

Room for Many More Investigating the Value of Creating Space for New Cells to Grow and for More Successful Meniscus Transplants

Replacing the structure in the knee responsible for stability and cushioning may become easier with longer-lasting results because of research conducted by **Cristin M. Ferguson, M.D.**, funded in part by a Clinician Scientist Award through OREF.

OREF named Dr. Ferguson a 2007 recipient of the award, which provides an annual stipend of \$100,000 for three years to compensate for the loss of income associated with devoting more time to research than to clinical practice. In return, OREF Clinician Scientists are asked to devote extensive time to research; serve as role models for orthopaedic residents, interns, and medical students; and organize and participate in conferences.

Dr. Ferguson's award will be funded by a contribution to OREF from *The Journal of Bone and Joint Surgery*.

"It is very easy to have all your research time taken up by clinical practice," Dr. Ferguson said. "You add on a surgery. You add on a clinic. It's very hard to carve out research time, and that's what this award enables someone to do. It helps develop the research part of a career and frees up time to serve as a mentor to people who have similar interests."

Getting to the Center

Dr. Ferguson's research concerns the meniscus, a C-shaped cartilage cushion that acts as a shock absorber and stabilizes the knee. One of the

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The meniscus tissue engineering research team
(Standing, left to right): **Mark Van Dyke, Ph.D.** (collaborator at the Wake Forest Institute for Regenerative Medicine), **Cristin Ferguson, M.D.** (Department of Orthopaedics). (Seated, left to right): **Mr. Devin Odom** (first-year medical student, Wake Forest University School of Medicine), **Kathryne Stabile, M.D., M.S.** (research resident, Department of Orthopaedics), **Ms. Julie Steen** (graduate student, School of Biomedical Engineering). Not pictured: **Tom Smith, Ph.D.** and **Beth Smith, Ph.D.** (Department of Orthopaedics).

Brought to Their Knees: How a Study That Began With OREF Funding Is Changing the Way Orthopaedists Think About ACL Reconstruction

Nearly 275,000 anterior cruciate ligament (ACL) reconstructions are performed in the United States each year. Hoping to improve patient outcomes, **Kurt P. Spindler, M.D.** is leading a clinical follow-up study, initially funded by OREF, to assess what makes some reconstructed ACLs last longer than others.

"I really want to know the answer to what happens to these ACLs, to know what predicts their failure or success so that we can improve our outcomes," he said. "OREF gave us the seed money to design a

study that proved we could follow up with patients years after their operations."

From Patient to Orthopaedist

Dr. Spindler, whose interest in orthopaedics and sports medicine resulted from his experience as a patient, after sustaining an injury during high school football practice, said he first became interested in research when he was asked to participate in a scientific investigation as a college student.

"I became hooked on evaluating things in a scientific way. I think that colors the way you

look at things. You begin to wonder, 'How do I want to experiment?' 'What is factual?' 'What is true?'"

Research remained a significant part of Dr. Spindler's training as he continued

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John J. Callaghan, M.D.
Board Chair

Stepping Up — OREF Grant Recipients Have Better Chance of Receiving NIH Funding

At recent sub-specialty meetings, I've heard many of my colleagues worry about the decrease in funds, especially from the National Institutes of Health (NIH), for large-scale orthopaedic research funding. However, the good news is OREF grant recipients have a better chance of getting a piece of the funding that is awarded — about 30% continue their research with funding from the NIH.

The researchers we support have proven some level of talent and commitment before they apply to OREF, yet may not be ready to secure regular, substantial NIH funding.

Because OREF's vigorous peer review process is modeled after the stringent parameters set by the NIH, each of our applicants acquires valuable knowledge and hands-on experience merely by submitting his or her application. Whether or not the applicants are funded, our peer review committee members offer specific suggestions for ways to improve their grants, and applicants are welcome to seek individual guidance.

And there are significant benefits for those who do receive funding from OREF. An OREF grant creates for the recipient an opportunity to fine-tune his or her research and compile the data required to apply and win at the NIH level.

The stories in this issue of *Impact* describe basic science research, clinical research, and the necessity of educating clinicians once better materials and methods have been established. We've included a story about **Kurt Spindler, M.D.'s** NIH-funded research, a clinical, follow-up study on ACL reconstruction that began with OREF funding. According to Dr. Spindler, it would not have been possible without the start-up funds he received from OREF.

As Dr. Spindler indicates in his story, we need to also support basic science research because it could be a critical next step in developing an element that improves clinical outcomes. OREF's requirement that Ph.D.s work closely with orthopaedic surgeons fulfills this need, and enables researchers, like **Steven A. Goldstein, Ph.D.**, to obtain funding at the NIH level.

Where do the next generations of solutions emerge? They emerge from those organizations that are willing to invest early; invest in brand new ideas and new investigators. OREF funds the new investigators, the new ideas.
— Steven A. Goldstein, Ph.D.

By funding these investigators early in their careers, OREF is ensuring they have the experience and data needed to obtain funding at the NIH level, so that they can carry on their quest to advance orthopaedics and improve patient care.

Sincerely,

John J. Callaghan, M.D.
Board Chair

"I think that most people who've been successful at research at the NIH level will have all started with OREF funds.... Without my OREF grant there would not have been an NIH grant."
— Kurt P. Spindler, M.D.

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Prosperous Partnerships

In the last issue of *Impact*, Dr. Callaghan discussed some new ways in which OREF is partnering with specialty orthopaedic partners. These new opportunities, such as our E-mail Services Program, are exciting enhancements to OREF's Designated Giving Program, which has been in place for more than 20 years.

Supporting the Spectrum of Research and Education Needs

OREF's Designated Giving Program is the means by which OREF simultaneously cultivates support for broad, middle-ground, and narrow research and education agendas. All are desperately needed if we are to maintain the quality of orthopaedic care that patients deserve.

\$500 or More for OREF, the Balance as You Designate

OREF's fundraising efforts generate support for our orthopaedic partners' programs as well as our own. Gifts of \$1,000 or more to the OREF Annual Campaign come with **Order of Merit** recognition and designation privileges, by which \$500 or more flows to OREF and the balance is directed to the donor's choice of orthopaedic partner(s).

Designation Opportunities in Print and Online

OREF facilitates gift sharing by listing our giving partners in *Impact*, on page 9 in this issue, in our brochures, and online at www.oref.org/donate. In addition, we provide gift-sharing tools for use at our partners' annual meetings, conferences, and workshops.

The Result? More than \$19.4 Million for OREF's Partners

Since OREF's Designated Giving Program began in 1995, OREF has raised more than \$19.4 million for our orthopaedic partners. By giving our partners an easy way to support their research and education missions, we can all work together to advance orthopaedics and improve patient care.

Sincerely,



Gene R. Wurth
President and CEO



Gene R. Wurth
President and CEO

About Impact

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Please direct comments about this publication to communications@oref.org

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Joseph C. McCarthy, M.D.
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Following the Leaders: Shands Members Have the Power to Increase Their Ranks

Increasing numbers of orthopaedic surgeons are making significant contributions to join OREF's highest recognition society, the **Alfred R. Shands Jr., M.D. Circle**. The Shands Circle acknowledges individuals who make long-term commitments to the OREF Endowment.

Shands Circle members cite various reasons for making such a notable commitment to OREF. Some are longtime Order of Merit donors — those who give \$1,000 or more to OREF's Annual Campaign — who want to help ensure that orthopaedic research is funded in perpetuity. Others are simply applying a personal philosophy that dictates they should give back what has been given to them.

But other Shands members were influenced by their peers or encouraged to give at the Shands Circle level because their mentors have done so. Such was the case for **Dr. Kim Templeton** who had never given to OREF until **Dr. Laura Tosi** asked her to begin donating in 2004. Soon thereafter Dr. Templeton became a Shands member to encourage young women and minorities to go into orthopaedic medicine. She decided her membership in the Shands Circle should support research and serve as an example for others.

Today, the Shands Circle includes nearly 500 members. New members were listed in the June/July 2007 *Impact*, representing more than 20 commitments OREF has received since January of this year. Fueled by knowledge that their friends and colleagues had the capacity and desire to give at the Shands level, **Drs. Behrooz Akbarnia, George Thompson, Charlie Rockwood, and Mr. Tim McTighe** are among those peers and mentors who reached out, successfully persuading these new Shands members to join.

In a personal letter Dr. Rockwood sent to those he asked to join he stated, "... I am writing to ask if you would consider becoming a member of the Shands Circle. There are many, many benefits in becoming a member of Shands and probably the most important is that you are making a contribution to the organization that consistently supports both basic and clinically relevant research in orthopaedic surgery."

The OREF Shands Circle recognizes those who make substantial endowment contributions — \$20,000 or more in cash or stock gifts within a 5-year period, or \$50,000 or more in deferred commitments, made through bequests, trusts, or life insurance policies. Shands Circle Members receive many benefits during the AAOS Annual Meeting, including priority

Tax-Saving Opportunity for Donors Aged 70^{1/2} or Older Expires Act Before December 31, 2007

On Aug. 17, 2006, President Bush signed into law new tax incentives for charitable gifts from donors who are 70^{1/2} or older. **The Pension Protection Act of 2006** encourages financial support of charitable organizations across the United States.

Under the law, you can make lifetime gifts using funds from your individual retirement accounts (IRAs) without undesirable tax effects. Previously you would have had to report any amount taken from your IRA as taxable income. You could then take a

charitable deduction for the gift, but only up to 50% of your adjusted gross income. In effect, this caused some donors to pay more in income taxes than they would have if they hadn't made a gift at all.

Fortunately, now these IRA gifts can be accomplished simply and without tax complications. Plus, you can make the gifts now — while you are living and able to witness the benefits of your generosity. But time is running out — this unique opportunity expires at the end of this year, so hurry!

You may contribute funds this way if:

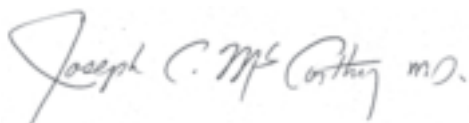
- You are age 70^{1/2} or older
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housing, an invitation to the exclusive Shands Circle Gala, and access to a private VIP suite. Plus, members and spouses receive an exclusively designed Shands Circle lapel pin, and special recognition from OREF throughout the year.

I encourage all Shands members to discuss joining the Shands Circle with anyone you know who has the means and the aspiration to give at this level. Our 20-plus new members are positive proof that as respected colleagues, you have the ability to persuade a friend and increase the number in our Circle. What a great boost it would be if every current Shands member invited one new Shands member.

If you are interested in asking someone to join the Shands Circle, **Ed Hoover**, associate vice president, development, can direct you on how to obtain materials and information you'll need. For more information on planned giving, please visit www.oref.org/giftplanningguide.

Sincerely,



Joseph C. McCarthy, M.D.
Chair, Shands Circle Committee

Shands Circle Benefits

Shands Circle members receive many benefits, including:

- **VIP housing** at the AAOS Annual Meeting
- Invitations to OREF's annual **Shands Circle Gala**, a black-tie optional dinner and reception
- Access to OREF's exclusive **Shands Circle VIP Suite** at the AAOS Annual Meeting
- A **gold lapel pin** featuring the Shands Circle logo
- **Significant recognition** at the AAOS Annual Meeting and through other vehicles, including OREF's publications

Contact OREF

To learn how to join the Shands Circle, or for more information on how to make a major gift to OREF, please visit www.oref.org/giftplanningguide or contact:

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Soon!

How the New Law Works

Pat, aged 80, has \$450,000 in an IRA and has pledged to give OREF \$100,000 or a smaller amount this year. If Pat transfers \$100,000 to OREF from the IRA, she will avoid paying income tax on that amount. She cannot, however, claim a charitable deduction — it is a pure wash. Pat has found an easy way to benefit us without tax complications. If Pat's spouse has an IRA and is 70½ or older, he can also give up to \$100,000 tax-free to a charitable organization.

How to Make a Gift

Contact your IRA custodian soon to transfer your desired gift amount to OREF or a charitable organization of your choice.

For More Information

If you are interested in making a lifetime gift from one of your IRA accounts, please contact your financial planning advisor or OREF. Additional planned giving information is now available at www.oref.org/giftplanningguide.



Room for Many More *continued from page 1*

most common procedures performed by orthopaedists, according to Dr. Ferguson, is knee arthroscopy to manage damaged cartilage structures. And the majority of these, Dr. Ferguson said, involve the trimming of torn menisci instead of repair, which has long-term implications for the knee.

“One of the more difficult things to see in your practice is a young, active person whose knee is, overall, very healthy, but they have a cartilage tear that can’t be fixed. Often a substantial portion of the injured meniscus needs to be taken out because it is biologically and mechanically unable to heal,” Dr. Ferguson said. “While current meniscus transplants with cadaver tissue are good, there are certain biological aspects that lead to earlier failure. They do not all appear to function as well as the original meniscus and they do not appear to last as long.”

Dr. Ferguson is seeking a solution to this problem, which she believes is caused by the nature of the cadaver transplant tissue.

“Studies show that the recipient of the transplant, or host’s, cells cannot grow into the central portion of the transplant, which is a dense tissue. Ultimately there are no cells living in the central portion of the transplant to help maintain its structure and strength, so it wears out.”

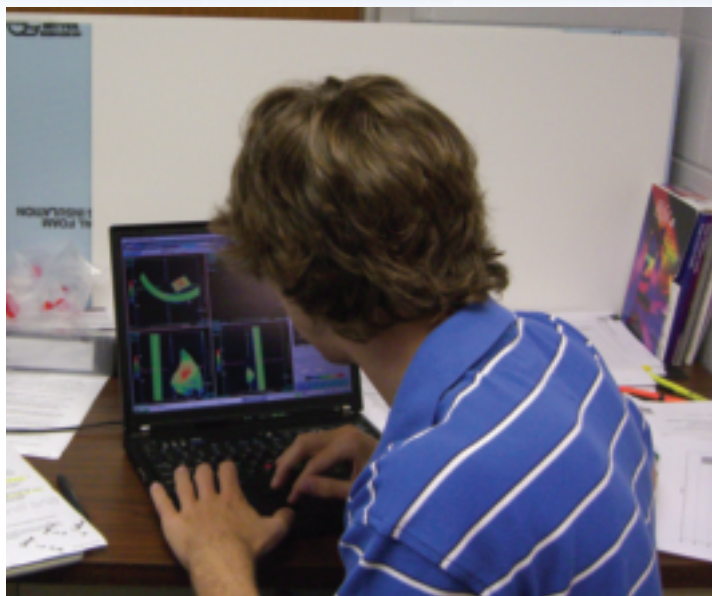
“It’s very hard to carve out research time, and that’s what this award enables someone to do. It helps develop the research part of a career and frees up time to serve as a mentor to people who have similar interests.”

— Cristin M. Ferguson, M.D.

To prevent this problem, Dr. Ferguson is investigating a way to transplant menisci with living cells in the center. Her research involves chemically processing a cadaver meniscus to not only remove the cadaver cells, but also create spaces (porosity) for new cells to grow. This should give the host’s cells room to grow into the center of the transplant tissue, or allograft.

An Amenable Allograft

In addition to making room for the host’s cells, Dr. Ferguson is working on another process to help the transplant patient accept the allograft. By deriving stem cells from the host’s own blood or bone marrow and inserting them into the transplant tissue, Dr. Ferguson hopes to create a meniscus that is already populated by the patient’s own cells before the transplant takes place.



Mr. Devin Odom, a first-year summer medical student, works on meniscus scaffold image analysis.

“I think the one thing that’s attractive about this method is that the fundamental structure of the meniscus — the natural arrangement, structure, and composition of collagen fibers — is maintained. We’re not trying to synthetically reproduce the meniscus. It is a complex tissue that would be very difficult to accurately recreate with synthetic materials. Instead, we’re preserving the natural structure, but making it more biologically compatible for the body’s cells to grow in and take over. The ingrowing cells can also take cues from the surrounding collagens and proteins to guide them to grow into the desired tissue. We’re capitalizing on the complex structure and biology of the meniscus scaffold that’s already there by making the allograft tissue more amenable for our bodies to incorporate and maintain it.”

The idea behind this, according to Dr. Ferguson, is that the living host cells that grow into the center of the tissue upon implantation should be better able to maintain the collagen and surrounding matrix proteins and, therefore, maintain the structural integrity of the meniscus tissue transplant. The fact that the host cells are added to the allograft also helps the recipient’s body accept the tissue because it already seems like the patient’s own.

These studies could have additional implications for older patients. As people age, the meniscus degenerates, and Dr. Ferguson would like to further her research by studying the processes of aging in the meniscus.

“Concurrent with meniscus degeneration, we also see the development of arthritis, and while the articular cartilage research that’s currently being done is very important, I think we’re missing information on another very important structure within the knee that contributes to the development of arthritis: the meniscus,” said Dr. Ferguson. “We need to understand the biology that is happening in the meniscus with aging and development of degenerative changes.”

Hope for Healthier Knees

If the biological studies show promise, Dr. Ferguson would like to move on to human clinical trials, comparing the new meniscus replacement to what she terms the current gold standard: allograft transplantation. If this new meniscus replacement shows promise, she hopes that it could someday be used to help patients who've experienced more extensive cartilage and arthritic injury than what is currently managed with standard meniscus allograft transplantation.

"I'm trying to work on the current technique to make it better so that patients will have better results with better long-term function. By creating a healthier knee, patients can stay more active longer, especially in their younger years, doing all of the activities that they like to do instead of giving them up."

"I'd like to understand why people tear their meniscus. I'd like to understand why the meniscus wears out. Research allows me the opportunity to ask these questions and, over time, answer them. I think the ultimate goal is to expand our knowledge so we can better treat patients."

— *Cristin M. Ferguson, M.D.*

Dr. Ferguson believes research is important, not only because she is herself a clinician scientist, but also to advance orthopaedics.

"There are so many things that I do every day that seem to work in clinical practice, but I don't really understand them. I'd like to understand why people tear their meniscus. I'd like to understand why the meniscus wears out. Research allows me the opportunity to ask these questions and, over time, answer them. I think the ultimate goal is to expand our knowledge so we can better treat patients."

Dr. Ferguson has focused her medical career around orthopaedic clinical training, sports medicine fellowship training, and basic-science orthopaedic research. She spent more than two years conducting orthopaedic research during her training, first at the University of California, San Francisco, and then at the University of Rochester. In 1999 she received an OREF Resident Research Grant for her study of the process of cartilage maturation. Currently, Dr. Ferguson is an assistant professor at Wake Forest University where she divides her time among teaching, clinical practice, and research. In addition to OREF, Dr. Ferguson will receive funding to support her meniscus transplant research from the Musculoskeletal Transplant Foundation and National Football League Charities. ■



(left to right) Beth Smith, Ph.D., Cristin Ferguson, M.D., and Tom Smith, Ph.D. review data in the orthopaedic research lab at Wake Forest University.

OREF Clinician Scientist Award Now in Its Fifth Year

The OREF Clinician Scientist Award was established by **Dr. Zachary B. and Mrs. Kathleen Friedenberg** in 2003 to encourage young orthopaedic surgeons to pursue careers as clinician scientists, with a special emphasis on continued research. After the creation of the first award, **Dr. Dane and Mrs. Mary Louise Miller** and **The Journal of Bone and Joint Surgery** also established Clinician Scientist Awards. **The Journal of Bone and Joint Surgery** will support Dr. Ferguson's Clinician Scientist Award.

Clinician Scientist Awards provide an annual stipend of \$100,000 for three years to compensate for the loss of income associated with devoting more time to research, and less time to clinical practice. In return, OREF Clinician Scientists are asked to devote extensive time to research; serve as role models for orthopaedic residents, interns, and medical students; and organize and participate in conferences.

Saluting our Corporate Associates

OREF is proud to acknowledge these companies for their generous support. A strong and productive alliance with industry enables OREF to fund quality programs that advance the orthopaedic profession, ultimately leading to improved patient care.

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Medtronic



Pain Management Initiative Results to be Published



Based on a collaboration between the Orthopaedic Research and Education Foundation (OREF) and the American Orthopaedic Association (AOA) and made possible through an educational grant provided by Pfizer Inc, the Pain Management Initiative surveyed orthopaedic surgeons to learn which pain management therapies, technologies, and techniques they administered to patients after total joint replacement, sports medicine, and spine-related surgery. You will find a highlights report of the OREF/AOA Pain Management Initiative with the November/December 2007 issue of *Impact*. A complete results report is being reviewed for publication. For more information and updates on publication of the full report, please visit www.oref.org or www.aoassn.org.

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- the balance to your choice of OREF orthopaedic partner(s)

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Gene Wurth
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wurth@oref.org

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The Building Blocks of Research and Development

Biomet Emphasizes Dedication to Research as OREF Corporate Associate

Following the lead of one of its founders and demonstrating a dedication to research, Biomet continues to be one of OREF's strongest Corporate Associates.

"Biomet began supporting research through OREF many years ago as a result of the company's strong commitment to research and development," said **Mr. Jeffrey R. Binder**, Biomet president and CEO. "Throughout the years, Biomet has been recognized as an entrepreneurial, engineering-driven orthopaedic company, producing many successful products and technologies with excellent, long-term clinical results. This could not have been achieved without a strong emphasis on research."



Mr. Jeffrey R. Binder

Biomet's Beginnings

In fact, Biomet was founded on the desire of **Dane A. Miller, Ph.D., Mr. Jerry L. Ferguson, Mr. M. Ray Harroff** and **Mr. Niles L. Noblitt** to use their individual expertise to compete within and contribute to the growing orthopaedic industry in Warsaw, Ind. Each of these individuals, having worked for device companies, took on personal risks, but through teamwork used their collective experience to found a new company that was responsive to the needs of orthopaedic surgeons and their patients.

"We need to invest in research to allow us to deliver a lot more care to our aging population," past Biomet President and CEO Dr. Miller explained. "Orthopaedic research gives the orthopaedic device industry and orthopaedic surgeons better tools, better equipment, better technology, and a better understanding of long-term clinical results. Better tools and a better understanding will ensure and improve efficient care of the orthopaedic patient."

Dr. Miller's desire to advance orthopaedic technology encouraged his decision to support research personally. The **Dr. Dane and Mrs. Mary Louise Miller Endowment Fund** has supported specific OREF grants, including two Clinician Scientist Awards, which encourage young orthopaedic surgeons to pursue careers as clinician scientists.

"While Biomet has been a significant contributor to OREF, we should also acknowledge the individual contributions of Dane and Mary Louise Miller to this Foundation," Mr. Binder indicated. "Dane Miller, a biomedical engineer and renowned visionary in orthopaedics, who was one of Biomet's founders and my predecessor, has been a longtime major supporter of OREF. Consequently, it should come as no surprise that OREF and Biomet became partners, with a common goal of supporting research for the advancement of orthopaedics."

Progress From Research

The strong partnership between Biomet and OREF continues under Mr. Binder's leadership. This is due in part, he said, to the positive effects research has had on the company. Products introduced in Biomet's formative years have stood the test of time. According to Mr. Binder, over the last three decades Biomet introduced numerous key advancements in orthopaedics. Developments include: use of titanium for hip stems, which provides better biocompatibility and elasticity; tapered hip stems to reduce stress shielding and improve bone viability and long-term fixation; porous plasma spray

coating created by heating the titanium coating rather than heating the implant itself to create a better bond and preserve the integrity of the implant; and improved wear characteristics for knee systems by using direct compression molded polyethylene for tibial bearings. Today, Mr. Binder said, Biomet continues its commitment to innovation with new technologies. In the last eight years Biomet has introduced more than 700 new products including a porous titanium construct and vitamin E stabilized highly crosslinked polyethylene.

"... one of the main benefits of supporting research through OREF is interaction with current and future opinion leaders, affording opportunities to collaborate on the development of new products and technologies."

— Mr. Jeffrey R. Binder

"These examples reflect only a few of the major improvements to implant design and manufacturing processes that are directly attributable to Biomet's innovation through research and development," Mr. Binder said. "Research is used by device manufacturers to create or modify products that have advantages over previous designs. An example of this is the use of alternative bearing materials designed to improve wear for total hip articulations, including metal-on-metal and ceramic-on-ceramic constructs. These technologies offer the potential for increased longevity of total joint replacements, which is certainly a direct benefit for patients, but also contributes to the advancement of the orthopaedic industry."

There was little question then that Biomet would support research, but why did it choose to do so through OREF? Mr. Binder said that the diversity of OREF's contributors and Board of Trustees make the Foundation qualified to assess projects and designate support for meaningful research and education.



Dane A. Miller, Ph.D.

"OREF is a widely recognized leader in orthopaedic education and research. As good corporate citizens, I believe we have an obligation to invest in the future development of orthopaedic technologies," Mr. Binder said. "And one of the main benefits of supporting research through OREF is interaction with current and future opinion leaders, affording opportunities to collaborate on the development of new products and technologies."

Ensuring orthopaedic surgeons are educated on such new technologies is also important to Biomet, and another reason its partnership with OREF remains strong.

"The support provided by industry to universities, teaching institutions, and organizations such as OREF is a key factor in advancing orthopaedic knowledge. As a leading orthopaedic device manufacturer, we believe that we should take a role in

"OREF helps provide guidance on what constitutes meaningful research and education by means of its various peer review committees. Without this guidance and foresight, many technological advances may not be fully recognized and further developed by the orthopaedic industry, ultimately affecting patient care."

— Mr. Jeffrey R. Binder

supporting the education of orthopaedic surgeons. OREF provides an opportunity to effectively achieve this goal," he said.

Collaborating on Common Goals

Wanting to learn more about opportunities provided by OREF, Biomet recently invited OREF Board Chair, **John J. Callaghan, M.D.**, former Board Chair **Victor M. Goldberg, M.D.**, and staff to meet with members of its management, research, engineering, and marketing departments.

"Our intention was to increase visibility of the goals of OREF and to investigate the potential for new areas of collaboration," said Mr. Binder.

The Biomet summit provided a heightened understanding of OREF's and Biomet's respective missions, operations, and goals. Representatives of both OREF and Biomet hoped this understanding would lead to more productive and beneficial collaborations in the future. They discussed collaborative opportunities, as well as other topics of interest such as marketing to clinicians not involved in research, researching topics outside the realm of orthopaedics, such as infection control, and the need for more clinical studies.

In addition, Biomet learned about OREF's new Independent Peer Review and Directed Research Services, which are offered to Platinum Level Corporate Associates. With this program, OREF's peer review process is available to evaluate basic science and clinical research proposals against OREF's criteria for scientific rigor and orthopaedic merit.

"I believe the Foundation fulfills a key role within the orthopaedic community," Mr. Binder said. "OREF helps provide guidance on what constitutes meaningful research and education by means of its various peer review committees. Without this guidance and foresight, many technological advances may not be fully recognized and further developed by the orthopaedic industry, ultimately affecting patient care." ■



Biomet, Warsaw, Ind.

Brought to Their Knees *continued from page 1*

participating in projects as a medical student and resident, and is still central to his work with the current generation of young orthopaedists. Today, Dr. Spindler is professor and vice-chairman of the department of orthopaedics and rehabilitation at Vanderbilt University Medical School where he is also director of the Vanderbilt Sports Medicine Center and Orthopaedic Patient Care Center, and serves as head team physician for Vanderbilt University's NCAA Division I varsity athletes.

"By going through scientific inquiring and using the best evidence-based medicine, you can be assured that you're applying the best care to your patients," he said, explaining his penchant for research. "And what being an orthopaedist really comes down to is taking excellent care of patients."

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— Kurt P. Spindler, M.D.*

First Funding

Dr. Spindler first became involved with OREF when he applied for and received funding for a basic science project that examined the role played by bone growth factors in the normal healing process. He wanted to know if they could be applied clinically to accelerate and seal healing in joints. The *Journal of Orthopaedic Research* published papers on his work in which he concluded that the

growth factors did not speed healing enough to warrant their use in clinical practice.

Still interested in the healing process, however, he searched for someone who shared his passion for research, looking outside Vanderbilt when he didn't find anyone at his own university.

"I found Martha Murray, who had received some OREF funding and now has an R01 NIH grant. I decided to collaborate with her and continue in the supporting role with that research."

With **Martha M. Murray, M.D.**, an assistant professor in orthopaedic surgery at Children's Hospital of Boston, Dr. Spindler continued to investigate what inhibits joint healing. Currently their studies show that platelets might play a significant role.

Dr. Spindler, however, was also interested in research beyond basic science, particularly in terms of ACL reconstruction.

"When you perform surgery on someone, you want to know what predicts their result. I think of result as being function. You want to know how well they function, what their activity level is, and what's the risk of them developing arthritis."

Survey Says

Adding to a database he had already developed as a fellow at Cleveland Clinic, Dr. Spindler collected prospective data from ACL reconstructions at Vanderbilt and from **Jack T. Andrish, M.D.** and **Richard D. Parker, M.D.** at Cleveland Clinic Foundation. With this data, he applied for and received an OREF Prospective Clinical Research Grant in 2002. The OREF funding allowed him to amplify the prospective data by contacting patients a few years after their operations. The study proved not only that a high percentage of follow-up was possible two to five years after ACL reconstruction, but also that valid information could be obtained from the previously validated questionnaires patients completed themselves.

"The forms are supposed to be interpreted and completed only by the patient and they are not to be changed by anyone," Dr. Spindler explained. "Their design is to be independent of any interviewer — physician or anyone else — so that the patient can interpret the questions reliably and accurately."

At two years after surgery, orthopaedists taking part in this study asked patients to answer four standardized questionnaires designed to gather outcome data.

The study used two general forms. Short Form 36 (SF36) contains 36 questions to measure health-related quality of life for all medical disciplines, and the Western Ontario MacMaster (WOMAC) form asks 24 questions about pain, disability, and joint stiffness to evaluate pain and function in knees and hips affected by osteoarthritis.

Dr. Spindler's research also used two sports-specific forms; the International Knee Documentation Committee (IKDC) form and the Knee Injury Outcome Osteoarthritis Score (KOOS) form, both of which measure activity level by asking such questions as, "Do you have problems with your knee in everyday life?" and "Do you limit your sports and recreational activities because your knee bothers you?"

Challenging the Status Quo

The research conducted under the OREF grant changed the way in which outcomes were evaluated. Before the OREF study, Dr. Spindler indicated, the standard methods to measure ACL reconstruction were based on structural factors, such as knee stability, range of motion, and laxity. Dr. Spindler's study did not measure structural changes, but relied instead on the questionnaires in which patients expressed how their knees felt years after their procedures. The questionnaires evaluated physical and mental health, function in sports, symptoms of arthritis, and overall quality of life. In August of 2005 *The Journal of Bone and Joint Surgery (JBJS)* published a paper on the study, highlighting validated questionnaires as a means to measure ACL reconstruction. Consistent with this, *JBJS* now recommends the WOMAC as the best form to evaluate osteoarthritis.



Kurt P. Spindler, M.D.

"Prior to the *JBJS* paper, everyone evaluated an ACL reconstruction by how stable your knee was. We said, 'we don't have that information, but we can tell you how well it's functioning by some valid sports-specific forms. We can tell you whether they have symptoms of arthritis,'" Dr. Spindler said.

"Without OREF there is no NIH grant. You can think of the NIH as a car race. No one is going to give you a Ferrari to race at first . . . The OREF allows you to race safely and appropriately at your level to build your skills set so that you have the opportunity to advance to the NIH, to get that Ferrari and win." —

Kurt P. Spindler, M.D.

"We changed the paradigm and said that measuring success in this way was equally important to the patient. *JBJS* agreed and this is the kind of shift the OREF paper made. Now people don't just focus on knee stability, they focus on stability but also on patient-reported outcomes."

To the MOON

Based on the success of the OREF-funded study, Dr. Spindler and his research partners established the Multicenter Orthopaedic Outcomes Network (MOON), a consortium of seven hospitals and universities throughout the United States, each of which adds ACL patient outcome data to the database.

In the first three years the members of MOON collected data on 1,600 patients, approaching a 90% follow-up rate. The high percentage of follow-up is due to the competitive nature of orthopaedists, Dr. Spindler indicated.

"We print out every surgeon's percent follow-up so that everyone else in the group sees, and it becomes them versus the rest of their friends. Since we're all at the same level and most of us run large sports medicine centers, we don't want to lose to each other. I don't want to lose to the guy in Cleveland, and the guy in Iowa doesn't want to lose to the orthopaedist at Vanderbilt or Cleveland."

Dr. Spindler explained that a high follow-up percentage is necessary because the minimum follow-up for Level 1 evidence-based medicine is 80%. Because some data,

such as revisions, must be excluded, the goal has to remain even higher to ensure percent follow-up remains above the minimum threshold.

From Hondas to Ferraris

After four years of collecting data and a little more than two years of writing grants, Dr. Spindler received, as the principal investigator, a \$1.2 million NIH R01 grant to continue the MOON cohort study.

According to Dr. Spindler, OREF funding was instrumental to the beginning of this long-term, follow-up research, and without it, NIH funding would have been impossible to obtain.

"Without OREF there is no NIH grant. You can think of the NIH as a car race. No one is going to give you a Ferrari to race at first. You're going to have to race cars that are more appropriate for your level. So you race Hondas for a while before you get good enough to go race with the big cars. That's exactly what OREF is. The OREF allows you to race safely and appropriately at your level to build your skills set so that you have the opportunity to advance to the NIH, to get that Ferrari and win."

Sophisticating MOON

The NIH funding will enhance data for the study. The four forms that the MOON members were using as follow-up are now used pre-operatively as well. Since the patients are asked the same questions before

continued on next page

surgery as they are at follow-up, Dr. Spindler said, the data paint a more accurate picture of how well reconstructed ACLs are functioning.

“We use the same valid outcome measures that we apply to patients at the time of their surgery, so when we follow up with the same measures our results are more powerful because we’re able to control for their initial baseline account.”

The database used by MOON affiliates has also become more sophisticated, having been customized by the Vanderbilt biostatistics department, headed by **Frank E. Harrell Jr., Ph.D.** and having received epidemiological support from **Robert S. Dittus, M.D., M.P.H.** at Vanderbilt’s Health Services Research Center.

In addition to improving the data aspects of the study, the NIH funding will allow further investigation. The members of MOON will take structural measurements. While the cost would be too great to have every patient in the database return to the MOON universities and hospitals to have their reconstructed ACLs structurally measured, a randomized sub-set of patients can act as a model for the whole group. Among other structural indicators, on follow-up the patient sub-set will be tested for laxity and function, and will have their ACLs X-rayed to measure joint space width.

Patient Patients

About 99% of MOON patients agree to participate in the cohort study. Dr. Spindler believes this is partly because patients realize that as subjects of the study they will receive the best possible care. But there are other benefits as well.

“When does a surgeon operate on you and then call you two years later to ask you to fill out a form to see how you’re doing? I think that patients realize that there’s no down side, other than the time it takes to fill out the form, but there’s a definite upside because you can improve ACL reconstruction for other people, and they may find improvements for themselves.”

In fact, Dr. Spindler said, much can be learned by evaluating the patient-reported data. The information will show whether patients are modifying sports and

“I think the insurance companies are going to have to take notice. Good clinical research can not only help the patients but it can also help you as physicians show that you’ve improved the quality and the efficacy of what you do and, therefore, should be reimbursed.”
— Kurt P. Spindler, M.D.

recreational activities due to knee-related pain, and how well their reconstructed ACLs are functioning compared to other patients who’ve had the same procedure. This data can be assessed to learn why some outcomes are better than others.

For example, Dr. Spindler said, a poor outcome could be the result of the partial loss of the meniscus. If they find this to be the case, orthopaedists would seek help from engineers to develop a meniscus substitute that could be implanted during the ACL reconstruction, hoping for a longer-lasting ACL graft.

The data assessment could also indicate other factors that lead to poor outcomes. Orthopaedists could then counsel their patients before and after surgery to teach them how to help their own recovery and maintain their reconstructed ACL.

This principle, based on the Framingham Study that showed high cholesterol, high blood pressure, family history, lack of exercise, and smoking to be the risk factors for cardiovascular diseases, is what Dr. Spindler would like to apply to knees and ACL reconstruction.



Dr. Spindler examines an ACL reconstruction patient.

"We're going to find out what the most important factors are in someone developing poor ACL function and we're going to see if we can modify them in the future to improve the outcome," he said. "Perhaps people who gain 50 pounds are doomed after surgery, for example. Weight may be a big thing, I don't know. That's what this study will tell us."

Satisfaction for Orthopaedists and Patients Both

Assessment of follow-up data has already led the surgeons involved in MOON to a few conclusions. They now know, for example, that the risk of tearing the graft in the reconstructed ACL is exactly the same as tearing the ACL in the knee that hadn't needed surgery. They have also found that body mass index, smoking status, arthritis on the medial femoral condyle, and pre-surgical activity level can predict how active a patient is two years after ACL reconstruction.

And the MOON cohort study could also directly benefit orthopaedists by changing insurance practices, Dr. Spindler indicated, since demonstrating that ACL reconstruction makes a difference in a patient's quality of life proves the effectiveness of the treatment.

"I think the insurance companies are going to have to take notice. Good clinical research can not only help the patients but it can also help you as physicians show that you've improved the quality and the efficacy of what you do and, therefore, should be reimbursed."

Dr. Spindler said he hopes that orthopaedists realize that clinical studies are research and development for orthopaedics and that supporting the research is critical, not only to prove the efficacy of orthopaedic procedures, but to improve patient care, which is, after all, why he became an orthopaedist.

"The most satisfying thing about being an orthopaedist is when a patient says 'thank you' for taking care of him or her. They don't have to thank me. I'm paid very well to take care of them, but they go out of their way to say 'thank you.'" ■

OREF...

Helping Residents Explore New Possibilities in Orthopaedics

OREF Resident DEVELOPMENT

The Orthopaedic Research and Education Foundation (OREF) has developed several resources we want to share, designed to help orthopaedic residents sharpen their skills and build a firm foundation for a rewarding career.

LEARNING FROM PEERS... Top-rated work (winning research abstract and poster submissions) from our Spring 2007 Resident Research Symposia competition are now posted on the OREF Resident Resources Web page: www.oref.org/residents.



GRANTS, WORKSHOPS & MORE...

OREF shared the work of 2007 Resident Research Symposia and 2007 State Society competition winners online and in print, through a call-for-grants poster, distributed to residents and candidates with the July 2007 issue of *The Journal of Bone and Joint Surgery*. Requests for extra copies of the poster, which also features the opportunities OREF provides for residents, may be sent to communications@oref.org.

RELATING TO INDUSTRY... Demand has been exceptionally high for *Essential Guidelines, Regulations and Ethical Considerations: The Evolving Relationship between Orthopaedists and Industry*, an article commissioned by OREF to help orthopaedic surgeons address health care compliance issues.

Congratulations

2007 Resident Research Symposia Winners

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Tax-Saving Opportunity Expires Soon

On Aug. 17, 2006, President Bush signed into law new tax incentives for charitable gifts from donors who are 70½ or older. **The Pension Protection Act of 2006** encourages financial support of charitable organizations across the United States. Under the law, you can make a lifetime gift using funds from your individual retirement account (IRA) without undesirable tax effects. For more information please turn to page 4.



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