Seeing through knees in quest to alleviate osteoarthritis [1]

From Our Labs [2]
Author: Elizabeth Dougherty

Chances are you have knee pain or know someone who does. Osteoarthritis, most commonly due to worn-down cartilage in the knee, affects over 230 million people worldwide, causing groans at best and an inability to live a full, mobile life at worst.

Novartis researchers are trying to regenerate functional cartilage in knees, but it’s hard to know if the experimental approach is working. Until now, the only way to find out has been to perform a biopsy to determine if the regenerated tissue is of high quality. To avoid the pain and injury of a biopsy, Novartis is collaborating with a scientist and his team at the Medical University of Vienna in Austria to measure the molecular makeup of regenerated cartilage using advanced magnetic resonance imaging (MRI) technology. This information could tell them if the regenerated tissue is the kind that will function like natural cartilage and help patients return to normal activities.

Their novel technique is giving them a way to see through knees.

Visualizing cartilage damage

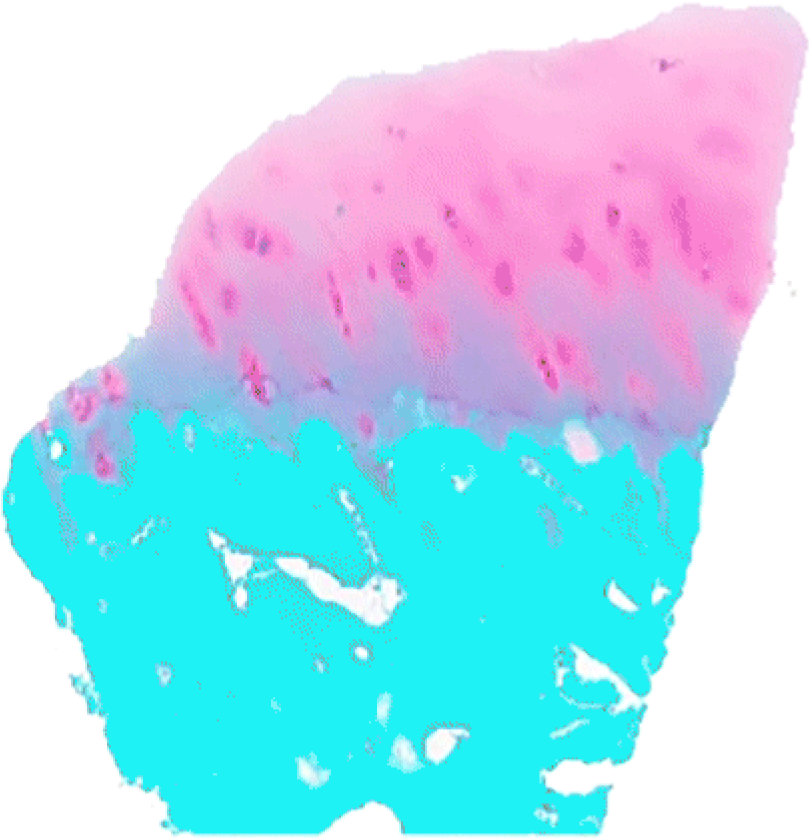

3-D movies of cartilage reveal structural details, including damaged spaces. Sections shown here are cartilage along the femur, or thigh bone. Image credit: Didier Laurent and Aparna Srikanth

What’s happening inside the knee to cause so much anguish? Underneath the kneecap lie several slips of tissue called cartilage.

Cartilage acts as a cushion that keeps bones from knocking together and has a smooth surface that enables joints to move freely. “The surface of cartilage is so slick, it’s like ice on ice,” says Didier Laurent, a Director in the Biomarker Development group at the Novartis Institutes for BioMedical Research (NIBR).

When osteoarthritis strikes, the cartilage breaks down. Pits form. That special springy and slippery function degrades. Joints become stiff and achy, and movement can become painful. The human body is not able to repair the damage.

Good cartilage defined

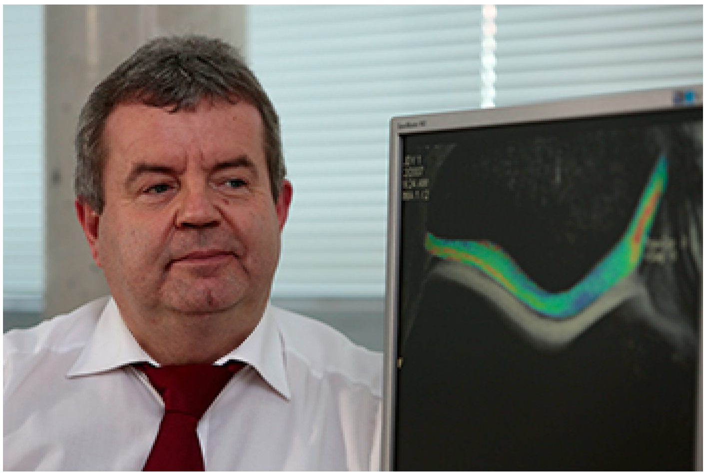


Biopsied cartilage can be stained to reveal the proteins present. Two slivers from the same tissue sample show that proteoglycans and collagen exist together in high-quality cartilage. Proteoglycans appear as a pink stain. Collagen appears as a brown stain. Image credit: PhenoPath Laboratories. Animation by Fidelis Onwubueke

A protein called proteoglycan is part of what gives cartilage its spring. The material naturally weaves itself together with another protein, collagen, to create a super-strong material a superhero would envy. High-quality cartilage is resilient enough to withstand constant pounding and still spring back, and it is smooth enough to enable bones to move fast and free.

Since damaged cartilage does not regenerate on its own, Novartis scientists are working on a way to prod the body to regenerate these building blocks and weave them together into high-quality tissue. The challenge is to confirm that the regenerated cartilage is a powerful weave of collagen and proteoglycans, without, through a biopsy, having to cut out part of what they've just grown back.

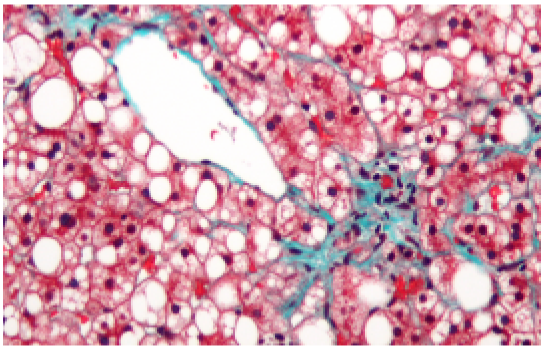
A view into the knee


NIBR collaborator Siegfried Trattnig, professor of radiology at the Medical University of Vienna. Image credit: Siegfried Trattnig

That’s where Siegfried Trattnig, an MRI expert at the Medical University of Vienna, and his MRI technology come in.

MRI machines in clinical use are typically 1.5 tesla or 3 tesla scanners (tesla is the measure of the magnetic field strength the machine produces). Trattnig, however, is working with a more powerful 7 tesla (7T) machine.

At 7T, it’s possible to see the finer details inside living bodies – such as knees – as small as 200 micrometers, slightly larger than the width of a human hair. The technology also generates information on tissue composition, which reflects how healthy the tissue is. This new capability is critical for picking up the subtle signals that reveal high-quality cartilage regeneration.


Discovery [3]

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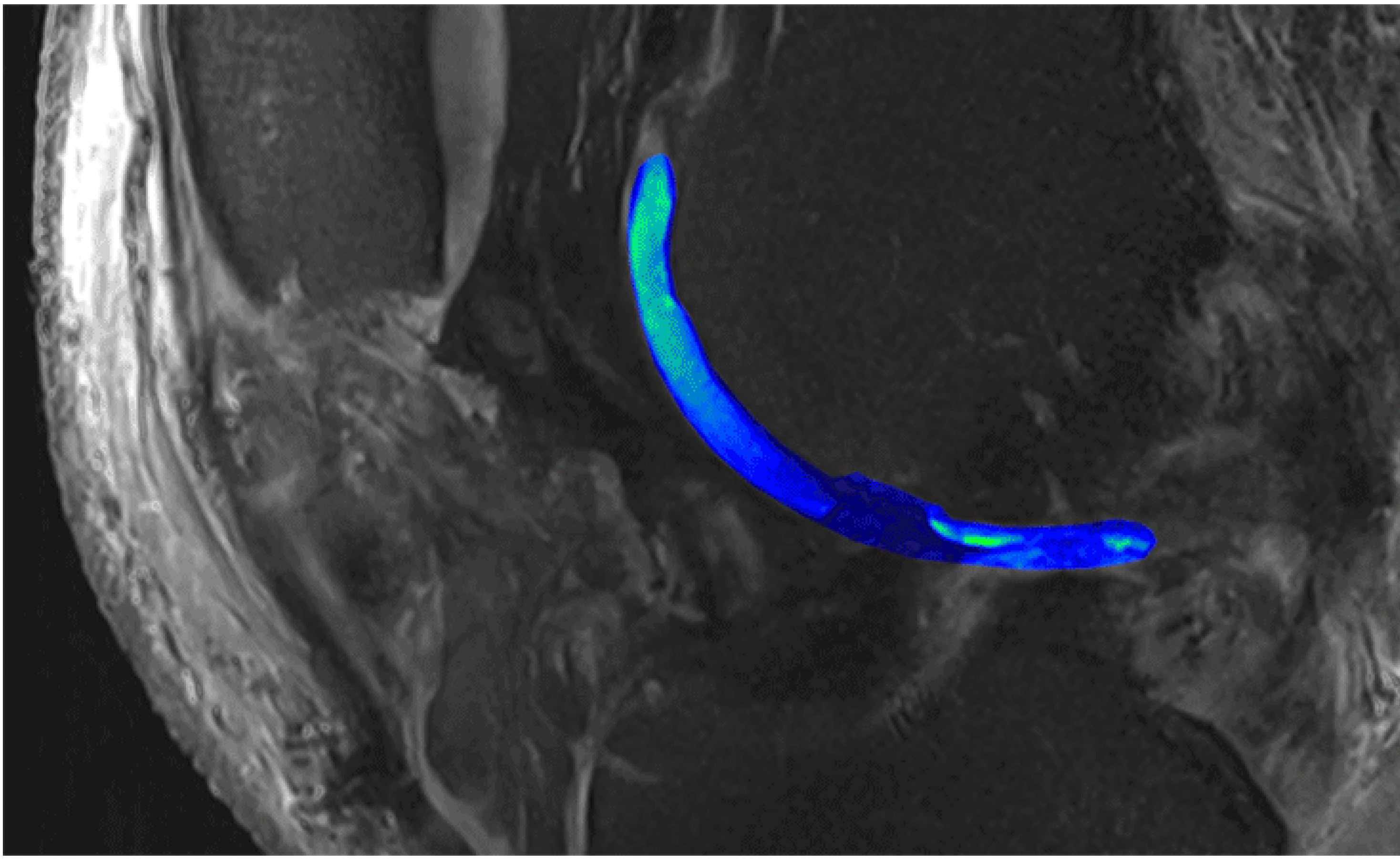
A view of how form meets function



Traditional MRI uses magnetic pulses to induce a signal from water molecules in the body. This technology differentiates cartilage (blue/light green) from bone. Advanced MRI uses the same approach but applies it to sodium. The tech identifies proteoglycans (bright green), the special ingredient in high-quality cartilage. Regions devoid of this sodium signal point to defective cartilage. Images courtesy Siegfried Trattnig (modified by Fidelis Onwubueke)

In addition to using a powerful MRI machine, Trattnig has developed techniques that expand the range of materials MRIs can detect. For instance, the technology can detect levels of proteoglycan, the special ingredient in high-quality cartilage.

These MRI images also show gaps in the cartilage (in darker blue above), which indicate damage. NIBR researchers are investigating a way to fill those gaps with high-quality cartilage using an experimental regenerative medicine. By using advanced MRI in their clinical trials, they could have a way to measure the quality of the cartilage regenerated without having to put patients through painful biopsies.

“We want to create good-quality cartilage that lasts a long time,” says Laurent. “With this technology, we have a way to see if we’re headed in that direction.”

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