LEARNING TOGETHER

Residents find benefits of OREF/ORS Research Symposia Part I

As they move toward their final year, residents must ask and answer questions about their careers. Should they go into academic or private practice? Should research be a major component? If they plan to conduct research, should it be basic science, translational, or clinical?

Residencies with a research component coupled with programs such as the OREF/ORS Resident Research Symposia give residents a taste of what it would mean to become a clinician scientist.

"I don't have a lot of experience presenting research and the symposium gave me the opportunity to communicate my research in a succinct manner, which can be difficult, and get people excited about it," said **Jacqueline Geissler, MD**, who tied for first place at the 2009 Minnesota Orthopaedic Society Annual Meeting Resident Research Symposium. "That's not a skill I've had a chance to develop, so it was a really valuable opportunity."

According to symposia participants, presenting their projects within tight time constraints — usually five minutes — improves their ability to synthesize and communicate their results.

"It's one thing to know your research and discuss it with an individual who has a background in your topic. The same task is much more challenging when you engage an audience that may know nothing about your area of investigation," said **Shen-Ying (Richard) Ma, MD**, whose poster earned first place at the 2009 Virginia Resident Research Symposium.

Communication among peers is another benefit residents say they gain from attending these symposia. Not only do they learn about potential advances in orthopaedics, they also may find that someone has a solution for a problem with which they've been struggling. And collaboration opportunities may arise when residents find their projects to be similar or complementary.

"Our orthopaedic program benefited because we're trying to start a bio-innovative institute where we work together with local universities, medical schools, and hospitals," observed **Andrew Bries, MD**, first-place winner at the 2009 Cleveland Resident Research Symposium. "I think this type of symposium supports that type of collaboration — everybody coming together to produce high-quality research."

Beyond opportunities to interact with each other, the symposia give residents a forum in which they can network and ask questions of attendings and established researchers, which may help them refine their career paths.

"Because the symposium I attended was combined with the Minnesota Orthopaedic Society's Annual Meeting, there were private practice and clinician orthopaedists there who were able to offer their insights and share their experiences," said **Mir H. Ali, MD, PhD**, the other first-place winner at the 2009 Minnesota Symposium.

In addition, constructive criticism given by those judging the competition can instruct residents on ways to adapt their research presentations for larger meetings.

"It's exciting to present your research to different audiences," said **Michael D. Tseng, MD**, whose presentation took first place in the basic science category at the 2009 Midwest Resident Research Symposium. "I gave my symposium presentation at the 2010 AAOS Annual Meeting and it was a good experience."

To Dr. Tseng, participating in the symposia put a cap on his residency. "The Resident Research Symposia are opportunities to culminate your research experience if you're in your fifth year of residency," he said. "I'm very glad I participated in the symposium and recommend it to future residents."

RESEARCH SYNOPSES part I

Andrew Bries, MD

A Study in Vivo of the Effects of a Static Compressive Load on the Proximal Tibial Physis in Rabbits

Slipped capital femoral epiphysis (SCFE) — a condition in which the femoral head slips backwards from the physis (growth plate) — is common among adolescents beginning puberty. But orthopaedists don't know whether this condition is caused by mechanical, hormonal, or other factors.

"There are several diseases we know are associated with heavier kids, but we don't know exactly if it's obesity that causes the disease or if other factors are involved," said **Andrew Bries, MD**, first-place winner at the 2009 Cleveland Resident Research Symposium. "We wanted to look specifically at force to determine if obesity causes the growth plate to be sick."

To determine the role played by obesity, Dr. Bries and his research team tested a rabbit model. Applying fixators — adjustable tension springs that add load to pins inserted through the physis and down the bone shaft — Dr. Bries induced mechanical forces on the growth plate.

"We looked to see if gene expression changed. We saw a change in the expression of Type 2 and Type 10 collagen aggrecan, which is similar to what is observed in humans with SCFE."

By conducting this research, Dr. Bries hopes that he and his research team will be able to determine if it's only force or if there are other factors contributing to SCFE.

"If we find out that the cause of these diseases is purely mechanical, we may need to reinforce that these kids need to lose weight, and perhaps could develop a growth factor or drug for at-risk kids that would prevent gene expression from changing in collagen, and prevent SCFE."

ABOUT OREF/ ORS RESIDENT RESEARCH SYMPOSIA

Resident Research Symposia give orthopaedic residents at area training programs an opportunity to present research papers to a panel of experienced investigators and clinicians. Panels critique and rank the work, and top presenters are acknowledged.

- OREF has held Resident Research Symposia for more than a decade.
- Since they began, with support from industry OREF has put more than $360,000 behind Resident Research Symposia.
- In 2010, the Orthopaedic Research Society (ORS) joins OREF in sponsoring the Resident Research Symposia. See p. 16 for other ways in which ORS partners with OREF.

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▲ Safdar N. Khan MD

Safdar N. Khan, MD

The Role of Leptin in the Local Control of Fracture Healing

Leptin, a molecule secreted by adipose tissue, seems to play contradictory roles when it comes to bone. When acting at the hypothalamic level in the central nervous system, it appears to be responsible for bone resorption. When acting locally at a fracture site, however, it is bone-forming.

"The dichotomy of a single molecule able to directly influence two different body systems is really fascinating," said **Safdar N. Khan, MD**, first-place winner at the 2009 San Francisco Resident Research Symposium. "And I questioned what role leptin plays during fracture repair."

Dr. Khan looked at the molecule from three aspects. First, he studied normal mice that have their own supply of leptin by fracturing their femurs and examining the fracture callus with Reverse Transcription Polymerase Chain Reaction, the most sensitive technique for messenger RNA detection.

"We showed for the first time that indeed the signal for leptin is present in fracture healing," Dr. Khan said.

Next, Dr. Khan and his research team investigated fracture healing in mice that did not have the leptin molecule (null mice) to learn if there were any differences. They found that when the leptin molecule was absent, there was a delay in bone formation.

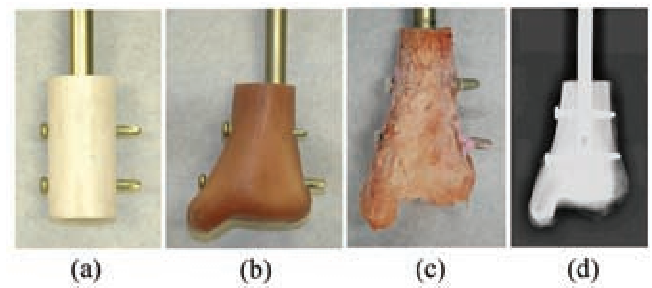
This led them to their third question: Could they reverse the effects of leptin deficiency in the null mice? After injecting two doses of leptin in separate groups of null mice at the fracture site, the researchers looked at CT scans to measure healing. The scans showed the injected leptin restored the healing characteristics they'd observed in the normal mice.

"The fact that we identified that the leptin molecule is present in fracture healing is important because the more we know about the basic biologic functions of numerous molecules during fracture healing, the more we will be able to understand impaired healing in fracture repair, spine fusion, or cartilage repair or regeneration," Dr. Khan explained.

▲ Brennen L. Lucas, MD

Brennen L. Lucas, MD

Biomechanical Comparison of Distal Locking Screws for Distal Tibia Fracture Intramedullary Nailing



▲ Samples of the experiment test specimens: a) Part I test specimen (PVC), b) Part II test specimen (composite analogue bone), c) Part III test specimen (cadaver), and d) Radiograph of Part III test specimen

Of the four long bones in the human body, the tibia is the most commonly fractured, but ideal methods for intramedullary nailing, a popular treatment, are unknown.*

"It is somewhat arbitrary how many screws orthopaedists decide to put into a distal tibia fracture to hold the intramedullary nails in place," said **Brennen L. Lucas, MD**, first-place winner at the 2009 Mid-Central States Orthopaedic Association Resident Research Symposium. "It was an unanswered question in orthopaedic literature and I thought it would be reasonable to answer in a residency research project."

Dr. Lucas and a team of biomechanical engineers developed two ways to simulate an unstable distal tibial fracture: a PVC pipe model and a cadaver model. The researchers treated the fabricated fractures with intramedullary nails and tested their stability with different screw configurations. They wanted to know what quantity and configuration was the most stable.

"We found that two medial-to-lateral screws were biomechanically equivalent to three distal locking screws," Dr. Lucas said.

While more tests need to be run, especially a clinical randomized trial that compares two screws versus three, Dr. Lucas indicated that results would benefit both patients and the health care industry.

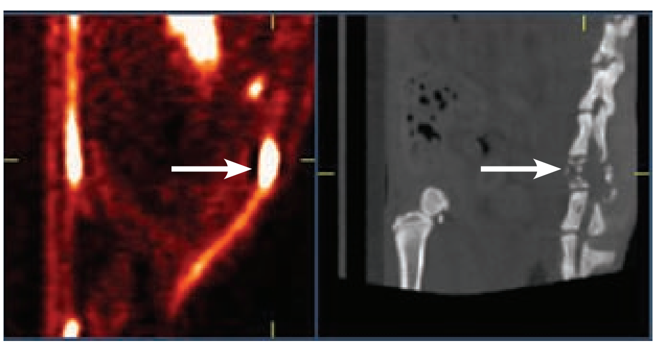
"It's beneficial for us to know how many screws we need to stabilize fractures until they heal," he said. "Also, in the long run it saves the health care industry money since there would be less fluoroscopy time, less operative time, and fewer implants."

*http://orthoinfo.aaos.org/topic.cfm?topic=A00522

▲ Shen-Ying (Richard) Ma, MD

Shen-Ying (Richard) Ma, MD

Metastatic Spine Disease: An Isolated Spine Tumor Model with Human Breast Cancer Cells



▲ Micro-PET (left) and CT (right) images demonstrating the implanted spine tumors and local spine destruction (arrows).

When malignant cells metastasize, they create complications for cancer patients, often resulting in malignant axial spine tumors. These tumors can severely compromise a patient's quality of life, through significant pain, reduced mobility, and if severe enough, paralysis.

"Many cancers spread to the spine, and right now the majority of our treatments are palliative and not necessarily curative," said **Shen-Ying (Richard) Ma, MD**, whose poster earned first place at the 2009 Virginia Resident Research Symposium.

With his mentor, OREF grant recipient **Francis H. Shen, MD**, Dr. Ma developed a rat model to research how tumor cells grow and behave. Dr. Ma and his research team implanted human breast cancer cells into rat spines. The researchers analyzed ways to image the cells and evaluate how they grew and spread to the adjacent vertebral bodies.

"We wanted to see if the human breast cancer cells we implanted in the rats would behave and spread like they do in humans," Dr. Ma explained. "In our model, when tumor cells spread from one segment of the spine to another, they behaved very much like they do in humans."

Because Dr. Ma wasn't able to accurately gauge tumor growth with X-rays alone, he decided to evaluate tumor growth using micro Positron Emission Topography (PET) and IVIS bioluminescence imaging.

"We found a radiology researcher who was evaluating small laboratory animal imaging including PET and IVIS, and we were able to test the technology with our cancer model," Dr. Ma said. "It worked really well. The exciting part was we could track the tumor cells' growth with both IVIS and PET. As the tumor cells multiplied and grew, they became brighter on the PET and IVIS pictures."

Although Dr. Ma is no longer in the research laboratory, Dr. Shen is continuing the research, which may evolve into testing treatment therapies aimed at altering tumor growth in the rat spine model developed with Dr. Ma.

Dr. Ma presented his findings at the 2010 AAOS Annual Meeting. "Hopefully my research will play a small part in a larger study that will lead to developing a treatment to improve the quality of life of individuals with spine metastases," said Dr. Ma.

▲ Nirav Pandya, MD

Nirav Pandya, MD

Child Abuse and Orthopaedic Injury Patterns: Analysis at a Level I Pediatric Trauma Center

More than 1 million cases of child maltreatment are investigated each year, about 16% of them for physical abuse.** Often, reporting abuse falls on emergency room physicians and general pediatricians, but according to **Nirav Pandya, MD**, first-place winner at the 2009 Philadelphia Resident Research Symposium, orthopaedic surgeons should bear part of the responsibility.

"As orthopaedic surgeons, we not only have to be good at fixing fractures, we have to be able to recognize if abuse is taking place and if it is, be one of the major players in ensuring children are given to child protective services," Dr. Pandya said. "We need to ensure the abuse stops rather than just fixing fractures."

Guidelines for identifying abuse have not been published, however, so Dr. Pandya and his team researched abuse patterns by retrospectively examining both the general trauma database and the child abuse and neglect database of the Children's Hospital of Philadelphia. Data they reviewed included patient demographics, time spent in the emergency room, and types of injuries treated.

Once they analyzed the data, Dr. Pandya and his research team created an algorithm orthopaedists could use to identify injuries caused by child abuse versus those that are the result of accidents.

"After reviewing data on 1,500 patients, we felt we could give some strict guidelines on consistent patterns to look for," Dr. Pandya said. "If orthopaedists keep these in mind, they'll have a better idea of when and how to effectively activate social protective services."

This study is important, Dr. Pandya indicated, not only for the well-being of injured children, but also to prevent families from having to endure unnecessary hardship.

"We want orthopaedists to be able to identify abuse and battery but we don't want them to accuse anyone wrongly and put patients and families through unnecessary interrogation from the police or social services," he said.

***Child Maltreatment 2008*, published by the U.S. Department of Health and Human Services.

▲ Erica D. Taylor, MD

Erica D. Taylor, MD

Nanostructured Scaffolds as Novel Therapeutic Replacement Options for Rotator Cuff Disease

Rotator cuff repairs are common orthopaedic treatments, but they don't always last.

"The nature of tendon healing is such that the repairs have a high propensity to fail when performed unaided," said **Erica D. Taylor, MD**, first-place winner at the 2009 Virginia Symposium. "The aging and athletic populations are growing, so there is definitely a need to find a device or a way to enhance the healing of rotator cuff repairs."

Because she was part of the Academic Orthopaedist Training Program at the University of Virginia, Dr. Taylor's mentor, **Cato T. Laurencin, MD, PhD**, asked her to develop in vitro and in vivo tests for new rotator cuff scaffolds that could be used as supportive structures in conjunction with tendon tissue engineering. Scaffolds would fill gaps until tissue regenerates.

Using a framework from previous research, Dr. Taylor learned to conduct tests on cells to assess their growth and whether they adhered to a scaffold. She also determined if the scaffold could be implanted into an animal model.

"Once Dr. Laurencin's team instructed me on how to electrospin nanofibers and do in vitro studies and cell work, I was able to then translate my clinical knowledge into a surgical procedure to test the scaffold in vivo," Dr. Taylor said.

Dr. Taylor implanted scaffolds into a rat model to evaluate how well they support new healing. She analyzed their gross histology and, testing their intrinsic tensile suture strength in an Instron machine, she also evaluated their biomechanics.

"I had a group of shoulders that were repaired after a supraspinatus injury and a group that were repaired and augmented with the scaffold. I compared the biomechanical properties at two different periods of time."

In addition, she observed when the rats regained use of their shoulders.

"Within a day or two they were all using their shoulders for feeding and crawling," Dr. Taylor noted. "None of them showed signs of infection, and when I made the final dissections to remove the scaffold, my repair was still in place."

Dr. Taylor presented these results at the 2010 AAOS Annual Meeting. She hopes the scaffolds could be used clinically.

"Dr. Laurencin is now at the University of Connecticut where they're advancing the tissue engineering applications of the scaffold," she said.

▼ Vidyadhar V. Upasani, MD

Vidyadhar V. Upasani, MD

Disk Health Preservation after Six Months of Spinal Growth Modulation: Expanding the Treatment Options for Fusionless Spinal Deformity Correction

For children with spinal deformities, treatment often means bracing, or in more severe cases, fusion. Orthopaedists specializing in spine care are searching for alternative solutions that preserve motion and prevent degeneration.

"Our long-term goal is to develop technology that straightens the spine while the child is growing," said **Vidyadhar V. Upasani, MD**, first-place winner at the 2009 Southwest Region Resident Research Symposium. "Hopefully, when the child is finished growing, the growth modulation device can be removed."

A growth modulation device could, however, create other, unwanted changes in the spine. Dr. Upasani investigated how tethering affects intervertebral disks.

"Picture a rigid shoelace. Screws are placed in vertebral bodies through the chest cavity and the tether — made of an ultrahigh molecular polyethylene — is attached between the screws, creating a compression of the vertebral bodies to straighten the spine."

Although there is no animal model for scoliosis, Dr. Upasani and his team were able to tether pig spines to create a curve, which compressed the vertebral bodies in the same way a tether would help correct a curve.

Dr. Upasani and his research team studied the resulting biomechanics, biochemistry, chemistry, and histology of the disks. They found that tethered disks were narrower and showed changes in annulus water content, but there was no significant degeneration. More studies need to be done, Dr. Upasani said.

If tethering shows promise for repairing spine deformity without risking spinal integrity, it could be used not only to preserve motion in severe cases requiring fusion, but also in milder cases that would usually be treated with bracing.

"Many current bracing studies have shown that bracing helps prevent curve progression at best, but it doesn't straighten the spine," explained Dr. Upasani. "And it's difficult to get children to comply with wearing the brace, especially when they're growing. The tether would act like an internal brace where it's performing the same function of preventing curving and also actually pulling the spine straight."