

MagnetOs Global Research Summary

Superior spinal fusions for today, and tomorrow

MagnetOs is a bone graft like no other: thanks to its *NeedleGrip™ surface technology*, it grows bone even in soft tissues. This surface technology provides traction for our body's vitally important '*pro-healing*' immune cells (M2 macrophages).^{*†1,2}

This in turn, unlocks previously untapped potential to stimulate stem cells - and form new bone throughout the graft.^{*3-5}

The growing body of science behind NeedleGrip is called *osteimmunology*. But for surgeons and their patients it means one thing: a more *predictable fusion*.^{*‡5}

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1. Scientific Evidence

From Benchtop to Clinic: A Translational Analysis of the Immune Response to Submicron Topography and Its Relevance to Bone Healing



Authors: van Dijk LA, de Groot F, Yuan H, Champion C, Patel A, Poelstra K, de Bruijn JD

Date: June, 2021

Publication: *European Cells and Materials*

Summary: This translational analysis of the immune response to submicron surface topography and its relevance to bone healing introduces the concept of osteoimmunology and immunomodulation through the polarization of M2 macrophages, and how that polarization is modulated through a bone graft with submicron needle-shaped surface topography. In vitro and in vivo data are analyzed, with the authors concluding that biomaterials with specific surface structures will induce a pro-healing immune response leading to bone formation. Furthermore, material-directed bone formation is translated into reliable spinal fusion outcomes in relevant pre-clinical models and human patients.

Citation: van Dijk LA, de Groot F, Yuan H, Champion C, Patel A, Poelstra K, de Bruijn JD. From benchtop to clinic: a translational analysis of the immune response to submicron topography and its relevance to bone healing. *Eur Cell Mater.* 2021;18;41:756-773. DOI: 10.22203/eCM.v041a48. PMID: 34151417.

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Calcium Phosphate with Submicron Topography Upregulates M2 Phenotype in Primary Human Macrophages, Enhancing Downstream Angiogenesis and Osteogenesis in Vitro



Authors: van Dijk LA, Utomo L, Yuan H, de Groot F, Gawlitta D, Rosenberg AJWP, and de Bruijn JD

Date/Publication: Manuscript in submission.

Summary: Calcium phosphates with submicron surface features such as MagnetOs have shown the ability to form bone in soft tissues, without the addition of cells or growth factors. It is hypothesized that an immune response to submicron topographies contributes to enhanced bone healing via upregulation of pro-healing 'M2' macrophages. In this in vitro study, the response of human macrophages to different calcium phosphate bone graft substitutes was assessed. Conditioned medium from macrophages cultured on MagnetOs resulted in enhanced in vitro pre-vascular network formation and osteogenic differentiation of mesenchymal stem cells, compared to conditioned medium from macrophages on TriCalcium Phosphate.

2. Pre-Clinical Evidence

Biphasic Calcium Phosphate with Submicron Surface Topography in an Ovine Model of Instrumented Posterolateral Spinal Fusion



Authors: van Dijk LA, Duan R, Luo X, Barbieri D, Pelletier M, Christou C, Rosenberg AJWP, Yuan H, Barrère-de Groot F, Walsh WR, and de Bruijn JD

Date: November, 2018

Publication: *Journal of Orthopedic Research Spine*

Summary: This study evaluated the performance of MagnetOs Granules and MagnetOs Putty used in posterolateral spine fusion against the gold standard of autograft in a clinically relevant, validated ovine model. Multiple endpoints were measured including manual palpation, range of motion, X-ray, CT, histology, and histomorphology. The authors concluded that the MagnetOs Granules and MagnetOs Putty fusions developed complete bridging bone which was equivalent to autograft.

Citation: van Dijk LA, Duan R, Luo X, Barbieri D, Pelletier M, Christou C, Rosenberg AJWP, Yuan H, Barrère-de Groot F, Walsh WR, de Bruijn JD. Biphasic calcium phosphate with submicron surface topography in an Ovine model of instrumented posterolateral spinal fusion. *JOR Spine*. 2018;28;1(4):e1039. DOI: 10.1002/jsp2.1039. PMID: 31463454; PMCID: PMC6686792.

Access: Scan or [click link](#) to access the publication



Efficacy of a Synthetic Calcium Phosphate with Submicron Surface Topography as Autograft Extender in Lapine Posterolateral Spinal Fusion



Authors: van Dijk LA, Barbieri D, Barrère-de Groot F, Yuan H, Oliver R, Christou C, Walsh WR, and de Bruijn JD

Date: December, 2018

Publication: *Journal of Biomedical Materials Research: Part B Applied Materials*

Summary: This study evaluated the performance of MagnetOs Granules and MagnetOs Putty against the gold standard of autograft in a lapine model. Multiple endpoints were measured including manual palpation, range of motion, radiography, histology, and histomorphology. The authors concluded that the MagnetOs Granules and MagnetOs Putty are effective autograft extenders for posterolateral fusion.

Citation: van Dijk LA, Barbieri D, Barrère-de Groot F, Yuan H, Oliver R, Christou C, Walsh WR, de Bruijn JD. Efficacy of a synthetic calcium phosphate with submicron surface topography as autograft extender in lapine posterolateral spinal fusion. *J Biomed Mater Res B Appl Biomater*. 2019;107(6):2080-2090. DOI: 10.1002/jbm.b.34301. Epub. 2019 Jan 7. PMID: 30614621; PMCID: PMC6690075.

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Accelerated Bone Formation by Biphasic Calcium Phosphate with a Novel Sub-Micron Surface Topography



Authors: Duan R, van Dijk LA, Barbieri D, de Groot F, Yuan H, and de Bruijn JD

Date: January, 2019

Publication: *European Cells and Materials*

Summary: In this study, four calcium phosphate bone grafts with different surface features and composition were implanted via blunt dissection into the soft tissue paraspinalis muscles in a canine model. The scientists found that calcium phosphates with submicron surface topography were able to form bone without added cells or growth factors, and that MagnetOs Granules with its needle-shaped surface features led to accelerated bone formation. The authors concluded that surface feature size has the most impact on bone growth in soft tissues, followed by the surface feature morphology.

Citation: Duan R, van Dijk LA, Barbieri D, de Groot F, Yuan H, de Bruijn JD. Accelerated bone formation by biphasic calcium phosphate with a novel sub-micron surface topography. *Eur Cell Mater.* 2019;28;37:60-73. DOI: 10.22203/eCM.v037a05. PMID: 30687909.

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MagnetOs, Vitoss, and Novabone in a Multi-Endpoint Study of Posterolateral Fusion, A True Fusion or Not?



Authors: van Dijk LA, Barrère-de Groot F, Rosenberg AJWP, Pelletier M, Christou C, de Bruijn JD, and Walsh WR

Date: July, 2020

Publication: *Clinical Spine Surgery*

Summary: This study compared autograft, MagnetOs Putty, Vitoss BA2X, and Novabone in a clinically relevant, validated ovine model for posterolateral spine fusion. Multiple endpoints were measured including manual palpation, range of motion, X-ray, CT, histology, and histomorphology. The study revealed clear differences in efficacy between commercially available bone grafts and demonstrated the efficacy of MagnetOs Putty, as this was the only material that showed equivalent performance to autograft in achieving spinal fusion.

Citation: van Dijk LA, Barrère-de Groot F, Rosenberg AJWP, Pelletier M, Christou C, de Bruijn JD, Walsh WR. MagnetOs, Vitoss, and Novabone in a Multi-endpoint Study of Posterolateral Fusion: A True Fusion or Not? *Clin Spine Surg.* 2020;33(6):E276-E287. DOI: 10.1097/BSD.0000000000000920. PMID: 31977334; PMCID: PMC7337107.

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Physico-Chemical Characteristics and Posterolateral Fusion Performance of Biphasic Calcium Phosphate with Submicron Needle-Shaped Surface Topography Combined with a Novel Polymer Binder



*MagnetOs Easypack Putty only commercially available in U.S.

Authors: Belluomo R, Arriola-Alvarez I, Kucko NW, Walsh WR, de Bruijn JD, Oliver RA, Wills D, Crowley J, Wang T, and Barrère-de Groot F

Date: February, 2022

Publication: *Materials*

Summary: This study evaluated the performance of MagnetOs Easypack Putty against the gold standard of autograft in a posterolateral fusion lapine model. Multiple endpoints were measured including manual palpation, range of motion, radiography, histology, and histomorphology. The authors concluded that MagnetOs Easypack Putty polymer hydrolyzes in physiological conditions, with the MagnetOs granules exposed to lapine tissue after 3 days of implantation. The authors also found similar fusion rates between autograft bone and MagnetOs Easypack Putty after 12 weeks of implantation, with no migration of the granules or adverse reactions.

Citation: Belluomo R, Arriola-Alvarez I, Kucko NW, Walsh WR, de Bruijn JD, Oliver RA, Wills D, Crowley J, Wang T, Barrère-de Groot F. Physico-Chemical Characteristics and Posterolateral Fusion Performance of Biphasic Calcium Phosphate with Submicron Needle-Shaped Surface Topography Combined with a Novel Polymer Binder. *Materials (Basel)*. 2022;11;15(4):1346. DOI: 10.3390/ma15041346. PMID: 35207887; PMCID: PMC8880136.

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3. Whitepapers

Favorable Preliminary Results of MagnetOs as Standalone Alternative to Autograft in a Prospective, Multi-center, Randomized, Intra-patient Controlled Trial



Authors: Delawi D¹, Hoebink EA², Kempen DHR³, van Susante JLC⁴, Kruyt M⁵

Affiliations: 1) St. Antonius Ziekenhuis 2) Amphia Breda 3) OLVG Amsterdam 4) Rijnstate Arnhem 5) UMC Utrecht

Date: April, 2022

Publication: Clinical Whitepaper

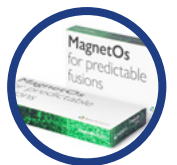
Study Design: Prospective, observer and patient blinded, multi-center, intra-patient, randomized controlled clinical trial

Summary: In this study, MagnetOs Granules were compared to the gold standard of autograft in human subjects undergoing posterolateral fusions of one to six-levels from T10-S2. MagnetOs Granules were used standalone, without added autograft or BMA. An intra-patient control was achieved by applying autograft to the contralateral side of the spine. Of the 100 subjects enrolled in this study, 50 subjects have thus far completed one year follow-up with fine-cut CTs, read independently by two blinded spine surgeons. Of the first 50 subjects, the fusion rate for MagnetOs Granules used standalone was 78% (39/50 subjects), while the autograft fusion rate was 42% (21/50 subjects).

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Use of a Novel Biphasic Calcium Phosphate with Submicron Surface Topography as an Extender to Autograft in Posterolateral Spinal Fusion



Authors: The Orthopedic Surgery Department

Affiliation: The University of California, San Diego

Date: April, 2022

Publication: Clinical Whitepaper

Study Design: Case Series

Summary: This whitepaper details the use of MagnetOs Putty used on-label as a bone graft extender in two challenging revision cases. Both subjects had predictable fusions and reduction in pain scores post-operatively.

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4. Clinical Evidence: Real-World Data

Effective Use of a Novel Biphasic Calcium Phosphate with Submicron Surface Topography in Posterolateral Spine Fusion



Author: Jones A, MD

Affiliation: Spire Cardiff Hospital

Date: April, 2021

Publication: *Juniper Online Journal of Case Studies*

Study Design: Case Series

Summary: In this case study, four female patients underwent a single or a two-level posterolateral lumbar fusion procedure for the treatment of degenerative spondylolisthesis or deformity. In all cases, MagnetOs Granules was used on label in the posterolateral spine. All four patients had predictable fusion on imaging post-operatively, as well as improvement in functionality and decrease in Oswestry Disability Index scores.

Citation: Alwyn J. Effective use of a novel biphasic calcium phosphate with submicron surface topography in posterolateral spine fusion. *JOJ Case Stud.* 2021;12(2):555834. DOI: 10.19080/JOJCS.2021.12.555834.

Access: Scan or [click link](#) to access the publication



Posterior Thoracolumbar Hemivertebra Resection and Fusion with a Biphasic Calcium Phosphate Bone Graft with a Novel Submicron Surface Topography



Author: Sandhu FA, MD

Affiliation: Georgetown University Hospital

Date: December, 2021

Publication: *Juniper Online Journal of Case Studies*

Study Design: Case Study

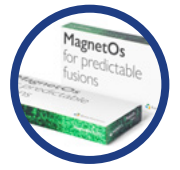
Summary: This case reports a 54-year-old female who underwent resection of a segmented T12 hemivertebra and T8-L3 fusion. Six weeks post-operatively, the patient had a sterile seroma requiring surgery, and the fusion mass was evaluated via second look surgery. At that time, the surgeon found robust bone formation and solid fusion mass with no granule migration.

Citation: Faheem S. Posterior thoracolumbar hemivertebra resection and fusion with a biphasic calcium phosphate bone graft with a novel submicron surface topography. *JOJ Case Stud.* 2021;12(2):555831. DOI: 10.19080/JOJCS.2021.12.555831.

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Clinical, Radiographic, and Histologic Outcomes of Ankle Arthrodesis in a Diabetic Patient using a Biphasic Calcium Phosphate Bone Graft with a Novel Submicron Needle-shaped Surface Topography



Authors: Fusco, TA, DPM¹, van Dijk LA, PhD², Sage K, DO²

Affiliations: 1) Orthopedic Associates, Florida 2) Kuros Biosciences

Date: February, 2022

Publication: *Juniper Online Journal of Case Studies*

Study Design: Case Study

Summary: This case details a patient with uncontrolled diabetes who underwent an uncomplicated ankle arthrodesis using MagnetOs Putty. Twelve-weeks post-operatively, the patient developed Charcot collapse of the subtalar joint and the fusion was converted to a tibiototalcalcaneal nail. On revision surgery, the ankle arthrodesis was palpated and visually inspected, and the surgeon found robust fusion mass and solid arthrodesis with no granule migration. Furthermore, histology taken from the fusion site confirmed mature lamellar bone at the arthrodesis and continued resorption of the bone graft at twelve-weeks post-operatively.

Citation: Fusco T, van Dijk L, Sage K. Clinical, Radiographic, and Histologic Outcomes of Ankle Arthrodesis in a Diabetic Patient using a Biphasic Calcium Phosphate Bone Graft with a Novel Submicron Needle-shaped Surface Topography. *JOJ Case Stud.* 2022;13(2):555857. DOI: 10.19080/JOJCS.2022.13.555857.

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5. Peer-Reviewed Publications

Arthrodesis of the Subtalar Joint Using a Novel Biphasic Calcium Phosphate Bone Graft



Authors: Fusco TA¹, Sage K², Rush S¹, Blom F¹, Colvin K¹

Affiliations: 1) Orthopedic Associates, Florida 2) Kuros Biosciences

Date: January, 2022

Publication: *Foot & Ankle Surgery: Techniques, Reports & Cases*

Study Design: Retrospective review

Summary: In this retrospective review, 32 consecutive patients undergoing subtalar arthrodesis surgery were evaluated: the first consecutive 15 patients were treated with various bone grafts including Demineralized Bone Matrices (DBM), Bone Morphogenetic Protein (BMP), Cell Based Allograft (CBA), and Platelet Derived Growth Factor (PDGF),, while the next consecutive 17 patients underwent fusion with MagnetOs Putty either as a standalone bone graft or mixed with BMA. The MagnetOs Putty group had a complete fusion rate of 70%, while the control group had a complete fusion rate of 46%, measured via plain radiograph (3 views) at twelve weeks.

Citation: Fusco TA, Sage K, Rush S, Blom F, and Colvin K. et al. Arthrodesis of the subtalar joint using a novel biphasic calcium phosphate bone graft. *Foot & Ankle Surgery: Techniques, Reports & Cases.* 2022;2(1):100150.

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6. Clinical Evidence: Ongoing Controlled Trials

MagnetOs Granules vs. Autograft in Instrumented Posterolateral Spinal Fusion (MaxA)



ClinicalTrials.gov Identifier: NCT03625544

Start Date: July, 2018

Estimated Completion Date: August, 2024

Study Design: Prospective, observer and patient blinded, multi-center, intra-patient, randomized controlled clinical trial

Summary: In this study, MagnetOs Granules were compared to the gold standard of autograft in human subjects undergoing posterolateral fusions of one to six-levels from T10-S2. MagnetOs Granules were used standalone, without added autograft or BMA. An intra-patient control was achieved by applying autograft to the contralateral side of the spine. Of the 100 subjects enrolled in this study, 50 subjects have thus far completed one year follow-up with fine-cut CTs, read independently by two blinded spine surgeons. Of the first 50 subjects, the fusion rate for MagnetOs Granules used standalone was 78% (39/50 subjects), while the autograft fusion rate was 42% (21/50 subjects).

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Post Marketing Study of MagnetOs Putty Compared to Autograft in Patients Undergoing Posterolateral Lumbar Fusion (PROOF)



ClinicalTrials.gov Identifier: NCT04679844

Start Date: February, 2021

Estimated Completion Date: August, 2024

Study Design: Prospective, Randomized, Intra-patient controlled, Multi-center Study

Summary: This study was initiated to assess the performance of MagnetOs Putty compared to local autograft in a total of 30 patients, requiring up to two-level instrumented posterolateral lumbar spine fusion. MagnetOs Putty is used as a bone graft extender mixed with autograft in a 1:1 volume ratio. The primary outcome measure is the rate of posterolateral lumbar/thoracolumbar fusion assessed by CT-scan at month 12.

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Post Marketing Study of MagnetOs Putty Compared to Local Autograft in Patients Undergoing Posterolateral Lumbar Fusion (PARTNER)



ClinicalTrials.gov Identifier: NCT04679896

Start Date: August, 2021

Estimated Completion Date: October, 2023

Study Design: Prospective, Randomized, Intra-patient controlled, Single-center Study

Summary: This study was initiated to assess the performance of MagnetOs Putty compared to local autograft in a total of 30 patients, requiring up to three-level instrumented posterolateral lumbar spine fusion. MagnetOs Putty is used as a bone graft extender mixed with autograft in a 1:1 volume ratio. The primary outcome measure is the rate of posterolateral lumbar/thoracolumbar fusion assessed by CT-scan at month 12.

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*Results from in vivo laboratory testing may not be predictive of clinical experience in humans. For important safety and intended use information please visit kurosbio.com. †MagnetOs is not cleared by the FDA or TGA as an osteoinductive bone graft. ‡MagnetOs has been proven to generate more predictable fusions than two commercially available alternatives in an ovine model of posterolateral fusion.

References: **1.** Van Dijk, et al. *eCM*. 2021;41:756-73. **2.** Duan, et al. *eCM*. 2019;37:60-73. **3.** Van Dijk, et al. *JOR Spine*. 2018;e1039. **4.** Van Dijk, et al. *J Biomed Mater Res. Part B: Appl Biomater*. 2019;107(6):2080-2090. **5.** Van Dijk, et al. *Clin Spine Surg*. 2020;33(6):E276-E287.

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