identified by amino-terminal microsequencing on a Porton 2090e gas phase sequencer equipped with on-line HPLC analysis of PTH-derivatives.

RESULTS AND DISCUSSION

Pepsin-extracted type II collagen from fetal bovine epiphyseal cartilage was fractionated on an agarose molecular sieve column. Analysis of protein across the chromatogram by SDS-PAGE revealed a higher molecular weight (150 kDa) fraction of type II collagen that appeared to be disulfide bonded. After disulfide bond cleavage with DTT, the reduced product migrated slightly slower than the α1(II) chain (Figure 2). Both the non-reduced and reduced bands were recognized by antibodies to type II collagen. N-terminal protein microsequencing of the reduced band after transblotting to a PVDF membrane gave two running sequences. One, GVMQGPM GPM GPRGPP*, matches the N-terminus of the main triple helical domain of the type II collagen molecule, while the other, LKRDPGAGLP*GPRG*, matches a sequence in the COL1 domain of pepsin-derived bovine α1(IX). The results indicate, therefore, that the parent fragment was α1(IX)COL1 linked covalently to the triple-helix of an α1(II) chain. The equivalent disulfide-bonded entity was also identified in digests of fetal human cartilage.

In addition to binding to antibodies against a triple-helical epitope in type II collagen, the human protein also reacted with monoclonal antibody 284. Monoclonal antibody 284 was originally developed and used to detect a proteolytic cleavage product of a Proline/Leucine bond in the α1(II) C-telopeptide found in cartilage and body fluids. The epitope recognized by the antibody is the -EKGPDP sequence, in which the C-terminal proline is essential for immunoreactivity. Coincidentally, the antibody also reacts with intact human α1(IX) chains, which end in a similar sequence, NKGDP at the C-terminus. Therefore, we used 284 antibody to track peptide fragments that contained the -KGPDP sequence. Conversely, bovine α1(IX) lacks this sequence it does not react with 284.

Figure 1: Molecular diagram showing the cartilage collagen heteropolymeric fibril and sites of covalent interactions.
To define precisely the sites of intermolecular cross-linking, a mAb 2B4 affinity column was used to purify cross-linked CB peptides that contained α1(IX)NC1 from a CB digest of human type II collagen. A methionine in this domain ensures its release as a short peptide. Peptides eluted from the affinity column were further purified by RP-HPLC then SDS-PAGE. Western blot analysis was performed with mAb 2B4.

Amino-terminal sequence analysis of the purified peptide identified it as α1(IX)NC1 cross-linked to a helical site in α1(II) CB9,7, which most likely is the known 930 hydroxylysine cross-linking residue. The discovery of this domain of type IX collagen linked to the type II collagen triple helix was not predicted from earlier methods of finding as cross-linking sites in the collagen IX molecule (Figure 1). It was known that type IX collagen is extensively cross-linked in cartilage matrix through lysyl oxidase-mediated bonds to both N- and C- telopeptides of type II collagen and between the type IX collagen molecules themselves through the α3(IX)NC1 domain. The finding of α1(IX)NC1 links to type II collagen, taken with other properties of fibril associated collagen molecules, suggest that the initial docking and cross-linking of type IX molecules on type II fibrils occurs through the COL2/NC1 domain interacting with the hole region of the quarter-staggered assembly (Figure 3).

**Recommended Reading**


Reproductive Hormone Effects on ACL Strength

Emma Woodhouse, M.D., Peter T. Simonian, M.D., Allan F. Tencer, Ph.D., and Phil Huber, Ph.D.

In the United States there are approximately 100,000 ACL injuries annually, corresponding to one injury per 3000 individuals per year. Epidemiologic studies show that female athletes suffer 2 to 8 times more ACL injuries than their male counterparts. Many young women athletes take oral contraceptive pills for menstrual regulation, to decrease acne or dysmenorrhea and for contraception. Cyclic fluctuations in estrogen levels have been implicated in the increased vulnerability of the female ACL, however no studies to date have investigated whether the hormonal milieu of normal menses vs oral contraceptive intake have differential effects on ACL response to stress. If there is a difference in their effect on the ACL, it could have important implications for female athletes of all levels.

In our study we attempt to use a rat model of normal menstrual cycle and oral contraceptive administration to investigate the chronic effect of two typical hormonal milieus on ACL collagen mechanics.

METHODS

Female rats undergo cyclic hormonal changes much like women only their cycle is 5 days in length rather than 28 days. 40 female Sprague-Dawley sexually mature rats (avg body weight 150g) were be obtained from a commercial laboratory. The rats were housed individually in cages and fed rat chow and water ad libidum. They were kept under standard conditions. The 40 female rats were divided evenly into two experimental groups called M and O. All rats were kept for 60 days which corresponds to 12 oestrus cycles. The rats in group O were given oral contraceptive steroids dissolved in 0.25ml propylene glycol orally by tube. The ethinylestradiol dose was 1.27ng. The levonorgestrel was 4.5ng. These doses were estimates of the rat equivalent dose of human oral contraceptive pills based on differential weight and bioavailability. The rats were given the combination steroid or placebo at the same time each day for 4 days and then it was held for 1 day to simulate the pill free week in human OCP's. After 40 days, 6 rats from each group were selected randomly to undergo daily phlabotomy for 5 days (0.75cc blood per day.) The blood was sent on ice for estrogen and progesterone levels at a commercial laboratory. At the end of 60 days, the rats were sacrificed in a CO2 chamber. One femur-ACL-tibia complex from each rat was then stripped of all soft tissue and the bones potted in methylmethacrylate. The experiment began with 21 rats in the control group and 19 in the experimental group. One of the experimental rats died in week four so eighteen experimental rats and twenty one control rat specimen were dissected. Two ACL's from the experimental group and two from the control group were ruined during the potting process. One was dropped on the floor and broke while the other three had methylnemethacrylate touch the ACL. These specimens were discarded. The remaining specimens (sixteen experimental and nineteen control) were tested using a custom drop fixture. The ACL was loaded in extension as it hung suspended from the proximal pot by a falling weight. Three values were recorded for each specimen using a load cell and computer: load to failure, energy to failure and elasticity. The statistical significance of differences between the two groups was evaluated by unpaired t-test.

RESULTS

The results of the blood hormone levels drawn from the rats on days 41-45 are shown in table 1. An unpaired t-test was used to compare the hormone levels of 6 rats from each of the experimental and placebo groups. The rats in the experimental group had significantly lower estrogen levels on cycle day three (p<0.025) than the placebo group. The rats in the experimental group also had significantly higher progesterone levels on days four and five compared with the placebo group. (p<0.005) Figures B and C graph the hormonal profile of the experimental and control group respectively. The control group have a midcycle estrogen surge and late cycle progesterone increase.

Table 2 shows the results of specimen loading. The Peak load, k-value and energy to failure were analyzed using an unpaired t-test. The ratACL's from the experimental group had a significantly decreased stiffness. There was no significant difference in peak load or energy to failure.

CONCLUSION

The influence of female sex hormones on collagen metabolism is complex. Estrogen acutely decreases the total amount of collagen in rat tendon, fascia, hip capsule and periodontal tissue. In rat uterus and primate sex skin, estrogen increases synthesis of new type 1 and 3 collagen.
while also increasing collagen degradation. Estrogen also increases collagen crosslinking, speeding the conversion of newly synthesized collagen to mature collagen. In post-menopausal women, estrogen and progesterone combined therapy at low doses decreases collagen type 1 while increasing type 3 collagen.

Liu et al have done several studies investigating the role of female sex steroids on ACL tissue. In 1996 they demonstrated estrogen and progesterone receptors on the ACL using immunohistochemical techniques. These receptors have also been localized on both human and rabbit ACL by reverse Polymerase Chain Reaction. Liu et al also found that physiologic doses of estrogen have a dose dependent effect on rabbit ACL tissue reducing fibroblast proliferation and rate of collagen synthesis. In a follow up study, the group noted that the dose dependent effect of estrogen seen on days 1 through 3 was attenuated on days 7, 10 and 14 of treatment. Also, type 1 collagen synthesis was decreased but not type 3 collagen. Type 3 collagen synthesis remained unaffected by estrogen exposure. Type 1 collagen tends to impart mechanical strength to connective tissue while type 3 collagen is correlated with elasticity. The authors concluded that sudden or cumulative fluctuations in serum estrogen concentration may induce metabolic changes in ACL fibroblasts which would predispose the ligament to injury.

Sciore et al demonstrated that estrogen and progesterone receptor transcripts are expressed in rabbit and human ligament (including anterior cruciate ligament) in both sexes. Message levels for the estrogen receptor were influenced during pregnancy while message levels for the progesterone receptor were unaltered. Ligament response during pregnancy and post-partum was ligament specific when comparing the MCL and ACL.

Slautebeck et al studied ovariectomized rabbits which were given high physiologic doses of estrogen for 30 days. A significant reduction in ACL load to failure was found in these rabbits vs ovariectomized rabbits without hormone administration (p=0.02) suggesting that estrogen has an acute deleterious effect on ACL strength. This study indicated that the effect of estrogen on ACL tissue metabolism seen by Liu et al may be responsible for the increased mechanical failure of the female ACL seen clinically.

Wojtys et al attempted to link menstrual cycle phase with incidence of ACL injury. 28 women with non-contact ACL injuries were evaluated for various factors including menstrual cycle phase. The study found fewer than expected injuries in the follicular phase and greater than expected injuries in the ovulatory phase although these results were not statistically significant. Moller-Nielsen et al investigated the role of oral contraceptives in the epidemiology of traumatic soccer injuries in a prospective study of 86 female athletes. They found a statistically significant reduction in "traumatic injuries" in athletes using oral contraceptives (p=0.05) however the injuries were not stratified and there is no specific data on ACL injuries. The authors attributed this difference to reduced premenstrual symptoms in OCP users. Mykelburst et al prospectively studied Norwegian handball players and found significantly fewer injuries during the midcycle. Of note half of the women studied by Mykelburst were taking oral contraceptive pills. These results indicated that further study was needed to determine whether cycle phase or oral contraceptive use impact ACL injury in female athletes.

Our study focused on the chronic effect of hormonal milieu (ovulatory vs OCP regulated cycle) on ACL mechanics. The different hormone
levels between the control and experimental groups suggest that the rats in the placebo group underwent an ovulatory cycle while the experimental group had more stable estrogen and progesterone levels as is typical of cycles under oral contraceptive control. Our results show that rats having undergone 12 oestrus cycles regulated by oral contraceptive steroids vs those that have undergone 12 oestrus cycles without exogenous steroids have different ACL response to mechanical stress. Specifically the hormone treated rats had significantly increased ACL stretch prior to failure than controls. There was, however, no significant difference in peak load before failure or energy to failure. The increased stretch prior to failure may be due to a higher concentration of type 3 collagen vs type 1 collagen as was found by Liu et al in their studies of acute estrogen exposure.

In contrast to Slaugtherbeck et al we did not find that the ultimate load to failure was different between our two groups as was found between ovariecotomized rabbits with and without exogenous estrogen. Instead we noted decreased stiffness in ACL’s exposed to cycles regulated by exogenous steroids. Slaughterbeck’s group did not specifically analyze the stiffness of their specimen. This discrepancy may be due to the fact that we did not ovariectomize the rats and so their overall hormonal milieu was not changed as drastically. Alternatively, it may be because we were concerned with chronic, cumulative effects rather than acute effects as was the case in their study.

Overall, our results suggest that menstrual cycles under the control of chronic exogenous contraceptive steroids are not associated with a change in ACL load to failure or energy to failure compared with controls. Therefore oral contraception is unlikely to clinically impact sex specific rates of ACL injury. However exogenous contraceptive steroids did alter the collagen mechanics of the ACLs tested by decreasing their stiffness. ACLs subjected to chronic oral contraceptive intake stretched further prior to failure than controls. The clinical implications of this are unclear. Much attention has recently been focused on the differences in neuromuscular control and proprioception between male and female athletes and its relationship to female ACL injury. Further investigation will be needed to discover whether or not hormonal modulation of ACL stiffness impacts proprioception.

ACKNOWLEDGEMENTS

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RECOMMENDED READING


Back Pain in Intercollegiate Rowers

Carol C. Teitz, M.D., John O’Kane, M.D., Bonnie K. Lind, M.S., and Jo A. Hannafin, M.D., Ph.D.

S tallard first reported back pain as a significant problem in rowers in 1980. He noted that rowing style had changed from a straight-backed swing to a flexion and rotation of the lumbar spine at the beginning of the stroke. The frequent complaints of back pain among current intercollegiate rowers, and the lack of a large-scale intercollegiate study, prompted the authors to question whether the prevalence of back pain had increased in recent years and, if so, what factors might be contributing to back problems.

Methods
Surveys were sent to 4680 former intercollegiate rowing athletes who had graduated between 1978 and 1998 from 5 schools with strong rowing programs. 2165 surveys were returned (46%). Subjects who had back pain before college rowing, those older than 45, and those who did not indicate whether or not they had back pain in college were omitted from the analysis leaving 1632 subjects.

Results
The 1632 subjects included 936 males, 694 females, and 2 subjects who did not report their sex; 71 were coxswains. The mean college height and weight of rowers who are currently under age 30 is significantly greater than that of rowers older than 30 (p<0.02 for men and p<0.003 for women). Higher mean college height and weight were significantly associated with back pain during college rowing in both males (p<0.007 and p=0.02), and females (p<0.001). 526 of 1632 subjects, including 11 coxswains, developed back pain during intercollegiate rowing: 297 males (31.7%) and 228 females (32.9%). In both males and females, the percentage of athletes who had back pain during college rowing increased from 18.8% of those who rowed 25 years ago to 45.1% of those who rowed in the last 10 years (p<0.001).

83 of 526 rowers with back pain (15.8%) ended their college rowing careers because of the pain. These 83 rowers constituted 5% of the entire cohort. An additional 11/526 (2%) lost an entire season due to pain, and 44/526 (8%) lost more than one month but less than a season.

287 athletes (18%) began rowing competitively before age 16. This percentage has increased from 14.2% of subjects currently between 41 and 45 years of age to 24.8% of subjects less than 30 years of age (p<0.001). In bivariate analysis, rowing competitively before age 16 was significantly associated with back pain during intercollegiate rowing (p<0.03) despite the fact that these athletes did not have pain prior to intercollegiate rowing.

Training with free weights, weight machines, and ergometers were each associated with an increased rate of back pain in bivariate analysis, as was ergometer duration greater than 30 minutes, mid-line ergometer cable position, and use of hatchet-style oars. Because many of these training variables reflect intensity of training, they were also considered as a group. Athletes who trained with 3 or 4 techniques had significantly higher rates of back pain compared with athletes who used 2 or fewer training techniques (33.5% vs 17.8%) (p<0.001). The percentage of athletes training with 3 or 4 techniques is significantly higher (p<0.001) among rowers who trained within the last 10 years than among those who trained 20 years ago.

Because of the many concurrent changes in rowing in the past 10-15 years, the bivariate analyses were repeated by decade of current age. In these analyses, only duration of ergometer rowing greater than 30 minutes and the use of free weights were associated with back pain in all decades. Moreover, multivariate logistic regression analyses found ergometer sessions greater than 30 minutes as the only significant predictor of back pain for men, (p<0.001). For women, ergometer sessions greater than 30 minutes (p=0.001) and college height (p<0.001) were both significant predictors of back pain.

Discussion
The prevalence of back pain in
intercollegiate rowing has increased over the last 25 years and may reflect a complex, interrelated set of changes in the sport over time, including changes in equipment, type and intensity of training, and rower physique, as well as beginning to row at a younger age. Nevertheless, ergometer training for longer than 30 minutes proved to be the most significant and consistent predictor of back pain, in every age decade and when all potential predictors were considered simultaneously.

This duration of ergometer training recently has become widespread due to increased ergometer availability and to standardized training protocols dispensed by US Rowing. Coaches suggest that ergometer training is more difficult than rowing in the boat, and that technique deteriorates during long ergometer sessions.

In addition to longer ergometer training times, height is significantly associated with back pain only in our female rowers. Although we don't know if the height increase is a function of torso length or leg length, greater torso length creates increased leverage that is advantageous for rowing, but may be disadvantageous for the spine. The legs initiate the drive phase of rowing during which the trunk-thigh angle must increase. Ideally, the quadriceps extend the knee while the hamstrings simultaneously rotate the trunk. Quadriceps dominance can lead to the buttocks moving back in the boat prematurely, thus hyperflexing the lumbar spine ("shooting the tail"). Hyperflexion also occurs when hamstrings are hyperflexible or when the scapular-stabilizing muscles are not strong enough to receive the force transferred from the lower limbs. Spine hyperextension occurs when the rower increases the trunk-thigh angle by extending the spine using spinal muscles rather than by rotating the pelvis posteriorly through the hip joints. Quadriceps dominance and hamstring hyperflexibility noted in female athletes may make compensating for increased leverage in a taller female rower more difficult. Koutedakis et al and Collander et al found a correlation between thigh-muscle imbalance and back pain. Moreover, Koutedakis et al significantly reduced time loss due to back pain by instituting a hamstring-strengthening program in 22 female rowers. To protect the spine, balanced strength and good rowing technique are critical.

**CONCLUSION**

Back pain in intercollegiate rowing has increased over the last 25 years affecting 32% of 1632 intercollegiate rowers in our study. The effect on the affected athlete's team is significant. In our study, 5.8% of rowers missed more than a month or the entire competitive season. Whether this back pain causes lifelong problems is the subject of additional data analysis underway.

**RECOMMENDED READING**


Moving Toward Knowledge Building Communities in Health Information Website Design

Tracey Wagner, Jennifer Turns, Kristen Shuyler, and Aaron Louie

The Arthritis Source is a web-based information resource created to help self-motivated, geographically dispersed learners gain access to information about arthritis (www.orthop.washington.edu/arthritis). It was developed to support the needs of everyone who interacts with it: the users, the site managers, and the content creators. For the past two years, the Program for Educational Transformation Through Technology (PETTT) and the U.W. Department of Orthopaedics and Sports Medicine have used a science of learning framework to develop an analysis process and content creation system that meets the needs of both learners and teachers using the Arthritis Source.

Our redesign of the Arthritis Source has been guided by both the current research on medical information websites and by our own specific concerns. A variety of current studies on the roles and effectiveness of medical websites have discussed some common shortcomings and related design decisions (e.g., Berland et al., 2001). In our research, we have moved away from describing the community of users and toward focusing on the users’ current knowledge and their goals in visiting the site. In this work we have attempted to address some of the known problems and also create a systematic solution to issues of content maintenance and site development that meets users’ changing needs. We are attempting to support the subject matter experts in creating content that is appropriate for the users. Most importantly, we wanted to help patients find answers to questions concerning their conditions. We are working on a system of site architecture and content development that can be driven explicitly by both our understanding of users’ information needs and by users’ interactions with the site over time. As people use the site, they will collaborate with the content authors to create an information resource that serves users’ purposes and will change with their needs.

This redesign transforms the Arthritis Source from its original state as a static, encyclopedic object into a community of inquiry and practice in which users learn from each other’s questions and shape the growth of the knowledge base. In this effort, the designers, content authors, and users of the website each learn from the others.

Redesigning to support knowledge building

The Arthritis Source has been a successful website since its inception about 1995. It was getting thousands of hits per day and users were submitting unsolicited compliments through emails. The site covered approximately 100 topics related to arthritis and incorporated a variety of media. Despite this success, we knew we wanted to make changes to the Arthritis Source—to update the information, to address the types of concerns emerging from studies of such informational websites, and to make the information more learner-centered. To address these issues, we wanted a solution that would be scalable (so we can continue to expand the website) and enhanceable (so we can make changes with reasonable levels of effort). We also recognized quickly that the information designers, content authors, and users needed to come together to collaborate on the most effective site.

In making our changes, we have adopted a knowledge building community perspective. In such a community, a variety of people contribute to the accumulation of knowledge, different people can contribute in different ways, the knowledge base builds up over time, and there are standards of quality for what belongs in the knowledge base. The members of the community learn from each other by being exposed to both the products and processes of the knowledge creation activities, which benefits them all. We are using this perspective as a way of thinking about how the users of the Arthritis Source will interact with the site, with the content authors, with the designers, and with each other.

Diverse learners, but shared needs

Our earliest work with the Arthritis Source consisted of various efforts to “know thy learner” so that we could create a site that was more learner-centered (Turns and Wagner, 2002). We used a variety of methods to learn who was visiting the website and what they were doing during their visits. One of our most comprehensive activities has been our use of an online survey in which users of the site provide us with information about themselves and their visit (Turns and Liu, 2000). Based on survey results, personal interviews, and emailed comments, we know that our...
user population is widely varied, but has some common needs and characteristics. The majority of the participants identified themselves as patients with arthritis (61%) or friends and relatives of an arthritis patient (8%). Patients have many different information needs and goals when they visit the site, but many patients share similar needs. The complexity of some of these needs as well as the shared nature of the various goals suggests that a potential community of learners already exists. Patients also come to the site with existing knowledge, and sometimes with existing misconceptions. Many of these misconceptions are also shared (or originate from common sources), suggesting that patients may be positioned to benefit from previous visitors’ learning—the essence of a knowledge building community.

From research to implementation
The extent and complexity of the questions brought to the site by our learners convinced us quickly that no static system could effectively satisfy all the users. The perspective of a knowledge building community suggested that we therefore should design a system in which the learners influence the content, tuning the system to their needs over time. The current version of the Arthritis Source has been changed in several distinct ways in response to this goal. Two are briefly discussed below.

Redesign element 1: Template-based content
We are moving toward a version of the Arthritis Source in which all content will be based on templates. The templates used in this context are a series of questions that pertain to a general class of topics and are used by the subject matter experts in the writing of articles within the topics. Templates perform several roles within the site:

- Templates are key to the learner-centered content—there are links between research and content.
- Template elements become navigation elements.
- Template-driven content has consistent structure across articles.
- Templates communicate to author what learners want to know.

Redesign element 2: Question-based navigation
The content of the site, while accessible in the usual browsing mode, is also tailored via the templates to support a question-based navigation system. This system allows learners to ask free text questions, and it responds to them with authoritative, relevant text that has been written based on a learner-centered approach. The system responds to such questions in two possible ways, each supporting a kind of community knowledge building. After a learner asks a question, the system returns several pre-answered questions within articles that may address the question. If the learner cannot find any useful information by asking or rephrasing the question, he or she is invited to submit the question to the content developers. These developers will then be able to add appropriate content to answer the question or improve the search system. The question-based search system provides several benefits to the site and the users:

- Permits users to start at natural starting point, questions.
- Helps users navigate through large body of information.
- Educational benefits (scaffolding) when seeing others’ questions.
- By collecting unanswered questions, our research continues.

CONCLUSION
This implementation transforms the Arthritis Source from a static information source to the continually evolving product of a knowledge building community. The boundaries between the creators (the content authors and the information designers) and the consumers (the users) of the information are blurred. This implementation of the Arthritis Source provides a means by which the users, content authors, and information designers become members of a community jointly influencing the scope and organization of the knowledge source. The ongoing choice of articles and the sequence of their content is the result of a collaboration.
between arthritis patients and site designers in which the designers learned about the patients’ information needs. Users’ efforts to construct their own knowledge with this site can now be seen as a collaboration between these users, earlier users who influenced the content, and the content authors and information designers.

**RECOMMENDED READING**


Optimizing the Intrinsic Stability of the Glenoid Fossa With Non-Prosthetic Glenoid Arthroplasty

Edward J. Weldon III, M.D., Richard S. Boorman, M.D., M.Sc., Kevin L. Smith, M.D., and Frederick A. Matsen III, M.D.

In shoulders requiring arthroplasty, the extant glenoid may provide insufficient intrinsic stability for the humeral head - for example if the glenoid is flat or biconcave. In such cases the surgeon can restore the desired intrinsic stability using a glenoid prosthesis with a known surface geometry. Alternatively, the surgeon can modify the surface of the glenoid to a geometry that provides the desired intrinsic stability. This study explores the feasibility, reliability and predictability with which glenoid intrinsic stability can be restored through spherical reaming of the glenoid bone around the glenoid centerline. It tests the hypothesis that the intrinsic stability of reamed glenoids can match that of clinically used polyethylene glenoid components.

METHODS

The intrinsic stability provided by the glenoid in a given direction can be characterized by the maximal angle the humeral joint reaction force can make with the glenoid centerline before the humeral head dislocates; this quantity is defined as the balance stability angle (BSA) in the specified direction (Figure 1). The BSA can be calculated by analysis of the shape of the glenoid surface (Figure 2). The BSA can also be measured directly by placing an unconstrained humeral head loaded only by gravity within the glenoid oriented with the centerline vertical and then tipping the glenoid until the humeral head dislocates (Figure 1). In this study, the balance stability angles were both calculated and measured in 8 different directions for 3 unused polyethylene glenoid components and 11 cadaveric glenoids in 4 different states: 1) native without capsule or rotator cuff, 2) denuded of cartilage and labrum, 3) after reaming the glenoid surface around the glenoid centerline using a spherical reamer with a radius of 25.0 millimeters, and 4) after reaming around the glenoid centerline using a spherical reamer with a radius of 22.5 millimeters (Figure 3). We also attempted to predict the BSAs achievable with reaming to each of the two different radii from measurement of the width of the glenoid before it was reamed.

RESULTS

Denuding the glenoids of their articular cartilage reduced the intrinsic stability, especially in the posterior direction (Figure 4 and Table 1). Reaming the glenoid restored the intrinsic stability back to values comparable to those of the normal glenoid. For example, the average calculated BSA in the posterior direction for all eleven glenoids was: native = 24° ± 9°, denuded = 14° ± 6°, reamed to radius 25.0 millimeter = 25° ± 5°, reamed to radius 22.5 millimeter = 33° ± 6°. The BSAs for the...
Figure 3: The different glenoid states. (a) The native glenoid in which the capsular tissues have been dissected from the labrum. (b) The denuded glenoid in which the articular cartilage and glenoid labrum have been curetted from the bony surface of the glenoid. (c) The glenoid reamed to 25.0 millimeters in which the glenoid has been spherically reamed to a radius of curvature of 25.0 millimeters around the glenoid centerline. (d) The glenoid reamed to 22.5 millimeters in which the glenoid has been spherically reamed to a radius of curvature of 22.5 millimeters around the glenoid centerline.

The proportions of the concavities of these glenoid cross-sections have been drawn based on the average depth (D) and width (W) from the 11 glenoids in each of the four states in the anterior to posterior (90º to 270º) direction. The representative photos below show glenoid #5 in each of its 4 states. a) native. b) denuded. c) reamed 25.0. d) reamed 22.5.

Figure 4: Intrinsic stability of the four different glenoid states, native, denuded, reamed to 25 mm, and reamed to 22.5 mm. The BSAs are shown in degrees. Note the particularly dramatic loss in posterior and posterior-inferior intrinsic stability with denuding the native glenoid of articular cartilage. Note also the restoration of the BSAs with spherical reaming to 25 and to 22.5 mm.
polyethylene glenoids, which had a manufactured radius of curvature of 25.0 millimeters, were not significantly different from those of the cadaveric glenoids following reaming to a 25.0 millimeter of curvature (p = .165) (see Figure 5 and Table 1). They were significantly less than the BSAs of the cadaveric glenoids following reaming to a 22.5 millimeter radius of curvature (p < .0001).

There was a high degree of correlation between the measured and the calculated BSAs for each of the different preparations (see Figure 6 and Table 2). The correlation coefficients ranged from .75 to .94. All correlations were significant (p<.0001). These strong correlations between results obtained with completely different techniques support the validity of the methods and indicates that factors other than glenoid surface geometry, such as friction, were not important in this model system.

The BSAs predicted prior to reaming were similar to those after the glenoid had been reamed (Figure 7). Considering the BSAs in the anterior and posterior directions (90° and 270°), the average absolute difference between the measured and predicted BSAs was 5.3° ± 3.6° with reaming to 25.0 millimeters and 3.4° ± 2.4° with reaming to 22.5 millimeters.

**Conclusion**

The intrinsic stability of human glenoids was decreased by removal of the cartilage and increased reliably and predictably through spherical reaming of its surface. Denudation of the glenoid surface had the most profound reduction of intrinsic stability in the posterior direction: a common...
Figure 7: Plot of calculated vs predicted BSA in degrees in the anterior and posterior directions.

### Average BSAs (degrees)

<table>
<thead>
<tr>
<th>Direction (degrees)</th>
<th>Native</th>
<th>Denuded</th>
<th>Ream 25.0</th>
<th>Ream 22.5</th>
<th>Global 44</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>31.3</td>
<td>29.1</td>
<td>34.8</td>
<td>40.6</td>
<td>36.3</td>
</tr>
<tr>
<td>45</td>
<td>24.5</td>
<td>25.8</td>
<td>30.4</td>
<td>36.5</td>
<td>31.9</td>
</tr>
<tr>
<td>90</td>
<td>21.9</td>
<td>17.9</td>
<td>27.2</td>
<td>33.2</td>
<td>25.8</td>
</tr>
<tr>
<td>135</td>
<td>28.4</td>
<td>23.0</td>
<td>32.6</td>
<td>38.0</td>
<td>31.9</td>
</tr>
<tr>
<td>180</td>
<td>32.1</td>
<td>23.3</td>
<td>32.2</td>
<td>37.3</td>
<td>36.2</td>
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<td>225</td>
<td>28.8</td>
<td>18.5</td>
<td>28.4</td>
<td>34.8</td>
<td>31.2</td>
</tr>
<tr>
<td>270</td>
<td>23.9</td>
<td>14.1</td>
<td>24.8</td>
<td>32.5</td>
<td>25.3</td>
</tr>
<tr>
<td>315</td>
<td>25.4</td>
<td>20.2</td>
<td>31.6</td>
<td>35.4</td>
<td>31.2</td>
</tr>
</tbody>
</table>

- * - significantly less than Native (p<.0001)
- ** - significantly greater than Denuded and Native (p<.0001)
- + - significantly greater than Reamed 25.0 and Global 44 (p<.0001)
- ++ - not significantly different from Reamed 25.0 (p=.165)

Table 1: A tabular presentation of the average calculated Balance Stability Angle, (in degrees) of the 11 glenoids, displayed according to directions tested in each of the 4 states. Included are the average calculated BSAs for the unused Global 44 polyethylene components.

### Clinical Relevance

Non-prosthetic glenoid arthroplasty through spherical reaming can achieve surface geometry and intrinsic stability similar to that of normal glenoids and that provided by a polyethylene glenoid.

### Recommended Reading


Department of Orthopaedics and Sports Medicine Faculty

Frederick A. Matsen III, M.D.
Professor and Chair
Christopher H. Allan, M.D.
Assistant Professor
David P. Barei, M.D.
Assistant Professor
Carlo Bellabarba, M.D.
Assistant Professor
Stephen K. Benirschke, M.D.
Professor
James D. Bruckner, M.D.
Associate Professor
Howard A. Chansky, M.D.
Associate Professor
Jens R. Chapman, M.D.
Professor
John M. Clark, M.D., Ph.D.
Associate Professor
Ernest U. Conrad III, M.D.
Professor
Mohammad Diab, M.D.
Assistant Professor
David R. Eyre, Ph.D.
Professor
John Green, M.D.
Assistant Professor
Theodore K. Greenlee, Jr., M.D.
Associate Professor
Ted Gross, Ph.D.
Associate Professor
Douglas P. Hanel, M.D.
Professor
Sigmund T. Hansen, Jr., M.D.
Professor
M. Bradford Henley, M.D.
Associate Professor
Todd Jarosz, M.D.
Assistant Professor
Nancy J. Kadel, M.D.
Assistant Professor
Roger V. Larson, M.D.
Associate Professor
Seth S. Leopold, M.D.
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Assistant Professor
Vincent S. Mosca, M.D.
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Research Assistant Professor
Lynn T. Staheli, M.D.
Professor Emeritus
Carol C. Teitz, M.D.
Professor
Allan F. Tencer, Ph.D.
Professor
Thomas E. Trumble, M.D.
Professor
Jiann-Jiu Wu, Ph.D.
Research Associate Professor
Liu Yang, Ph.D.
Research Assistant Professor
Adjunct Faculty
Basia R. Belza, R.N., Ph.D.
Associate Professor, Physiological Nursing
Jack W. Berryman, Ph.D.
Professor, Medical History & Ethics
Charles H. Chesnut, M.D.
Professor, Nuclear Medicine
Randal P. Ching, Ph.D.
Assistant Professor, Mechanical Engineering
Eva M. Escobedo, M.D.
Assistant Professor, Radiology
Gregory C. Gardner, M.D.
Associate Professor, Rheumatology
Thurman Gillespy, M.D.
Associate Professor, Radiology
Daniel O. Graney, Ph.D.
Associate Professor, Biological Structure
John C. Hunter, M.D.
Associate Professor, Radiology
Frederick A. Mann, M.D.
Professor, Radiology
David W. Newell, M.D.
Professor, Neuroscience
Susan M. Ott, M.D.
Associate Professor, Division of Metabolism
Wendy Raskind, M.D., Ph.D.
Associate Professor, General Internal Medicine
Michael L. Richardson, M.D.
Professor, Radiology
Christopher I. Shaffrey, M.D.
Associate Professor, Neuroscience
Robert B. Schoene, M.D.
Associate Professor, Medicine
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Assistant Professor, Rehab Medicine
John E. Olerud, M.D.
Professor, Division of Dermatology
Nathan J. Smith, M.D.
Professor Emeritus, Pediatrics
Michael D. Strong, Ph.D.
Research Professor, Surgery
Nicholas B. Vedder, M.D.
Associate Professor, Plastic Surgery
Clinical Faculty
Sarah E. Jackins, R.P.T.
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University of Washington School of Medicine

Department of Orthopaedics and Sports Medicine

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Children's Hospital and Regional Medical Center
4800 Sand Point Way NE
Seattle, WA 98105
(206) 526-2000

Harborview Medical Center
325 Ninth Avenue
Seattle, WA 98104
(206) 731-3462

University of Washington Medical Center
Bone and Joint Center
4245 Roosevelt Way NE
Seattle, WA 98105
(206) 598-4288

VA Puget Sound Health Care System
1660 South Columbian Way
Seattle, WA 98108
(206) 764-2215
Graduating Residents  
**Class of 2002**

Timothy DuMontier, M.D.: Tim will begin a one-year foot and ankle fellowship with Art Manoli in Michigan. Thereafter he will return to Montana to start a general orthopaedic practice.

Scott Hacker, M.D.: Scott will begin a one-year sports medicine fellowship in Vail, Colorado. Following his fellowship he hopes to return to the west coast.

Timothy Rapp, M.D.: Following his residency he will begin an oncology fellowship at the University of Washington Medical Center.

Carla Smith, M.D.: Carla will begin an AO trauma fellowship at the University of Zurich, followed by volunteering in general orthopaedics in Bhutan and pediatric orthopaedics in Nepal. She will return to Harborview to do a trauma fellowship.

William Sims, M.D.: Bill will begin a one-year fellowship with Dr. Champ Baker at the Hughston Clinic in Columbus, Georgia.
Incoming Residents

Heidi Ambrose: Heidi attended the University of San Diego where she received a BA in Chemistry. She received her medical degree from the University of Washington. She is completing her surgical internship at the University of Washington. Her interests outside of medicine include basketball, snow skiing, as well as piano and ceramics.

Stacey Donion: Stacey attended the University of Washington where she received a BS in Psychology and Physical Therapy. She also received her M.D. from the University of Washington. She is finishing her surgical internship at the University of Washington. Personal interests include swimming, soccer and skiing.

Eric Klineberg: Eric received his BA in Biology and Studio Art from Rice University. This was followed by obtaining a Master of Science in zoology - neural science from the University of Maryland. Eric received his medical degree from the University of Maryland. He is currently completing his internship at the University of Washington. His interests include basketball, football and golf.

Melvin Wahl: Mel received his BS in Human Biology from Eastern Washington University. He earned his medical degree from the University of Washington. He is currently completing his internship at the University of Washington. Outside interests include sports such as basketball, wrestling, fishing and golf.

William Montgomery: Bill obtained his BS degree in Early Childhood Education from the University of Vermont and a Masters degree in Public Health at the University of Hawaii. He also received his M.D. from the University of Hawaii. He is currently completing his internship at the University of Washington. Bill enjoys spending time with his wife and children, hiking, swimming.

Burt Yaszay: Burt received his BS in Biochemistry and Cell Biology from UC-San Diego. He earned his M.D. from Stanford. He is currently completing his internship at the University of Washington. His personal interests include working out at the gym, biking and travelling.
2002 Department of Orthopaedics
New Faculty

John Green, M.D.

Dr. Green received his undergraduate degree in Biopsychology as well as his medical degree from the University of Cincinnati. His internship and residency training in orthopaedic surgery were completed at Michigan State University/McLaren Regional Medical Center. Dr. Green then went on to complete his sports medicine fellowship training at the Minneapolis Sports Medicine Center. In 1997 he was recruited to begin a sports medicine program at LSU Health Sciences Center in Shreveport, Louisiana. Dr. Green is the new director of the University of Washington Sports Medicine Clinic in the Hec Edmundson Pavilion where he specializes in the surgical treatment of sports injuries.

Todd Jarosz, M.D.

Dr. Jarosz completed his undergraduate education at Albright College in Reading, Pennsylvania. He then, received his medical degree from the University of Medicine & Dentistry Robert Wood Johnson Medical School@Camden. He completed a General Surgical Internship and Residency in Orthopaedic Surgery at the University of Virginia. He also completed three additional years of advanced training by completing a two-year Sportsmedicine fellowship in Orlando, Florida, and a fellowship in Spinal/Reconstructive Surgery at the University of Maryland. He has a special interest in sports-related spinal injury, complex spinal reconstructive surgery, and shoulder and knee arthroscopy. He is involved with patient care at the University of Washington Hospital, Harborview Medical Center, and the Eastside Clinic.

Seth Leopold, M.D.

Dr. Leopold received his medical degree with honors in research from Cornell University in 1993. Subsequently, he completed an orthopaedic surgery residency at the University of Chicago, and pursued subspecialty training in joint replacement at Rush-Presbyterian-St. Luke’s Medical Center, an internationally-known referral hospital for complex joint reconstruction. Dr. Leopold comes to UW after serving three years in the US Army Medical Corps, where he taught and performed joint replacement surgery, and pursued research interests related to both basic science and clinical aspects of arthritis surgery. His practice serves patients with arthritis, especially of the hips and knees, as well as individuals suffering with persistently painful or failed joint replacements. In addition, Dr. Leopold is experienced at a variety of minimally-invasive joint replacement techniques, which can significantly shorten the recovery period following surgery in properly-selected patients. Dr. Leopold sees patients on the Eastside and at UWM C-Roosevelt.
### Research Grants

**Department of Orthopaedics and Sports Medicine**

**National Institutes of Health (NIH)**

- Augmentation of Peak Bone Mass  
  Ted S. Gross, Ph.D.

- Collagens of Cartilage and the Intervertebral Disc  
  David R. Eyre, Ph.D.

- Disuse Induced Osteocyte Hypoxia  
  Ted S. Gross, Ph.D.

- Imaging of Molecules by Oscillator-Coupled Resonance  
  John A. Sidles, Ph.D.

- Outcomes Following Limb Reconstruction Vs Amputation  
  Douglas G. Smith, M.D.

- Pathology of Inborn Skeletal Diseases  
  David R. Eyre, Ph.D.

- Skeletal Dysplasias  
  David R. Eyre, Ph.D.

- TLS and TLS Fusion Proteins in Leukemia  
  Liu Yang, Ph.D.

**Veterans Affairs Medical Center Review Grants**

- Effect of Motor Imbalance on Bony Deformity and Plantar Pressure  
  Bruce J. Sangeorzan, M.D.

- Ewing’s Sarcoma Fusion Proteins and mRNA Splicing Factors  
  Howard A. Chansky, M.D.

- Rehabilitation Research and Development Center of Excellence for Limb Loss Prevention and Prosthetic Engineering  
  Bruce J. Sangeorzan, M.D.

**Centers for Disease Control**

- Age-Related Cervical Spine Mechanics and Injury Tolerance  
  Randal P. Ching, Ph.D.

- Development of a Device to Reduce Cervical Whiplash Potential in Rear-End Car Accidents  
  Allan F. Tencer, Ph.D.
RESEARCH GRANTS
DEPARTMENT OF ORTHOPAEDICS AND SPORTS MEDICINE

Orthopaedic Research and Education Foundation (OREF)

Overcoming Nerve Defect by Growth Factor Stimulated Regeneration Along Intact Nerves
Thomas E. Trumble, M.D.
Ben Dubois, M.D.

Reproductive Hormone Effects on ACL Strength
Emma Woodhouse, M.D.
Peter T. Simonian, M.D.

Toward Clinical Application of the Intact Nerve Bridge Technique: Longer Term Study in a Rabbit Model
Thomas E. Trumble, M.D.
Wren V. M Callister, M.D.

American Federation for Aging Research

Rest-Inserted Loading: Examination of a Novel Osteogenic Stimulus For the Aged Skeleton
Sundar Srinivasan, Ph.D.

Alberta Heritage Foundation for Medical Research

Shoulder Laxity
Richard S. Boorman, M.D.

American Society for Surgery of the Hand

Bridging Versus Non-Bridging External Fixation of Distal Radius Fractures: a Measure of Structural Rigidity in an Unstable Fracture Model
Thomas E. Trumble, M.D.

Prospective Randomized Clinical Trial of Hand Therapy Following Carpal Tunnel Surgery
Thomas E. Trumble, M.D.

Defense Advanced Research Projects Agency

The Accelerated Development of MRFM
John A. Sidelis, Ph.D.


**RESEARCH GRANTS**

**DEPARTMENT OF ORTHOPAEDICS AND SPORTS MEDICINE**

**DePuy Orthopaedics, Inc.**

THA Range Of Motion Study  
Randal R. Ching, Ph.D.

Thermal Effects of Two Different Glenoid Fixation Techniques  
Sean R. Churchill, M.D.  
Frederick A. Matsen III, M.D.

**Ethicon**

Role of Bone in Cartilage Transplantation  
Peter T. Simonian, M.D.

**Genetics Institute**

A Feasibility and Safety Study of rhBM-P-2/ACS and Allograft Compared to Autogenous Bone Graft for Patients with Severe Tibial Shaft Fractures  
Sohail K. Mirza, M.D.

**Leukemia Research Foundation**

Disruption of RNA Splicing by TLS/ERG Leukemia Fusion Protein  
Liu Yang, Ph.D.

**National Childhood Cancer Foundation**

Childrens Cancer Group  
Ernest U. Conrad III, M.D.

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April 2001 Through March 2002

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