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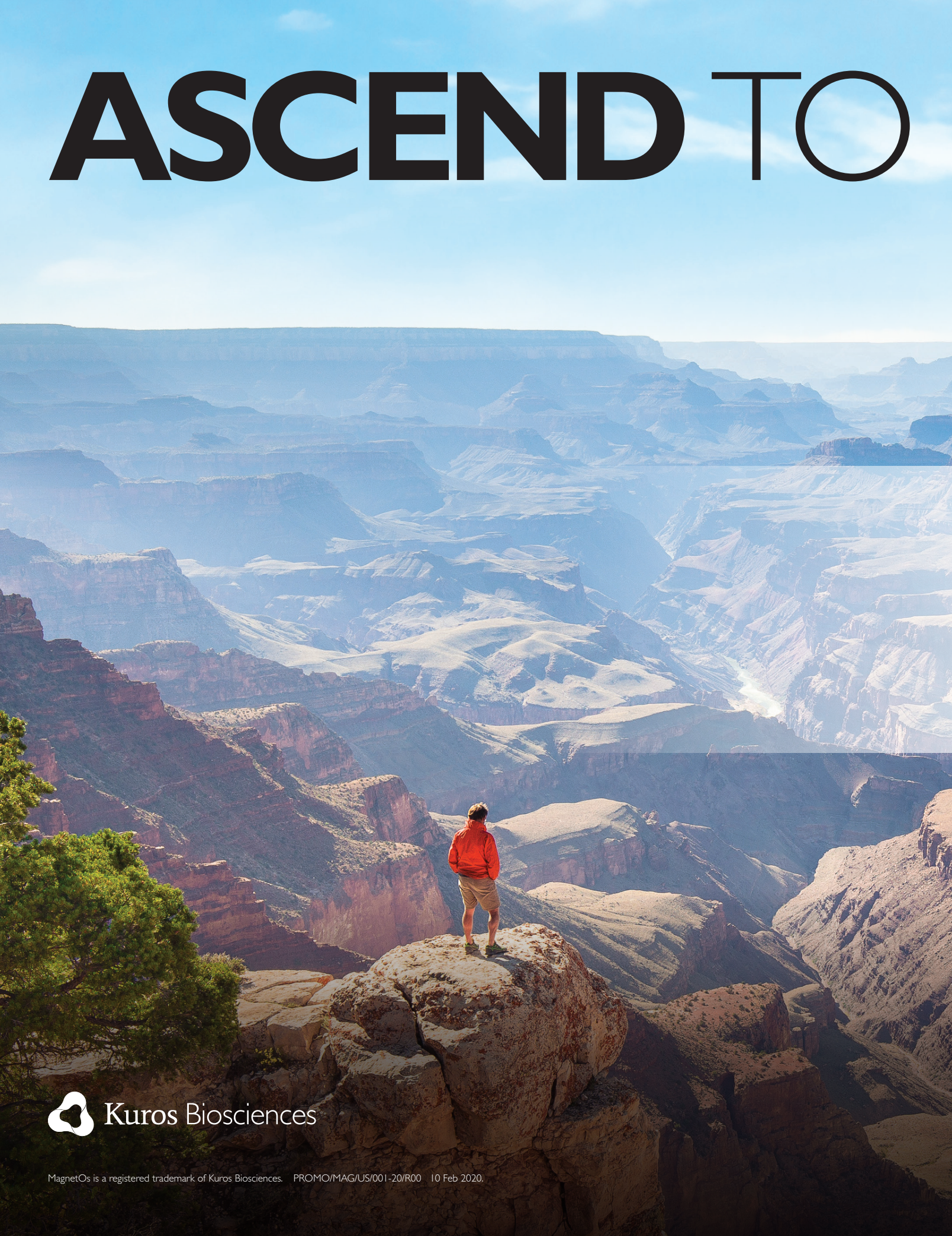
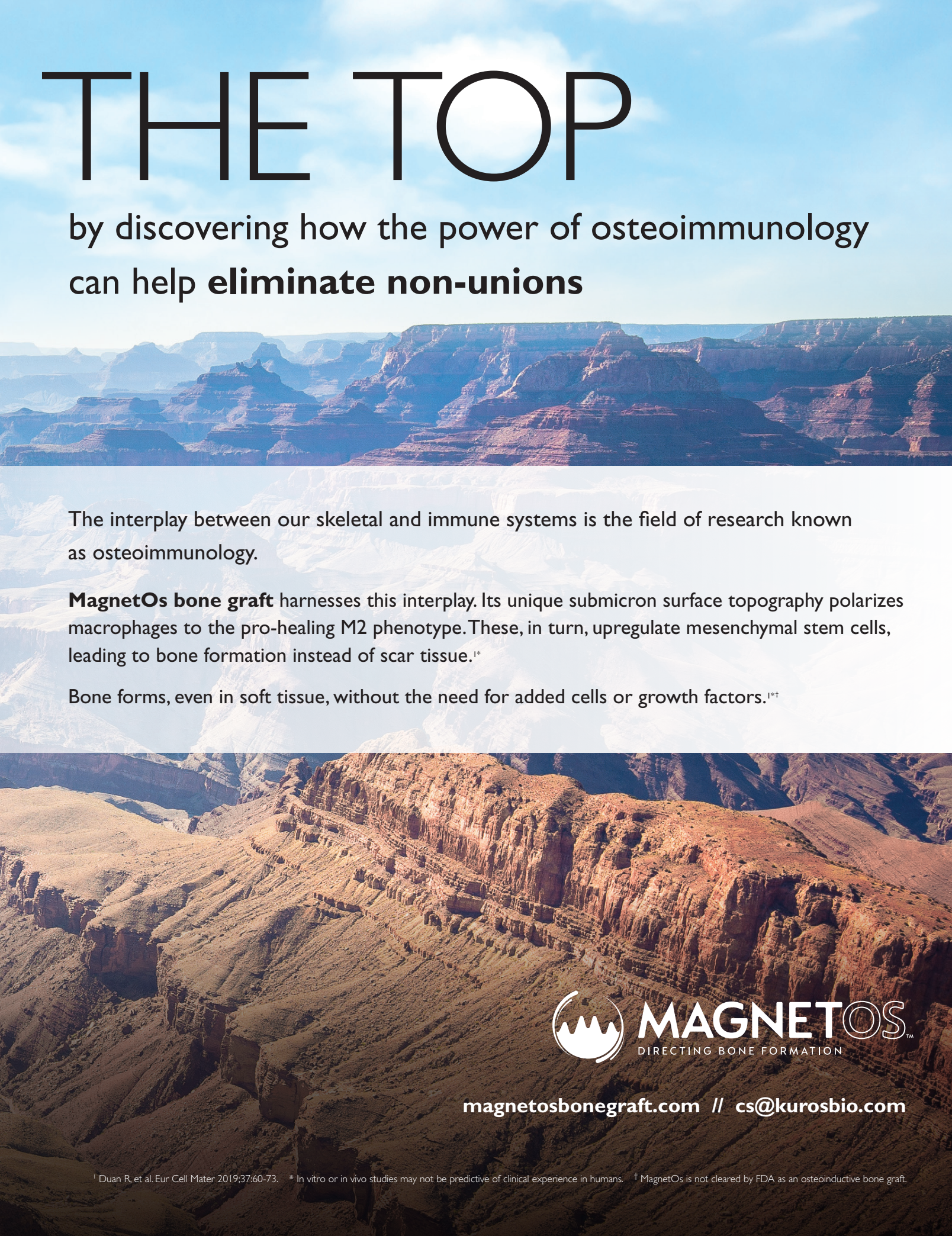


Kuros Biosciences



THE TOP

by discovering how the power of osteoimmunology can help **eliminate non-unions**

The interplay between our skeletal and immune systems is the field of research known as osteoimmunology.

MagnetOs bone graft harnesses this interplay. Its unique submicron surface topography polarizes macrophages to the pro-healing M2 phenotype. These, in turn, upregulate mesenchymal stem cells, leading to bone formation instead of scar tissue.[1*]

Bone forms, even in soft tissue, without the need for added cells or growth factors.[1*†]

MAGNETOS™
DIRECTING BONE FORMATION

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[1] Duan R, et al. Eur Cell Mater 2019;37:60-73. * In vitro or in vivo studies may not be predictive of clinical experience in humans. † MagnetOs is not cleared by FDA as an osteoinductive bone graft.

Kuros Biosciences

BECKER'S SPINE REVIEW

This data-backed graft promotes bone formation, lowers costs in spinal fusion

More than 1.2 million spinal surgeries are performed in the U.S. each year, including spinal fusion, decompression and discectomy procedures, according to the National Center for Health Statistics. And the volume of elective lumbar fusions is rising across the U.S., research published in *Spine* indicates.

As spine fusion volumes increase, so do the numbers of patients who will develop pseudarthrosis, a related complication. A number of surgeons are turning to advanced techniques to help reduce non-union rates and the resulting expenditures. For instance, bone grafts are used in 59 percent of lumbar spinal fusion procedures and 91 percent of cervical spinal fusion procedures, according to GlobalData published in 2017.

"There's a ton of biologics everywhere, and companies are continually approaching surgeons trying to get them to use or switch to their 'better' or 'improved' biologic," said Pierce Nunley, MD, director of the Shreveport-based Spine Institute of Louisiana.

Because of all this noise, Dr. Nunley paid little mind at first when a Netherlands-based company called Kuros Biosciences came knocking. But then he saw Kuros' work on a novel fibrin parathyroid hormone-based bone graft product candidate, which recently received Investigational New Drug approval from the FDA. This product made him realize the company wasn't approaching biologics like the other vendors; it was taking a much more scientific approach. That's when he learned about MagnetOs bone graft.

"[Kuros] showed me some real data," Dr. Nunley said. "And I thought, 'Wow. That's pretty compelling.' So, quite frankly, that's why I started using MagnetOs."

Research examining how MagnetOs facilitated bone formation through cell differentiation is what convinced Dr. Nunley that the product was worth its salt for use in spinal fusions. In animal models, MagnetOs formed a bone fusion mass that was comparable – if not better – than other calcium phosphates, he said.

A strong foundation

What Dr. Nunley found even more compelling was why, physiologically and biologically, the product works. Essentially, MagnetOs' advanced submicron surface technology is configured in such a way that it "turns on" the M2 macrophage phenotype, which promotes bone formation, as opposed to the M1 macrophage phenotype that lead to problematic inflammation and fibrous tissue formation.

This technology is based on a strong understanding of osteoimmunology and the benefits of 3D-implant porosity, according to Richard Todd Allen, MD, PhD, chief of spine surgery at UC San Diego (Calif.) Health System. MagnetOs' unique surface features are what enables the product to alter cellular reactivity to draw appropriate cells into the area and drive bone formation, he said.

"This has been one of the most exciting fields of study over the past 15 years or so in terms of bone healing," Dr. Allen said. "Rather than identifying what affect an inflammatory response has to bone healing and fusion, our understanding of the specific cell types and integrated mechanisms involved in coordinating bone formation has improved, versus those cells generating a fibrous non-union."

While this osteoimmunologic research behind MagnetOs looked promising, Dr. Nunley was cautious about introducing it into his practice, having tried seemingly effective products in the past that ended up causing severe inflammation and pain for patients.

He performed a few cases with MagnetOs and followed the patients closely to see if there were any issues. No issues were discovered and it appeared to work well, so he decided the bone graft technology was worth continuing to use.

"I've not had any – to my knowledge – negative events from the use of MagnetOs," he said. "I've only been using it a year or so, but I've not had a single non-union or concern currently about any of my MagnetOs patients having a non-union."

Not your average white, powdery crystal

While other companies offer beta tricalcium phosphate products – white, powdery crystals that are similar in appearance to MagnetOs bone graft – no other product facilitates the M1 to M2 macrophage response that the Kuros product does, according to Kornelis Poelstra, MD, PhD, director of The Robotic Spine Institute of Silicon Valley in Los Gatos, Calif.

"There are a lot of papers now that directly compare, in very strong animal models, the class-leading (by sale) beta tricalcium phosphate products to MagnetOs," Dr. Poelstra said. "And the data is extremely strong for the surface modification and the direct bone formation with MagnetOs."

Other products lead to fibrous bridging bone, which looks like good, bony fusion on X-rays and CT scans, according to Dr. Poelstra. The problem, however, is that the mass actually contains small particles of remaining bone graft material surrounded by fibrous tissue. In contrast, MagnetOs creates a solid block of

*this article continues on the back cover

bone, he said.

The product also beats other graft materials in terms of handling characteristics, whether it's used in posterior cervical, lumbar or thoracic spine surgeries, according to Dr. Allen.

"The polymer used to make it malleable also makes it moldable," he said, "and its ability to stick down to the facets, transverse processes and lamina is truly impressive and unlike any demineralized bone matrix or other graft material I have used."

More effective, but at what cost?

Outcomes and handling characteristics are two vital considerations when introducing a new product. But as prices for lumbar spinal fusions soar, costs are at the top of surgeons' minds.

Today, estimates for the price of a lumbar spinal fusion range from $60,000 to $110,000 per procedure, according to SpinalCord.com, an injury resource center. In part because of non-unions, spinal fusion costs an estimated $118,945 per quality-adjusted life year gained, an April 2015 study by Nashville, Tenn.-based Vanderbilt University Medical Center researchers found.

MagnetOs represent a cost-effective option for spine fusions, according to Dr. Poelstra. Not only does MagnetOs' promote solid bone formation to help surgeons avoid costly non-unions, but it also doesn't use added cells or growth factors that come at a price.

"Based on the evidence we have about the product, I know that it's extremely effective and that I most likely don't have to use anything that is more expensive in the operating room," he said. "If you look at all of the products that have growth factors in them or are cell-based, they're usually three to four times as expensive as MagnetOs."

Moreover, Kuros' cost-effective option has worked "extremely well" inside of a cage for patients with immunologic diseases such as rheumatoid arthritis or severe psoriatic arthritis, as well as older patients whose healing processes might not be as successful, Dr. Poelstra said.

For these cases, Dr. Poelstra combines a small amount of local autograft with MagnetOs putty, resulting in a "tremendous buildup of bone" and more predictable bone growth than he's achieved with bone morphogenetic protein products. Plus, he doesn't have to fill the entire interbody fusion cage with MagnetOs.

Dr. Allen has also used MagnetOs in some of his toughest cases, including one where a patient referred from an outside hospital presented with a large seroma surrounded by what seemed to be a shell of early bone after rhBMP-2use.

Concerned about the difficult fusion environment, bony eburnation and soft tissue surfaces with an avascular appearance, Dr. Allen performed a pedicle subtraction osteotomy at L3 and revision fusion with a small amount of autograft and MagnetOs, filling in areas with cancellous chips and demineralized bone matrix.

At eight months after the surgery, the patient's implants are stable, his alignment is maintained, and radiographs and CT scans indicate he's making mature bone in areas not previously fused at about six and a half months.

"He is significantly better functionally, increasing his daily walking and has markedly improved pain scores," Dr. Allen said.

Over a decade of work coming to fruition

The MagnetOs technology that creates the kinds of outcomes Dr. Allen described is not derived from brand-new science. Kuros Biosciences has spent more than a decade refining its bone repair technologies and the surface science of orthobiologics. Continuous efforts to mimic the best features of biologically robust autograft bone has led to the creation of MagnetOs as it is today.

In February 2017, the FDA approved Kuros' MagnetOs granules, and in August of that year, the MagnetOs putty received clearance. Dr. Poelstra introduced MagnetOs into his practice as soon as it got the FDA's green light.

Though Kuros hasn't yet pursued an osteoinductive indication in the U.S., MagnetOs' ability to promote bone formation – even in soft tissues – without added cells or growth factors gained the product an osteoinductive indication in Europe. Drs. Poelstra and Allen agreed that MagnetOs' osteoinductive abilities are clear.

Wherever it's used, the advantage of MagnetOs' ability to make bone endogenously, cost-effectively and without added cells or growth factors boils down to one thing: patient outcomes.

"This architecture is unlike conventional and most current bone synthetic bone grafts," Dr. Allen said. "Having the ability to locally apply this type of graft material, alter the local inflammatory environment after surgery in favor of bone healing and repair, and do that based on the graft applied is an exciting potential opportunity to improve fusion rates in our patients."

Disclaimer: The views, opinions and positions expressed by surgeons in this article are those of the surgeon alone and do not represent those of Kuros Biosciences. In the US, MagnetOs is cleared for standalone use in the extremities and as an autograft extender in posterolateral spine. MagnetOs is not cleared by FDA as an osteoinductive bone graft. Please refer to the product instructions for use for a full list of indications, contraindications, warnings, and precautions.

Kuros Biosciences

Kuros Biosciences aims to deliver decreased complications, advanced functional rehabilitation and to eliminate non-unions for spine surgeons and their patients. Their flagship product, MagnetOs bone graft, has an advanced submicron surface topography that leads to the formation of bone, rather than scar tissue, following implantation. Within their pipeline is an investigational drug/biologic combination product candidate consisting of a fibrin-based healing matrix with a targeted bone growth factor (truncated parathyroid hormone (PTH) analog). Visit www.kurosbio.com for additional information on Kuros Biosciences, its people, science and product pipeline.

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