Evaluation of a Calcium Phosphate-collagen Matrix Bone Graft with Needle-shaped Submicron Surface Topography in a Clinically Relevant Sheep Posterolateral Lumbar Spine Fusion Model

Nathan W. Kucko[1], James Crowley[2], Daniel Wills[2], Tian Wang[2], Matthew Pelletier[2], Huipin Yuan[1], Guido Houtzager[1], Charlie Campion[1], William R. Walsh[2], Joost de Bruijn[1], Florence Barrère-de Groot[1]
Presenting Author: Nathan W. Kucko, nathan.kucko@kurosbio.com

Disclosures: Nathan W. Kucko (3A, Kuros Biosciences), James Crowley (N), Daniel Wills (N), Tian Wang (N), Matthew Pelletier (N), Huipin Yuan (3A, 3C, Kuros Biosciences), Guido Houtzager (3A, Kuros Biosciences), Charlie Campion (3A, 3C, Kuros Biosciences), William R. Walsh (3B, Kuros Biosciences), Joost de Bruijn (3A, 3C, 9, Kuros Biosciences), Florence Barrère-de Groot (3A, Kuros Biosciences)

INTRODUCTION: Biphasic calcium phosphate (BCP) with a characteristic needle-shaped submicron surface topography (MagnetOs™) has attracted much attention due to its unique bone-forming ability which is essential for repairing critical-size bone defects such as those found in the posterolateral spine [1,2]. Previous in vitro and ex-vivo data performed by van Dijk LA [3] and Yuan H [4] demonstrated that these specific surface characteristics drive a favorable response from the innate immune system. This study aimed to evaluate and compare the in vivo performance of three commercially-available synthetic bone grafts, (1) i-FACTOR Putty®, (2) OssDsign® Catalyst Putty and (3) FIBERGRAFT® BG Matrix, with that of a novel synthetic bone graft in a clinically-relevant instrumented sheep posterolateral lumbar spine fusion (PLF) model. The novel synthetic bone graft comprised of BCP granules with a needle-shaped submicron surface topography (MagnetOs) embedded in a highly porous and fibrillar collagen matrix (MagnetOs Flex Matrix).

METHODS: Six female, skeletally mature sheep (*Ovis Aries*, Border Leicester Merino Cross, 4–5 y, 80–90 kg) were used at the University of New South Wales, Australia, following approval from the local Animal Care and Ethics Committee (ACEC). Four synthetic bone grafts were implanted as standalone in an instrumented sheep posterolateral lumbar fusion (PLF) model for 12 weeks (n=3 bilateral levels per group; levels L2/3 & L4/5), after which spinal fusion was determined by manual palpation, radiograph and µCT imaging (based on the Lenke scale), range-of-motion mechanical testing, and histological and histomorphological evaluation.

RESULTS: Radiographic fusion assessment determined bilateral robust bone bridging (Lenke scale A) in 3/3 levels for MagnetOs Flex Matrix compared to 1/3 for all other groups. For µCT, bilateral fusion (Lenke scale A) was found in 2/3 levels for MagnetOs Flex Matrix, compared to 0/3 for i-FACTOR Putty®, 1/3 for OssDsign® Catalyst Putty and 0/3 for FIBERGRAFT® BG Matrix. Fusion assessment for MagnetOs Flex Matrix was further substantiated by histology which revealed significant graft resorption complemented by abundant bone tissue and continuous bony bridging between vertebral transverse processes resulting in bilateral spinal fusion in 3/3 implants. Statistical analysis was performed using GraphPad Prism. Fusion grading data from manual palpation, x-ray, µCT, and histology were analyzed by the Fisher-Freeman-Halton exact test. Data from µCT volume quantification, biomechanical ROM testing, and histomorphometry were analyzed by analysis of variance followed by Tukey honest significant difference test for post hoc analysis. Normal distribution of data was assessed by the Shapiro-Wilk normality test. For all statistical tests, a significance level of $p<0.05$ was utilized.

DISCUSSION: This study shows clear differences in efficacy between commercially available bone graft substitutes, emphasizing the importance of clinically relevant animal models with multi-endpoint analyses for the evaluation of bone graft materials. MagnetOs Flex Matrix achieved better fusion rates compared to three commercially-available synthetic bone grafts when used as a standalone in a clinically-relevant instrumented sheep PLF model.

SIGNIFICANCE/CLINICAL RELEVANCE: The current rate of non-unions in the spine is estimated to be 17%, which results in over 10% of all spinal fusion patients requiring a second intervention to relieve their symptoms. Using the most effective bone graft can improve fusion outcomes by up to 60%. This study demonstrates the ability of MagnetOs Flex Matrix to improve fusion outcomes compared to other synthetic bone void fillers when used standalone in a clinically-relevant, critical-size defect sheep PLF model, which can translate into improved fusion outcomes in the clinic.

REFERENCES: **1.** L. van Dijk et al., *J Biomed Mater Res Part B*, 107(2019) 2080-2090; **2.** L. van Dijk et al., *JOR Spine*, 1:e1039(2018); **3.** L. van Dijk et al., *The Spine Journal*, 20 (9), S25, 2020; **4.** H. Yuan et al., *The Spine Journal*, 20 (9), S116-117, 2020

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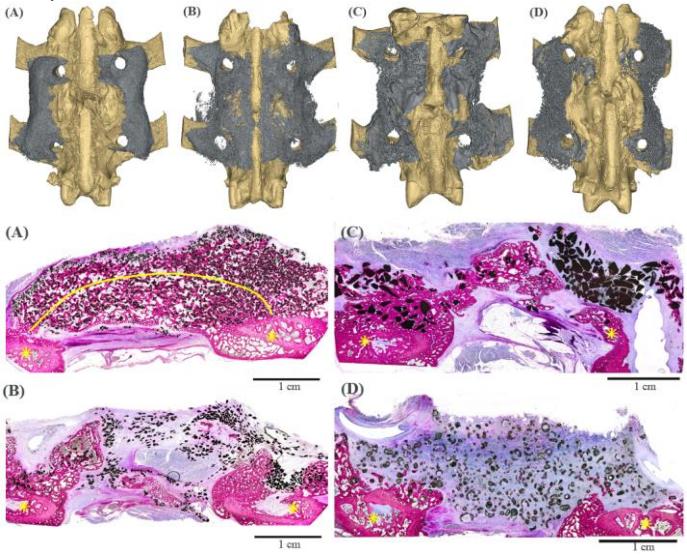

Figure 1: Representative examples of 3D µCT reconstructions (A–D) of spinal levels treated with MagnetOs Flex Matrix (A), i-FACTOR Putty (B), Catalyst Putty (C), and FIBERGRAFT BG Matrix (D). The host spinal bone (off-white) and fusion mass (grey) including (new) bone and residual implant material are shown as individual segmentations. MagnetOs Flex Matrix exhibited robust bone bridging that was well consolidated between the intertransverse space. Conversely i-FACTOR Putty and Catalyst Putty spread to towards the lamina and facet joints, suggesting graft migration.

Figure 2: Representative, low-magnification micrographs of sagittal histologic sections (methylene blue/basic fuchsin) taken from the intertransverse process regions of spinal levels treated MagnetOs Flex Matrix (A), i-FACTOR Putty (B), Catalyst Putty (C), and FIBERGRAFT BG Matrix (D). Bone matrix is shown in pink, soft tissues in blue, and residual graft material in black. The low magnification micrographs were graded for fusion, evident from a continuous bone bridge between adjacent transverse processes (yellow line). MagnetOs had a fusion score of 6 of 6 segments while Catalyst Putty had a score of 3 of 6 segments, and i-FACTOR Putty and FIBERGRAFT BG Matrix both scored 0 of 6 segments as fused.