Evaluation of the efficacy of *E. coli*-derived rhBMP-2 in mini-pig spinal posterolateral fusion

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HA & *E. coli*-derived rhBMP-2

- **Posterolateral lumbar fusion with rhBMP-2 /HA-TCP after laminectomy in the nonhuman primate**
- **Lower dose of rhBMP-2 achieves spine fusion when combined with an osteoconductive bulking agent in non-human primates**
- **RhBMP-2 produced by mammalian cells : too expensive → major obstacle to its clinical application**
- **Bacterial expression system (eg, *Escherichia coli*) : cost-effective production of rhBMP-2**

Purpose of This Study

- To determine whether HA granule could be an adequate carrier for E-BMP-2

- To assess the osteoinductivity of HA granule-E-BMP-2 composite

- To evaluate the bone forming ability depending on the different dosages of E-BMP-2

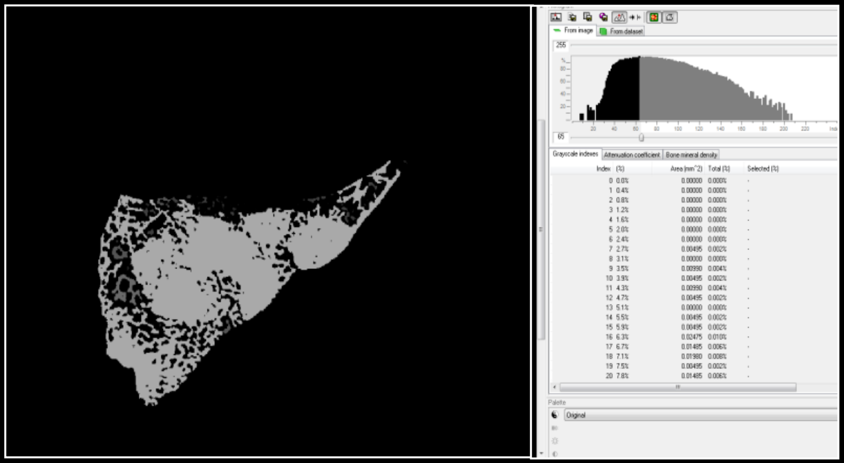
Materials and Methods

- 31 skeletally mature male Yucatan mini-pigs
- Single control group (n = 8) without E-BMP-2 and two experimental groups (1.0 mg/side, n = 8 and 3.0 mg/side, n = 15)
- To evaluate the bone forming ability depending on the different dosages of E-BMP-2
- *E. coli*-derived rhBMP-2 (3 mg/vial, Daewoong)
- Synthetic HA granules (Bongros® -HA, Bio-Alpha)

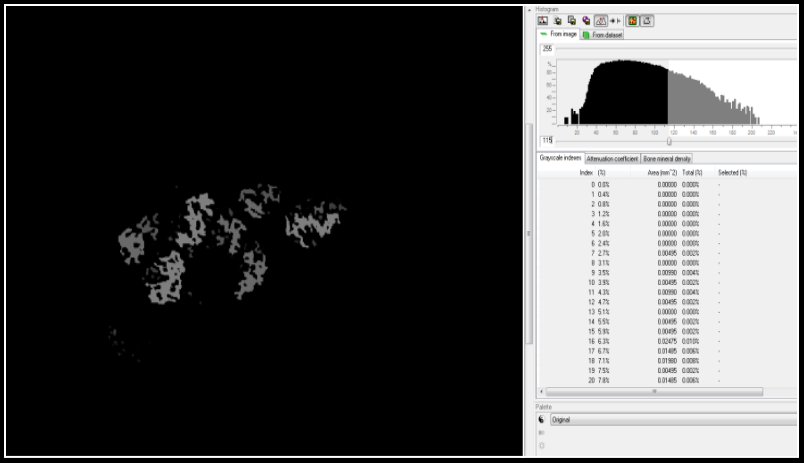
Fusion Assessment

- Radiographic analysis
- Manual palpation
- 3D CT (Toshiba, Tokyo, Japan)
- 3D μCT (SKYSCAN, Skyscan-1173, Belgium)
- Histologic examinations

μCT Analysis



Bone Volume Fraction



HA Volume Fraction

Bone volume fraction (%) = BV/TV × 100 (lower gray threshold = 65)

HA volume fraction (%) = HA volume/TV × 100 (lower gray threshold = 115)

New bone volume fraction (%) = BV fraction – HV volume fraction

Wound Complication

	Group			N
	Control	1 mg	3 mg	
Developed	1 (12.5%)	2 (28.6%)	4 (30.8%)	7
Not developed	7 (87.5%)	5 (71.4%)	9 (69.2%)	21
N	8	7	13	28

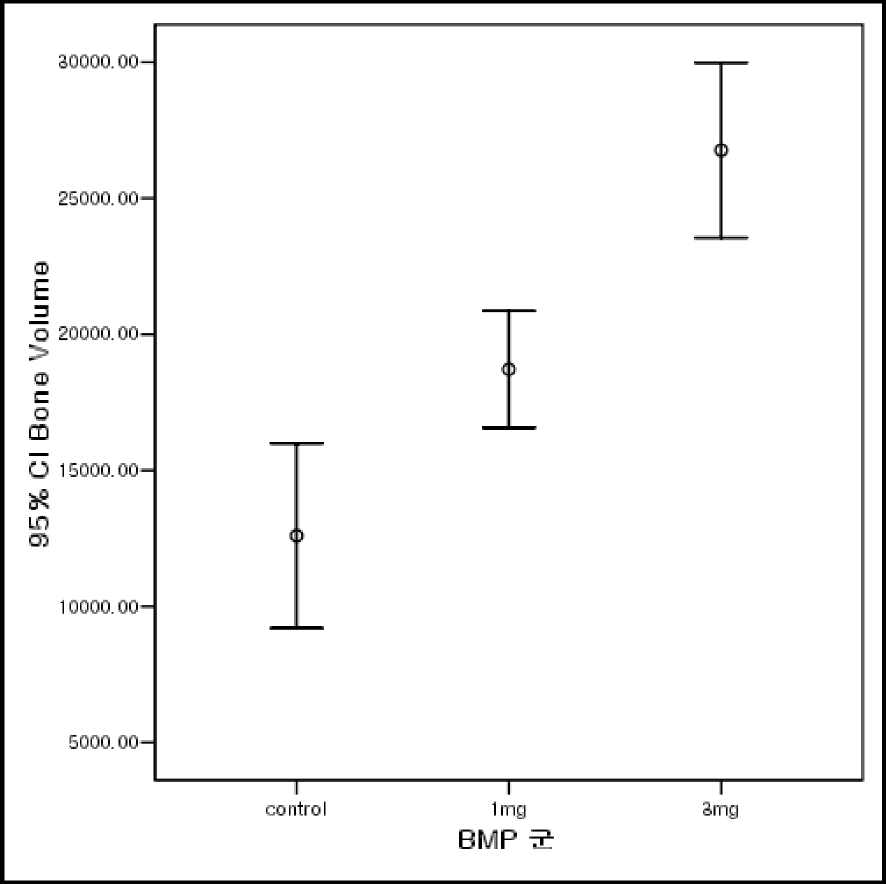
$P = 0.623$

Bony Union

	Group			N
	Control	1 mg	3 mg	
Union	3 (37.5%)	5 (71.4%)	11 (84.6%)	19
Non-union	5 (62.5%)	2 (28.6%)	2 (15.4%)	9
N	8	7	13	28

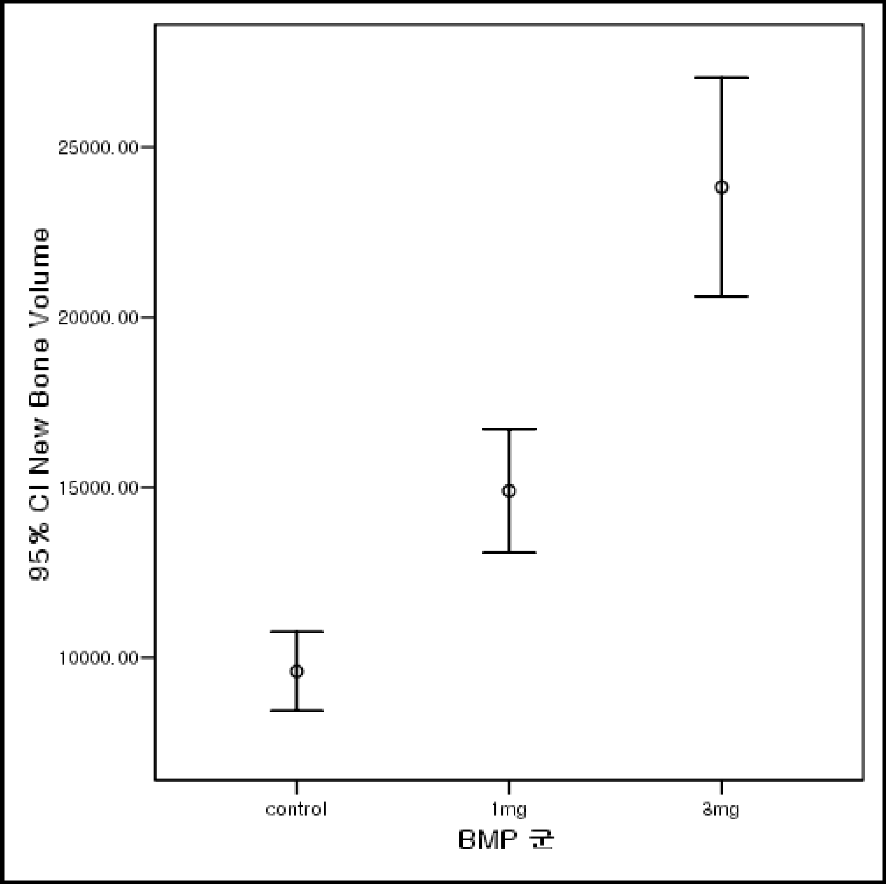
$P = 0.031$

Bone Volume



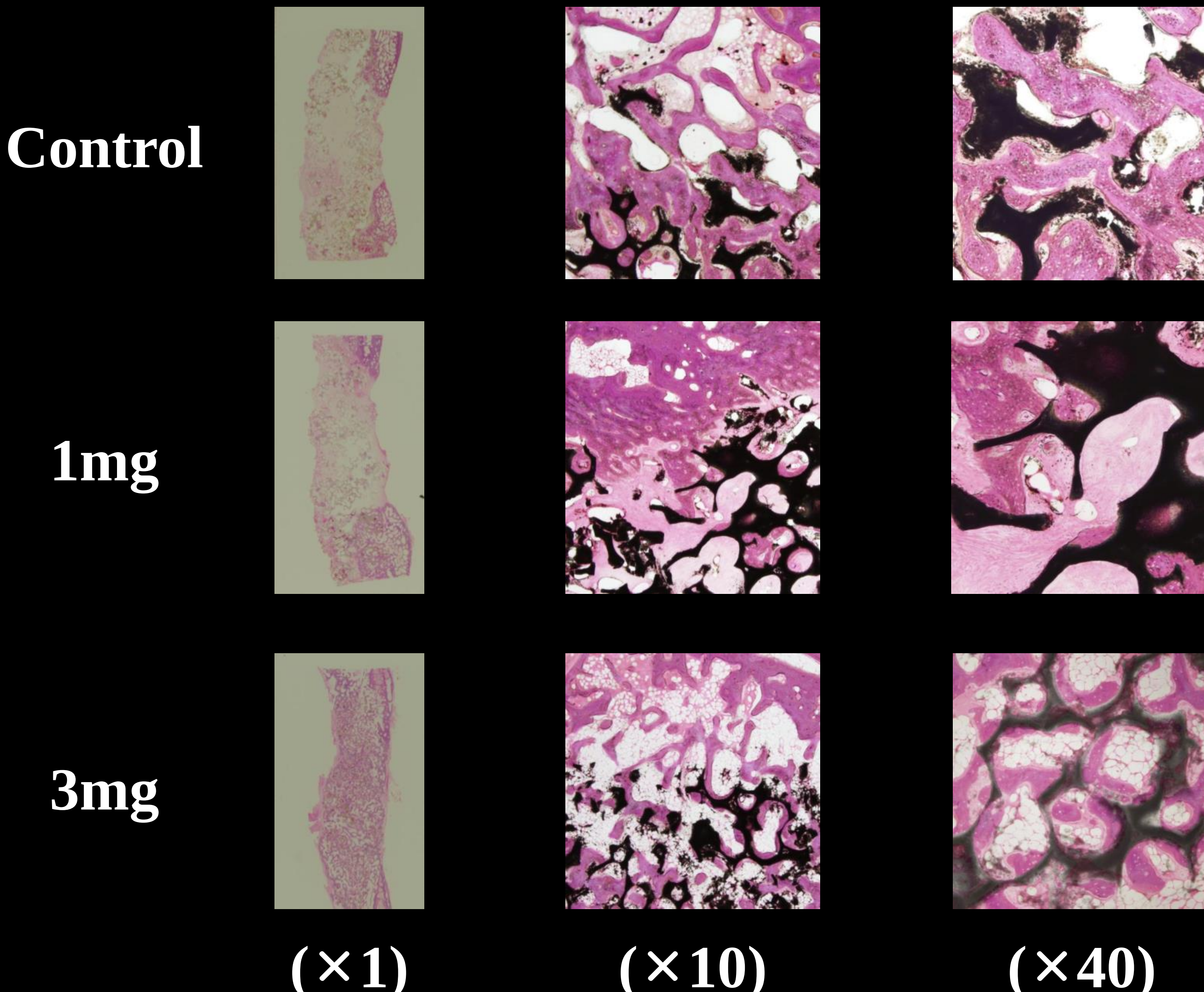
P < 0.001

New Bone Volume



P < 0.001

Histologic Analysis (×1)



Discussion

- **One of major obstacle in fusion surgery using rhBMP-2 is its high cost**
- **Cost-effective production of rhBMP-2 using an *E. coli* system was introduced and several animal studies demonstrated the osteoinductivity of E-BMP-2 in dose-dependent fashion**
- **Our porcine posterolateral fusion model showed addition of E-BMP-2 significantly increased the fusion rates**

HA carrier-E-BMP-2 Combination

- **HA is a major mineral constituent of bone and osteoblasts can deposit bone directly onto this osteoconductive carrier material**

- **Considering the mechanical and biologic environment for posterolateral spine fusion, HA is also useful for rhBMP-2 carrier because of its mechanical resistance to compression force and high affinity for rhBMP-2**

Conclusions

- E-BMP-2 adsorbed HA granule could be an alternative to autogenous iliac bone graft

- Dosage of 1 mg/side E-BMP-2 could be effective in posterolateral spine fusion in porcine model when combined with HA carrier

DISCLOSURE STATEMENT

The authors have nothing to disclose