Managing Tendinopathies and Tendon Tears: Nanoscale Mesh Scaffolding Promotes Biological Healing

Tendinopathy is a common clinical syndrome that can affect any tendon. Patients present across an age and activity spectrum with pain, swelling and impaired function. Previously described by the diagnostic terms “tendinitis” or “tendinosis,” the clinical condition is now more accurately referred to as tendinopathy. Chronic tendinopathies can weaken tendons and cause overt tendon tears.

“When patients have a tendinopathy, it represents a failure of the body’s normal repair mechanisms. Although there is some evidence that it may begin as an inflammatory condition, the pathology is better characterized as a degenerative condition,” explains Mayo Clinic orthopedic surgeon Mark E. Morrey, M.D. As a specialist in tendinopathies and soft-tissue healing conditions, Dr. Morrey also conducts research focused on using novel scaffolds to direct growth in different types of soft tissues, utilizing rotator cuff injuries as a model. Adds his Mayo orthopedic surgeon colleague John W. Sperling, M.D.: “The clinical potential of this approach is significant because it promises, for the first time, to enable the physician to restore high-quality tendon tissue needed for optimal function.”

Role of inflammation

Clinical symptoms of tendinopathies are still often treated with corticosteroids. “This approach has been utilized for decades and appeared to have some benefit for our patients. Unfortunately, well-designed, randomized, controlled, long-term studies have shown that although this treatment has worked in the short term, it can lead to more recurrences and poor tendon health in the long term,” Dr. Morrey says. “When

Figure 1. 20x magnification of normal tendon (left) compared to normal cartilage cells (right) shows the typical elongate phenotype of tendon and rounded phenotype of cartilage cells.
considering an injection of corticosteroids for tendinopathies, physicians should look very carefully at emerging data regarding tendon quality and potential long-term risks and benefits to patients.”

Dr. Morrey’s research seeks to characterize the underlying molecular and biological causes of failed healing in rotator cuff tear models. The goal is to correct them so the tendon can recover its natural healing ability. His results suggest a major factor contributing to failure to heal is the absence of requisite mechanical cues such as tension and extracellular architecture. These cues direct tendon cells to regenerate.

**Cellular confusion**

Lacking these cues within the cellular microenvironment, ruptured tendon cells fail to elongate, a morphological deficit that impairs the cells’ function to produce the normal proteins needed for healthy tendon. Explains Dr. Morrey: “In healthy tendon, as cells are dividing, they change their shape and they become more elongated as a direct response to the extracellular architecture.” Injured cells take on a rounder shape, resembling cartilage cells, a condition known as chondroid metaplasia. “This is what we are seeing at the histologic level,” Dr. Morrey explains. “These cells don’t know what to become—they’re confused, in a sense, because they lack the appropriate inputs to guide healthy growth. As a result they resemble cartilage cells and produce a cartilage-like extracellular matrix instead of a tendon-like matrix.”

Researchers at both Mayo and England’s Oxford University are collaborating to apply these insights to promote tendon healing. By restoring the necessary conditions within the matrix to cue the proper growth of tendon cells, they aim to regenerate tendon structure.

**Guiding growth**

To create conditions that favor the growth of new tendon cells, Dr. Morrey and Oxford colleagues are developing a synthetic, degradable mesh patch to provide a scaffold for tendon regeneration. “A scaffold is a means of recreating those mechanical cues so the cells can recover their natural architecture and hopefully promote normal healing,” he explains.

When placed over a traditional surgical rotator cuff repair, the patch can augment healing by providing the cues that guide the regenerating cells to grow into a tendon-like structure (Fig. 2).

Once that is achieved, the scaffold degrades and leaves behind normal, healthy, tendon tissue. “The cells are initially told what to become because of the architecture of the patch,” Dr. Morrey says. “It is partially a mechanical signal to guide tendon cell

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**Figure 2. Schematic of scaffold degradation and repair shows cells migrate into the scaffold, attracted by the orientation and chemical composition of the fibers. Cells progressively and preferentially differentiate toward the desired cell phenotype while the scaffold degrades, leaving behind only regenerated tissue in the correct orientation and morphology of normal tendon tissue.**

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**Figure 3. A photomicrograph shows cuing effects of the patch material on cell morphology, with elongated tendon-cell-like cells appearing within the patch fibers (red lines), while cells not in contact with the patch are more rounded and resemble non-tendon cell types.**
prompts powerful biochemical changes within the tissue (Fig. 4). When injury occurs the cellular response begins with neutrophils, which release reactive oxygen species. These damage the tissue further and also recruit other cells, including the first responders in a healing situation, macrophages.

- **Macrophages: heal or harm?**
  Biomaterials, such as scaffolds which are implanted to aid healing during the injury response, may alter the healing response. Depending on biomaterial features such as fiber size and the types and level of degradation products, macrophages recruited to the area of injury can heal or harm. If given the right cues, they can help promote healing in a regenerative, tissue-responsive macrophage form that basically accepts the material as its own. But if a macrophage takes the form of a foreign-body giant cell, it may become harmful as it tries to deal with the byproducts of injury. This can lead to excessive fibrosis and encapsulation.
  
  An important focus of Dr. Morrey’s research is directed at controlling signals to macrophages with the goal of downplaying the rejection response and promoting a healing response. Says Dr. Morrey: “We need better approaches to treating tendinopathies and tendon tears. With biologic approaches utilizing scaffolds, I believe we are one step closer to developing them.”

**Biocompatibility issues**

- **Fiber size**
  In designing any biological implant it is important that the materials used do not promote an unwanted immune response. “We know the body responds differently to different materials. This includes varied responses to the chemical degradation products of these materials, and to the sizes of fibers utilized in these patches,” Dr. Morrey says.
  
  As the fiber size of the patch changes, the immune system responds differently to it from a biocompatibility standpoint: It may reject and wall off the material, rather than incorporating it. “To be successful, you have to get the right mixture of fiber size and chemical structure to tell the cells what to do.”

- **Injury response**
  In addition to mechanical changes, injury

![Figure 4](image-url)  
**Figure 4.** Tissue injury prompts powerful biochemical changes within the cell, setting in motion a process of cellular responses that affect the healing response, depending on whether macrophages heal or harm. Biomaterials such as those used in the patch can help cue macrophages to regenerate healthy tendon tissue.
First Nationwide Prevalence Study of Hip and Knee Arthroplasty Shows 7.2 Million Americans Living With Implants

The orthopedic community and public are well aware that hip and knee replacement operations are among the most commonly performed operations in the U.S. Figures show that around 1 million of these procedures are performed each year. But how many people actually are living with a hip or knee replacement in the United States? This important measure of the impact of joint arthroplasty on public health, known as prevalence, has been missing until the recent release of a Mayo Clinic Orthopedics study (Fig. 1).

Presented in March 2014 at the annual meeting of the American Association of Orthopaedic Surgeons (AAOS) in New Orleans, the Mayo study is the first of its kind. Its prevalence estimates for 2010 show that:

- An estimated 4.7 million Americans have undergone total knee arthroplasty (TKA) and 2.5 million have undergone total hip arthroplasty (THA) and are living with implants.
- Prevalence is higher in women than in men: 1.4 million women and 1.1 million men have THA and 3 million women and 1.7 million men have TKA.
- Prevalence increases with age. In adults ages 80 to 89 years, about 6 percent and 10 percent have a history of total hip and knee replacement, respectively.

Prevalence matters

Daniel J. Berry, M.D., lead Mayo investigator on the team, describes the importance of the groundbreaking prevalence estimates for TKA and THA this way: “These numbers underscore the significant positive impact on health and quality of life that total joint replacement surgeries have made since the era of total joint replacement began in 1969—the year that Mayo Clinic became the first in the U.S. to perform total hip implant surgery. Development of the total knee replacement technique followed in 1971. This large number highlights how these operations have kept a substantial part of our population mobile despite severe arthritis, something that wouldn’t have been possible before these technologies were available.” For perspective on future planning of health care services, Dr. Berry notes that there are approximately 1.5 times more people living in the U.S. with a hip or knee replacement as there are people living with heart failure.

The study also provides valuable insights into possible future trends in orthopedic care. These include the need to provide specialized health care services for individuals with joint replacements, ranging from chronic care of aging implants to the management of revision surgeries and long-term complications from wear debris or other issues.

Explains Dr. Berry: “Individuals with joint replacement constitute a special population with distinct needs that extend beyond the immediate hospitalization course and the post-operative period.” Adds his colleague on the study, Mayo epidemiologist Hilal Maradit Kremers, M.D.,
Mayo Clinic orthopedists made unusually strong and topically diverse contributions to the program offerings of the 2014 American Association of Orthopaedic Surgeons (AAOS) annual meeting in New Orleans in March. The effort reflects the department’s commitment to continual improvement through collegial learning and teaching to enhance patient care.

More than 60 Mayo specialists participated in over 120 sessions, including practice leadership, faculty development, event planning and program organization and serving as panel moderators, symposia chairs, expert panelists, instructional leaders and topical presenters for paper and poster sessions. Michael J. Stuart, M.D., completed his five-year term as a member of the Central Program Committee and Mark W. Pagnano, M.D., completed his five-year term as a member of the Instructional Course Committee.

A small sampling of Mayo AAOS annual meeting contributions includes participation by:

- **Diane L. Dahm, M.D.**: Chair of the educational committee, Sports Medicine and Arthroscopy
- **Arlen D. Hanssen, M.D.**: Symposium Presenter: Essential Surgical Techniques for Total Hip Arthroplasty: A Video-Based Symposium
- **Bruce A. Levy, M.D.**: Moderator, Paper Presentation: The Multiple Ligament-Injured and Dislocated Knee
- **Ahmad Nassr, M.D.**: Panel Member, Instructional Course Lecture: Avoiding and Managing Complications in Cervical Spine Surgery
- **Mary I. O’Connor, M.D.**: Moderator, Faculty Development Course I: Getting Your Great Ideas Supported—Effective Techniques for Women in Orthopaedics
- **Rafael J. Sierra, M.D.**: Moderator, Surgical Skills Course: Unicompartmental and Primary Total Knee Arthroplasty: Measured Resection Vs. Gap Balancing
- **Scott P. Steinmann, M.D.**: Moderator, Instructional Course Lecture: Complex Elbow Injuries: New Techniques for Operative Management and Avoiding Complications
Mayo Clinic Sports Medicine Center Partners with Minnesota Timberwolves and Lynx in New Downtown Minneapolis Facility

To meet the growing demand for orthopedic expertise among patients with diverse goals—from general fitness, to functional rehabilitation to professional performance enhancement—Mayo Clinic is opening a new 20,000-square-foot Sports Medicine Center in downtown Minneapolis in partnership with two professional basketball teams, the Minnesota Timberwolves and Lynx. Located on the third floor of a now-unoccupied building at 600 Hennepin Avenue, the newly remodeled shared-space facility will be named Mayo Clinic Square and is adjacent to the Target Center and Target Field. It is scheduled to open in the fall of 2014.

Under the partnership, the teams will also develop a new practice facility at the site—including four practice courts—and the Mayo Sports Medicine Center specialists will be the preferred provider of medical care. Mayo Clinic specialists will diagnose, treat, and rehabilitate musculoskeletal injuries, as well as implement programs for optimal performance and injury prevention. The teams’ marketing platforms will help Mayo Clinic provide public education on a variety of wellness topics, including nutrition and physical fitness.

Collaboration is key
Collaboration with the Timberwolves and Lynx will utilize the teams’ international reach to educate the public on health and wellness topics, according to Michael J. Stuart, M.D., Sports Medicine Center co-director, USA Hockey chief medical officer and U.S. men’s Olympic ice hockey team physician, most recently in Sochi, Russia:

“This partnership provides an excellent opportunity to extend the Mayo model of care to Twin Cities residents,” Dr. Stuart explains. “We’re also thrilled to have the privilege of interacting closely with world-class athletes of the Timberwolves and Lynx with the goal of helping them optimize performance and avoid injury. Through our relationship with these fine athletes we hope to inspire the public to learn more about evidence-based fitness and health practices.”

Adds Edward R. Laskowski, M.D., co-director, Mayo Clinic Sports Medicine Center:
“We are proud to provide a team of renowned clinical experts, including orthopedic and physical medicine and rehabilitation specialists, who care for elite level professional and Olympic athletes. We want to have this same level of care available to meet the fitness and performance needs of all ages and types of athletes, and for individuals interested in improving general overall fitness.” The new center will be similar to the new 25,000-square-foot Mayo Clinic Sports Medicine Center expansion at Mayo’s Dan Abraham Healthy Living Center in Rochester, Minnesota.

**Advanced services**

Mayo staff on site will include physicians who specialize in orthopedics and physical medicine and rehabilitation. Other staff members include physical therapists, athletic trainers, and strength and conditioning experts. A Mayo Clinic employee will be available to help navigate scheduling for patients seeking to integrate their sports medicine workup with integrated care at Mayo Clinic in Rochester, 80 miles south of the new center.

**Mayo Clinic Sports Medicine Center offerings include:**
- sports injury evaluation and treatment
- sport-specific training and conditioning
- health and well-being programs
- diagnostic imaging, including digital radiographs, MRI and musculoskeletal ultrasound
- injury prevention
- performance solution programs for elite and amateur athletes
- regenerative medicine
- ongoing orthopedic and sports medicine research

Notes John T. Wald, M.D., Mayo Clinic radiologist and medical director for marketing and public affairs: “The partnership reflects Mayo’s strong commitment to serving the needs of patients in the Twin Cities and our core value of sharing knowledge to improve people’s health and wellness around the nation and world.”

*Figure 1. This artist’s rendering shows the redevelopment plan for a downtown Minneapolis building into the new Mayo Clinic Sports Medicine Center, which will partner and share space with two professional basketball teams, the Minnesota Timberwolves and Lynx, while also providing services to the general public. Scheduled to open in 2014 at 600 Hennepin Avenue near Target Center and Target Field, the 20,000-square-foot facility will offer state-of-the-art, evidence-based training, rehabilitation, conditioning, diagnosis and selected treatments and performance enhancement solutions for everyone—from pro athletes, to those just starting a fitness regimen or recovering from injury or surgery, to weekend warriors. Under the partnership, Mayo Clinic sports medicine specialists will be the preferred medical provider to the teams. The teams’ marketing services will provide Mayo Clinic with a global platform for providing wellness and fitness education linked to evidence-based research on the vital role of activity in long-term health.*
Continuing Medical Education

Diagnostic and Interventional Musculoskeletal Ultrasound
July 10-12, 2014-Mayo Clinic, Rochester, Minnesota.

A collaboration between Mayo Clinic and the American Institute for Ultrasound in Medicine (AIUM), this three-day course is appropriate for physiatrists, sports medicine physicians, radiologists, orthopedic surgeons, anesthesiologists, rheumatologists, sonographers and other clinicians who evaluate and treat patients with musculoskeletal and neurological diseases, from beginner to intermediate/advanced levels. Registration available online at www.aium.org.
Contact: Call 800-323-2688 (toll-free) or email cme@mayo.edu

Knee Dislocation and Multiligament Knee Reconstruction
September 18-19, 2014-Mayo Clinic, Rochester, Minnesota

Designed for high-level arthroscopists, this anatomy-intensive course focuses on the current techniques for multiligament knee reconstruction. The latest in ACL, PCL, MCL/Posteromedical corner and FCL/Posterolateral corner surgical techniques are addressed. To maximize surgical experience, the course is structured to have two attendees with one faculty member per lab station, short didactic sessions followed by lab time and opportunities to recap and discuss with experts.
Contact: Call 800-323-2688 (toll-free) or email cme@mayo.edu

24th Annual Mayo Clinic Symposium on Sports Medicine
November 7-8, 2014- Rochester, Minnesota

Through a multidisciplinary focus, this course is designed to provide physicians, physical therapists, athletic trainers and other sports medicine professionals with the latest diagnostic and treatment strategies for sports-related and musculoskeletal conditions. Expert lecturers representing various sports medicine fields will deploy multiple educational formats including case presentations, live demonstrations of physical examination, anatomy and arthroscopy techniques.
Contact: Call 800-323-2688 (toll-free) or email cme@mayo.edu

Next Department Chair Named

In spring 2014, Daniel J. Berry, M.D., completed his term as Chair of the Department of Orthopedic Surgery, Mayo Clinic Rochester. He served in that role for the past decade. Mark W. Pagnano, M.D., will succeed Dr. Berry as the next Chair of the Department.