

UC SANTA BARBARA

THE *Current*

August 2, 2010

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UCSB Professor Sees Medical Breakthrough in New Bone Measurement Tool

Paul Hansma's face lights up when he talks about what his latest research might mean for people who suffer after breaking their hips or other bones that become more and more brittle as they age. Statistics show that a woman is more likely to die in the next year after a hip fracture than if she's had a heart attack.

Hansma, a professor of physics at UC Santa Barbara who has spent much of the past 20 years developing Atomic Force Microscopes, has focused on biophysical research and the study of human bones. His renowned bone tissue research has led him to what he believes will be a significant step in the study of biomaterials: development of a new medical diagnostic tool -- the Reference Point Indentation (RPI) instrument.

Hansma is a co-author of a new study published in the Journal of Bone and Mineral Research. In the study, "Microindentation for in vivo Measurement of Bone Tissue Mechanical Properties in Humans," Hansma and his co-authors say they have validated the RPI as a new tool for measuring the strength and quality of bones by using live human test subjects.

"This is a revolutionary breakthrough," Hansma said of the RPI. "People get excited when they hear about this."

The study documents the first clinical trials of the RPI, which uses a mechanically driven test probe enclosed in a microscopically small cylinder about the size of a hypodermic needle. The test probe is driven like a tiny piston into the bone of the test subject for about 10 seconds, creating microscopic indentations. The indentations are repeated and the microfractures are measured to determine the bone's strength and quality.

"The properties of bone materials are an important part of fracture risk," Hansma said. "In normal, everyday life, you wonder about whether something is going to break or not. It depends. How big is it? How thick is it? Is it made of balsa wood, or walnut? In the field of bone fracture risk, there has not been any instrument that can measure the material properties of bone relative to fracture risk, so it's been ignored."

Conventional measurement is currently done for bone mineral density. It's done with X-rays, called DEXA (dual energy X-ray absorptiometry). "This is a measure of how much bone you have," Hansma said. "As people age, they lose bone. This bone loss can be monitored with DEXA. If you've lost a certain amount, you'll typically be prescribed drugs like Fosamax or Boniva. They help the bones get bigger, help mitigate bone loss and, in some cases, rebuild bone. It's a \$6 billion market right now, growing at 25 percent per year. All they're doing is dealing with bone quantity. They're dealing with half the problem."

What's been missing is a way to measure bone quality. Using the RPI, a doctor would be able to determine bone quality by studying the microfractures created in the bones of tested patients. "There's been no way to measure this until now," Hansma said. "This is just a local measurement of how easily the bone is fractured. Since there was no way to measure this, there was no way to develop therapies. But with the RPI, we can measure how easily a bone could be fractured. So now we have a goal -- let's try to do something to the bone to lower the total indentation distance as measured by the RPI, because we would like the bone to be less easily fractured."

All clinical trials have taken place in Barcelona, Spain, under the supervision of Hansma and Dr. Adolfo Diez-Perez, a physician at Hospital del Mar in Barcelona and the study's first author. Hospital patients -- victims of hip fractures and other ailments

-- were injected with a local anesthetic in their tibia. The leg bone was then tested using the RPI instrument. The RPI's probe creates microfractures in the tibia, measuring the force that's being applied and the distance that the probe goes into the bone.

"What you can see from the tests is that everyone whose bone was easily fractured by the RPI's indentations -- very easily fractured at a probe depth of 40 microns -- every single one was someone who had previously suffered a bone fracture," Hansma said. "And below 30 microns of probe depth, no one had suffered a fracture. It's very statistically significant. Clearly, there's a big difference."

The ability to do these tests on live patients was a key factor in the success of the research. "You can't cut a section out of a lot of peoples' bones, test them with a conventional mechanical testing device, and then follow the people for 10 years to see who has fractures," Hansma said. "A small community of scientists has been working on bone material properties, but there has been a lack of any kind of connection to clinical trials. That's what this paper represents: a bridge between the people who have been working on bone materials properties, and the physicians who are needing to make decisions about treating patients."

So far, the only site approved for clinical trials is in Spain. The Food and Drug Administration (FDA) has not approved the RPI for tests in the United States. What would it take to get FDA approval? "Several million dollars for clinical studies in the U.S.," Hansma said.

A new Santa Barbara company, Active Life Scientific, is currently selling the instruments to researchers for laboratory studies and hopes to raise the funds necessary to fund clinical studies and receive FDA approval. For now, the company is focusing on preclinical and clinical research applications. It hopes to eventually develop diagnostic tools, making this new technology available to people who want to know about their risk of bone fracture and how to reduce it.

Hansma is chief scientific officer for Active Life, which was founded by two UCSB graduates, Davis Brimer and Alex Proctor. "This company was started by two students without deep pockets," Hansma said. "They have been funded to date by friends and family, and are now receiving fund from visionary investors who see the promise in this technology. They've sold nine instruments, including one to an equine veterinarian who believes the technology can be used to diagnose and treat

racehorses. Active Life doesn't yet have the resources to fund clinical trials, or to give instruments to people who can do clinical trials. That's why we're grateful to Adolfo. He funded the trials himself. With the results of his work in Barcelona being published, maybe there will be some new Adolfos in the United States who emerge to help move the technology to the clinic."

Hansma's next project will be a collaboration with UCSB Chancellor Henry T. Yang, who's also a professor of engineering, and Srinivasan Chandrasekar, a professor of industrial and materials engineering at Purdue University. The research, funded by a grant from the National Science Foundation, will focus on developing optimized cutting methodologies for bone. The RPI will be used to evaluate the quality of the bone surface after it has been cut. The long-term goal, according to Hansma, is to minimize damage to bone and tissue during surgery.

Co-authors with Hansma on the RPI study are Dan Morse, Connor Randall, Daniel Bridges, and James Weaver, all of UC Santa Barbara; Perez, Roberto Guerri, and Maria Jesus Pena, of Hospital del Mar in Barcelona; Xavier Nogues, Leonardo Mellibovsky, and Enric Caceres, of RETICEF, Instituto Carlos III in Madrid, Spain; Kurt J. Koester and Robert O. Ritchie, of UC Berkeley; and Proctor and Brimer, of Active Life Scientific. Helping Hansma with the RPI in his lab are undergraduates Sasha Cohen, Bryan Kaye, Omar Ahmady, Max Myers, and Brianna Miner. Hal Kopeikin helped with the statistical analysis.

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