

COWELL BMP

Osteoinductive Bone Graft rhBMP-2 + BCP/DCP



The world's first E.rhBMP-2 (E.Coli derived Recombinant Human Bone Morphogenetic Protein type 2), as a growth factor that induces bone and cartilage formation. It is a retinoid mediator that plays a key role in osteoblast differentiation.

Composition

- COWELL BMP is bone graft material based on the E.rhBMP-2, developed for the first time in the world. It is supported by 10 years of clinical data and over 40 studies.
- BCP/DCP as a carrier allows maintenance of space.

Features

- Primary closure for soft tissue regeneration is not required.
- Regenerates adherent gingiva.
- Simplifies challenging bone grafting and soft tissue regeneration.
- Acts directly on stem cells.
- Induces bone regeneration without infection in extraction socket.
- Contains 1mg of bone morphogenic protein per 1g of the particle (1g of autologous bone contains 2ng of bone morphogenic protein).

Experience innovation

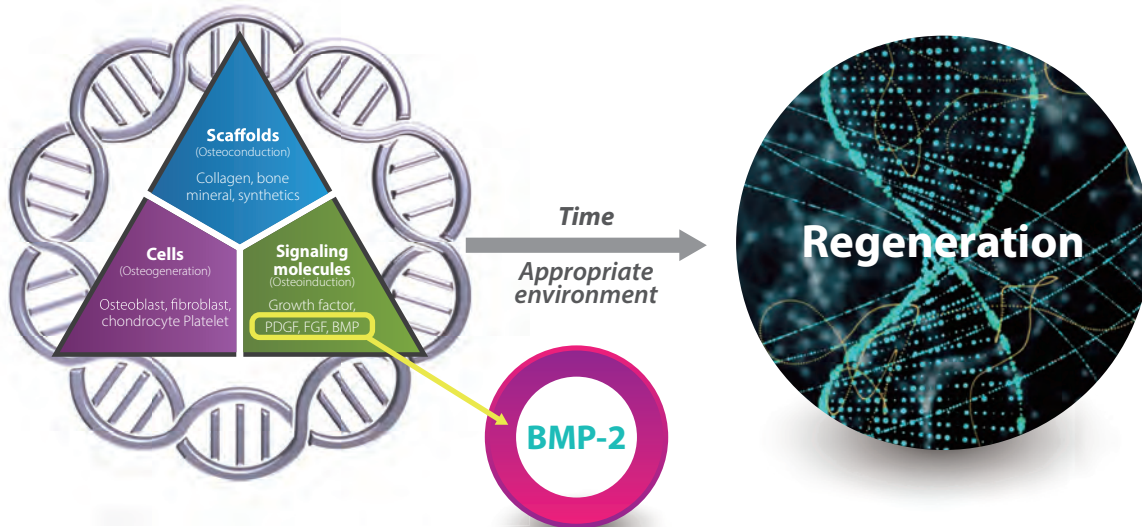
COWELL BMP



THE WORLD FIRST E.rhBMP-2-based bone graft, supported by
10 YEARS OF CLINICAL DATA AND 40+ STUDIES.

Development Background

Triad of Tissue Engineering



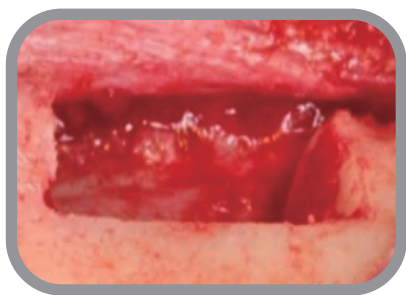
Autologous stem cell transplantation

- Less effective due to difficulty of the engraftment in early stage of tissue regeneration
- Cell cultivation causes enormous expense

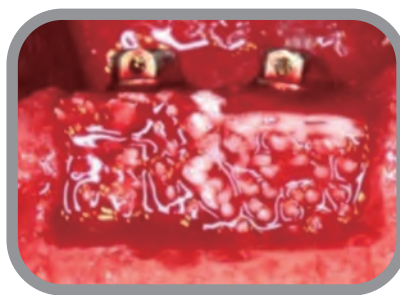
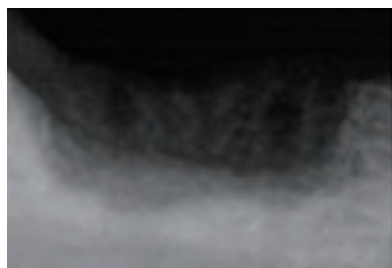
However, Stem cell growth factors

- Effective in tissue regeneration for all vertebrates
- Even human growth factor is effective in both human and animals

Stem cell transplantation VS rhBMP-2



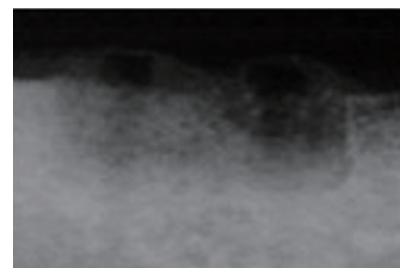
Stem cell transplantation



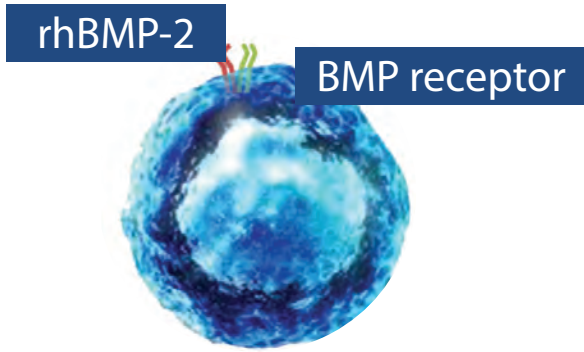
Stem cell & rhBMP-2



rhBMP-2

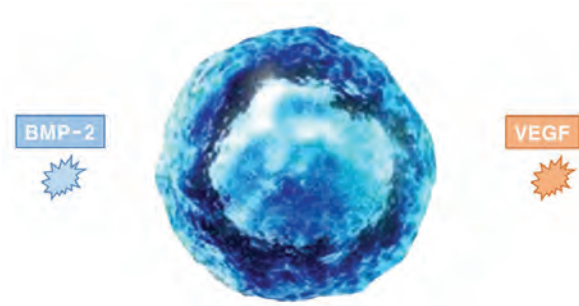


Mechanism of Action of COWELL BMP



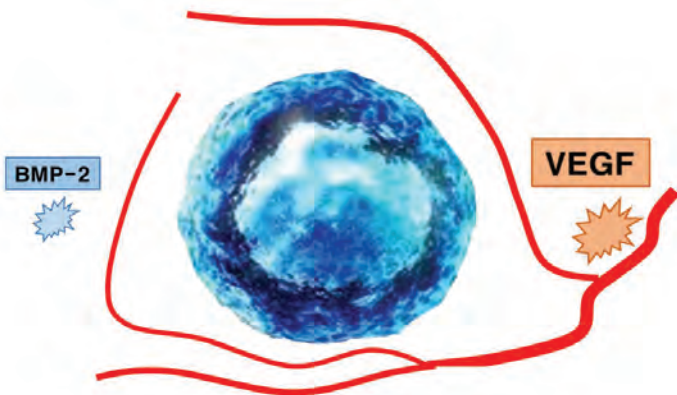
Mesenchymal Stem cell

1. rhBMP-2 bonds with BMP-2 receptor of Stem cell to **activate intracellular phosphorylating enzyme.**

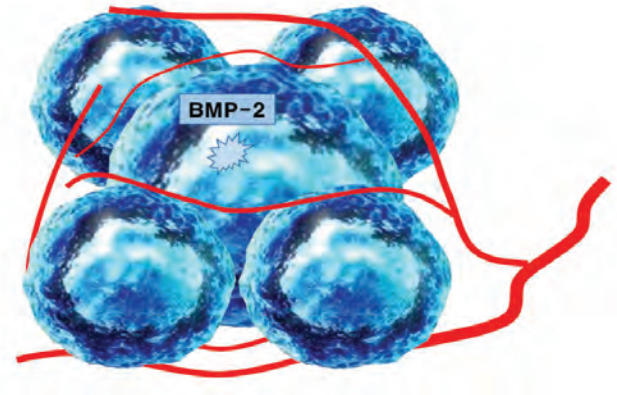


2. BMP-2 of Stem cell and VEGF activates for **protein synthesis and secretion.**

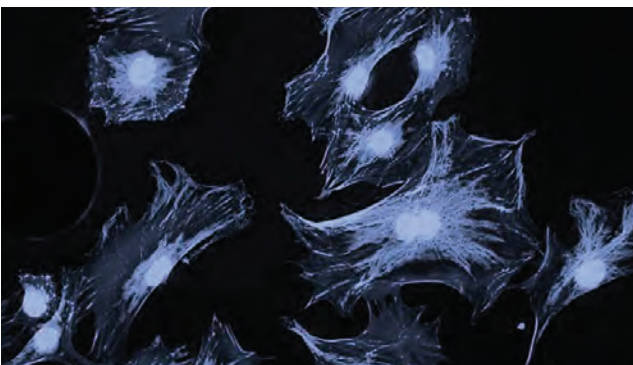
* VEGF : Vascular Endothelial Growth Factor



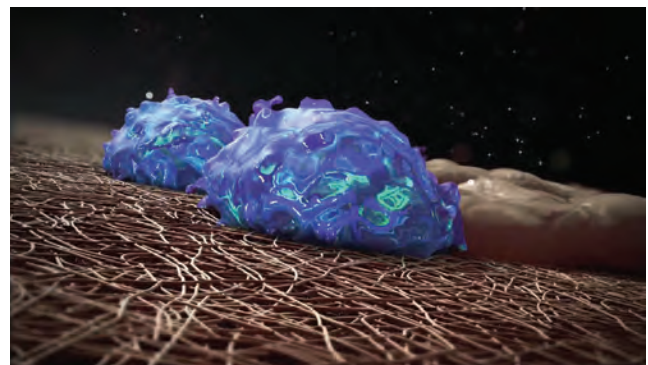
3. VEGF **promotes cell growth** by inducing angiogenesis to nourish Stem cell.



4. BMP-2, activates **cell division** of surrounding Stem cell and promotes rapid proliferation.



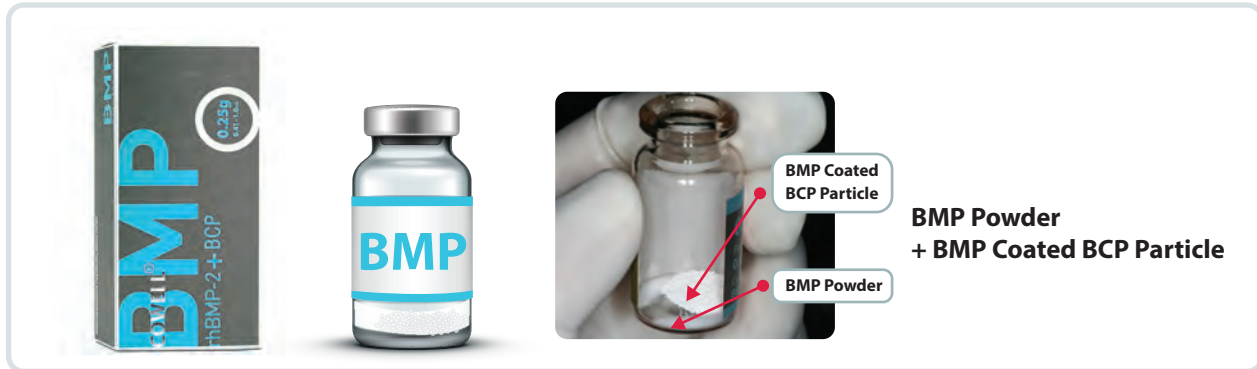
5. Proliferated Stem cells, **differentiate into various cells** according to surrounding tissues.



6. Differentiated cells **form neoplastic tissues** and remodel them according to the surrounding environment.

Product Type

COWELL BMP (One vial)



- Dose and particle size of the COWELL BMP



0.1g

Product Code	Particle Size
BB1010	0.41~1.0mm



0.25g

Product Code	Particle Size
BB1025	0.41~1.0mm



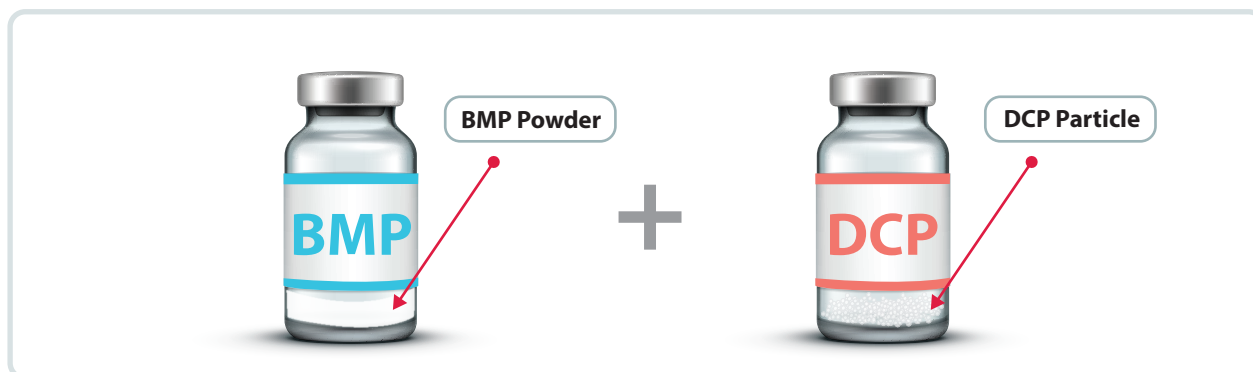
0.5g

Product Code	Particle Size
BB1050	0.41~1.0mm

* A vial of 0.1g can be used for less than one extraction socket, while 0.25g/0.5g can be used for maxillary sinus or for the wide bone defect area.



COWELL BMP Plus (Two vials)



• Dose and particle size of the COWELL BMP Plus.

BMP 0.1mg

Product Code	BMP Dose	Particle Dose	Particle Size
EBB0125	0.1mg	0.25g	0.41~1.0mm
EBB0105	0.1mg	0.5g	0.41~1.0mm
EBB1110	0.1mg	1g	0.41~1.0mm
EBB1220	0.1mg	2g	0.41~1.0mm

BMP 0.25mg

Product Code	BMP Dose	Particle Dose	Particle Size
EBB2525	0.25mg	0.25g	0.41~1.0mm
EBB2505	0.25mg	0.5g	0.41~1.0mm
EBB1125	0.25mg	1g	0.41~1.0mm
EBB1225	0.25mg	2g	0.41~1.0mm

BMP 0.5mg

Product Code	BMP Dose	Particle Dose	Particle Size
EBB0525	0.5mg	0.25g	0.41~1.0mm
EBB0505	0.5mg	0.5g	0.41~1.0mm
EBB1150	0.5mg	1g	0.41~1.0mm
EBB1250	0.5mg	2g	0.41~1.0mm

BMP 1mg

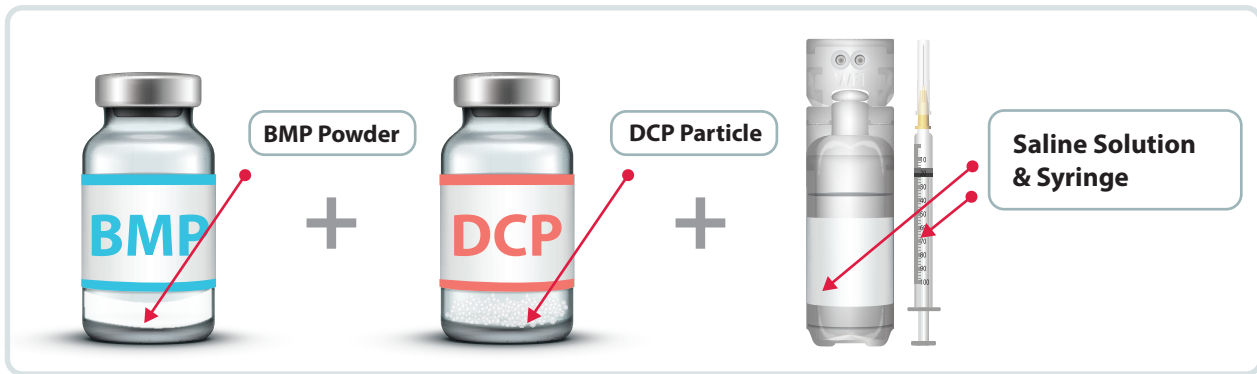
Product Code	BMP Dose	Particle Dose	Particle Size
EBB1025	1mg	0.25g	0.41~1.0mm
EBB1050	1mg	0.5g	0.41~1.0mm
EBB1011	1mg	1g	0.41~1.0mm
EBB1012	1mg	2g	0.41~1.0mm

BMP 2mg

Product Code	BMP Dose	Particle Dose	Particle Size
EBB2025	2mg	0.25g	0.41~1.0mm
EBB2050	2mg	0.5g	0.41~1.0mm
EBB2011	2mg	1g	0.41~1.0mm
EBB2012	2mg	2g	0.41~1.0mm



INNO GF Kit (Two vials + Saline Solution + Syringe)



• Dose and particle size of the INNO GF Kit.

BMP 0.1mg

Product Code	BMP Dose	Particle Dose	Particle Size
IBB0125	0.1mg	0.25g	0.41~1.0mm
IBB0105	0.1mg	0.5g	0.41~1.0mm
IBB1110	0.1mg	1g	0.41~1.0mm
IBB1220	0.1mg	2g	0.41~1.0mm

BMP 0.25mg

Product Code	BMP Dose	Particle Dose	Particle Size
IBB2525	0.25mg	0.25g	0.41~1.0mm
IBB2505	0.25mg	0.5g	0.41~1.0mm
IBB1125	0.25mg	1g	0.41~1.0mm
IBB1225	0.25mg	2g	0.41~1.0mm

BMP 0.5mg

Product Code	BMP Dose	Particle Dose	Particle Size
IBB0525	0.5mg	0.25g	0.41~1.0mm
IBB0505	0.5mg	0.5g	0.41~1.0mm
IBB1150	0.5mg	1g	0.41~1.0mm
IBB1250	0.5mg	2g	0.41~1.0mm

BMP 1mg

Product Code	BMP Dose	Particle Dose	Particle Size
IBB1025	1mg	0.25g	0.41~1.0mm
IBB1050	1mg	0.5g	0.41~1.0mm
IBB1011	1mg	1g	0.41~1.0mm
IBB1012	1mg	2g	0.41~1.0mm

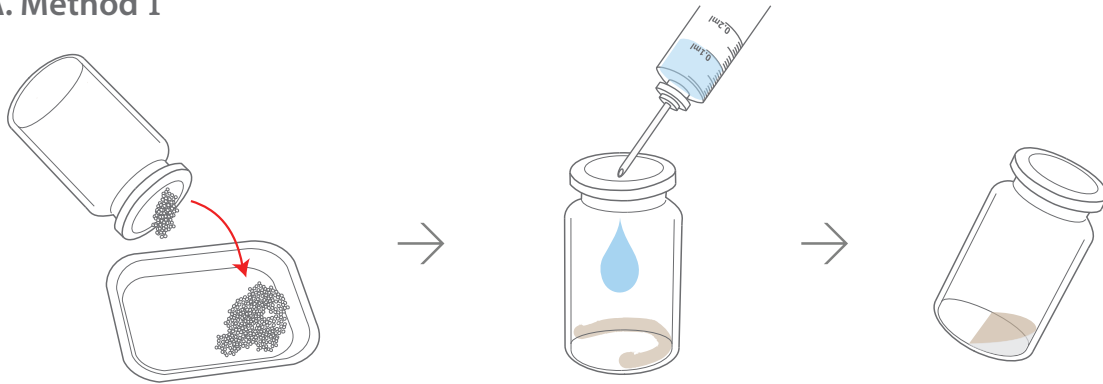
BMP 2mg

Product Code	BMP Dose	Particle Dose	Particle Size
IBB2025	2mg	0.25g	0.41~1.0mm
IBB2050	2mg	0.5g	0.41~1.0mm
IBB2011	2mg	1g	0.41~1.0mm
IBB2012	2mg	2g	0.41~1.0mm



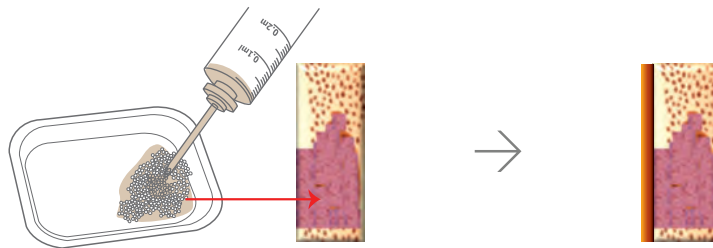
User Guide COWELL BMP

A. Method I



a. Transfer DCP graft material (Vial I).

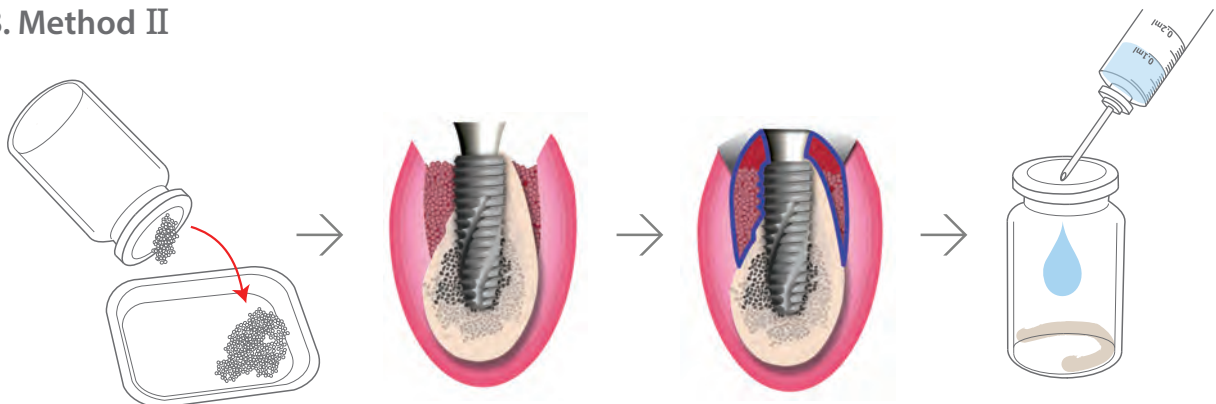
b. Inject distilled water into vial II with lyophilized rhBMP-2 powder in it and mix with the powder.



c. Mix BMP solution with DCP or plus autogenic / allograft and, apply to the recipient site.

d. Cover the defect area using a barrier membrane or suture natural soft tissue without membrane.

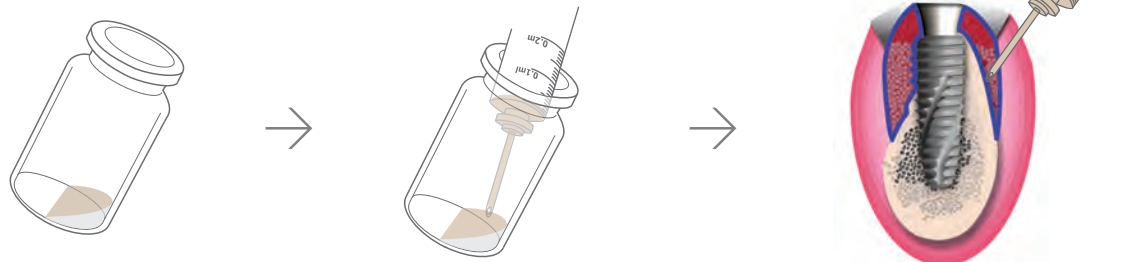
B. Method II



a. Transfer DCP graft material (Vial I) into a container.

b. Apply DCP into the recipient site and cover the defect area using a barrier membrane or suture natural soft tissue without membrane.

c. Inject distilled water into lyophilized rhBMP-2 powder (vial II).

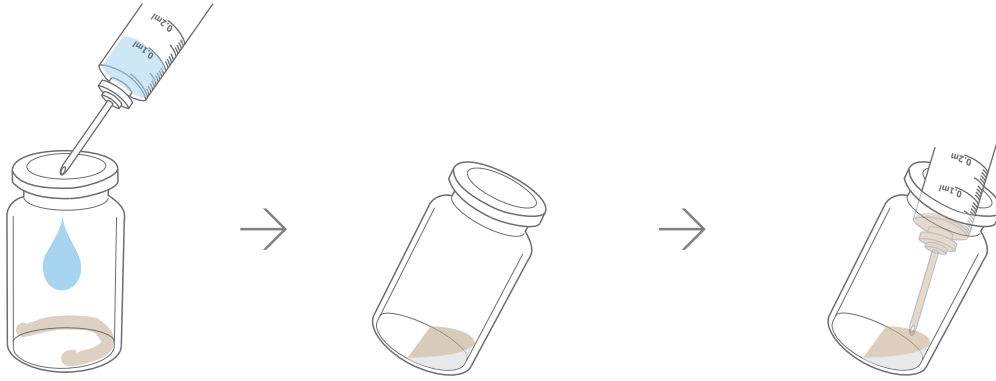


d. Mix rhBMP-2 with distilled water (saline solution) and wait for 10 to 15 seconds before using.

e. Aspirate the mixture using a syringe.

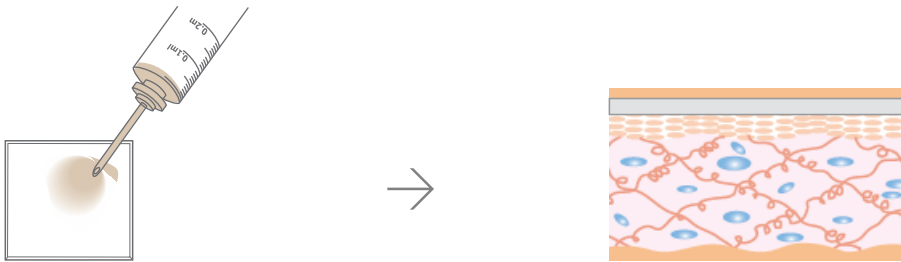
f. Inject BMP solution through soft tissue until needle of syringe reaches bone.

C. Method III



a. Inject distilled water into vial **II** with lyophilized rhBMP-2 power in it and mix with the powder.

b. Aspirate the mixture using a syringe.



c. Hydrate BMP-2 solution into membrane.

d. Apply BMP-2 solution soaked membrane to damaged site.

Dose of distilled water to make the mixture (BMP-2 Solution)

BMP Dose	Distilled Water Dose	BMP Dose	Distilled Water Dose
0.1mg	0.1ml	2mg	1.6ml
0.25mg	0.2ml	5mg	4ml
0.5mg	0.4ml	10mg	8ml
1mg	0.8ml	20mg	16ml

Video

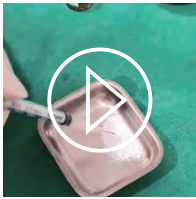
* Scan above QR code to watch videos of user guide of COWELL BMP

1. Mixture with bone graft material

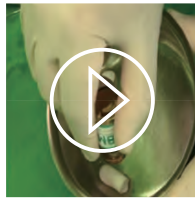
Full dose of COWELL BMP

Excess leakage of COWELL BMP

Douse bone graft material immediately before the graft to minimize the time for rhBMP-2 protein to adsorb to bone graft calcium ingredient.



Particle bone graft



Collagen Plug



Bone matrix

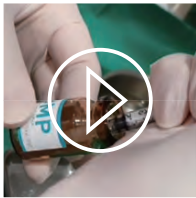


2. Injection into bone graft site

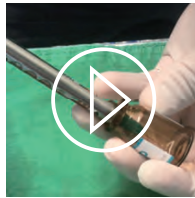
½ dose of COWELL BMP

Moderate leakage of COWELL BMP

Even if the solution leaks out of the gingival after the injection, the effect is the same since the minimum effective drug dose has reached the stem cells.



General Syringe



Lidocaine Syringe

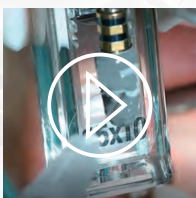


3. COWELL BMP coated implant

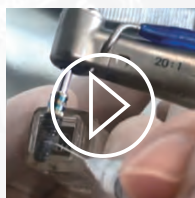
½ dose of COWELL BMP

Moderate leakage of COWELL BMP

The bone marrow stem cells are directly activated by placement of rhBMP-2 coated implant.



INNO Implant_1



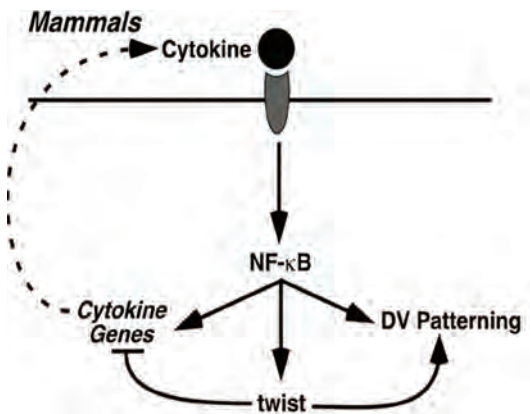
INNO Implant_2



Safety of COWELL BMP

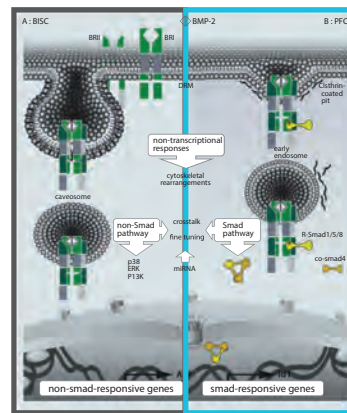
Q : Bone overgrowth by rhBMP-2?

A : rhBMP-2 is safe from bone overgrowth because Twist-2 is synthesized in Stem cells to stop cell division when bone formation period is completed.



Cell, Vol. 112, 169-180, January 24, 2003

European Journal of Endocrinology (2000) 142 9-21



Cell proliferation **Cell differentiation**

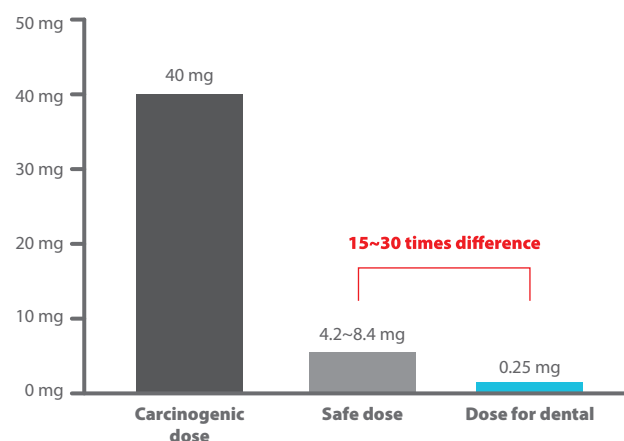
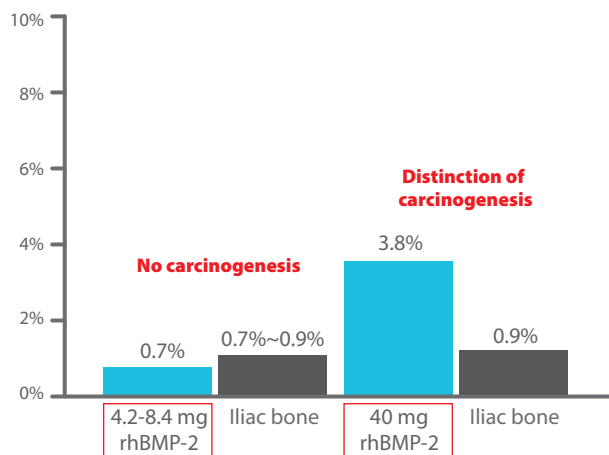
- Bonding to BMP-2 receptor
- Signal pathway
- Nuclear activation
- **VEGF, BMP Synthesis**

Q : Correlation between cancer incidence and usual dose of rhBMP-2?

A : Generally, rhBMP-2 may be related to cancer incidence only when total dose is over 40mg.

Countless research has proven that the safety standard dose is 4.2~8.4mg. COWELL BMP is supplied below the safety standard dose only.

(E.g. COWELLBMP 0.25g contains 0.25mg of rhBMP-2 which is 15 to 30 times lower than the safety standard.)



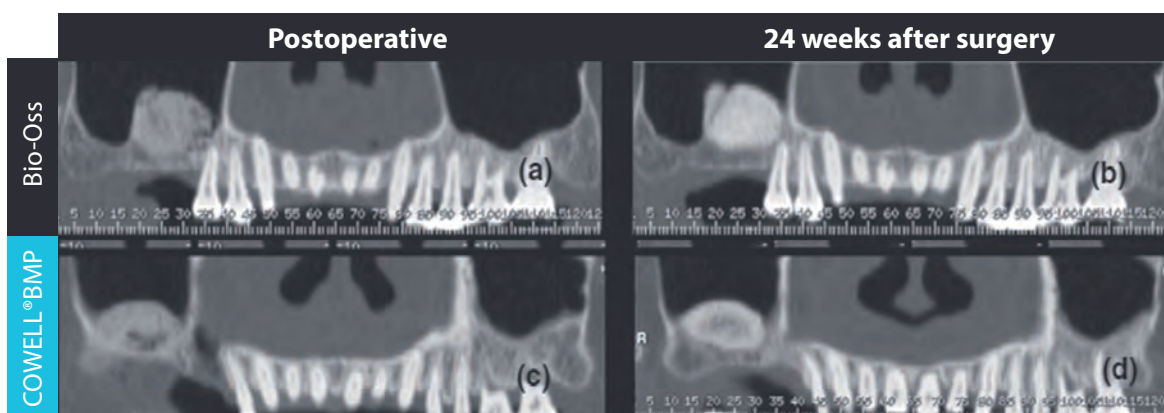
Q : Swelling occurrence after using rhBMP-2?

A : Relief incision may cause swelling due to angiogenesis proliferation in muscle but it is pain-free. Also, swelling is a transitional phenomenon and it is not a side effect.



Q : Seroma occurrence after using rhBMP-2?

A : After sinus lift surgery, excessive secretion of exudate during healing period may undertow in the grafted site of sealed maxillary sinus and develop into seroma but soon disappear. To limit the use to a maximum of 0.25 mg is safer rather than a high dose.



Effectiveness of COWELL BMP

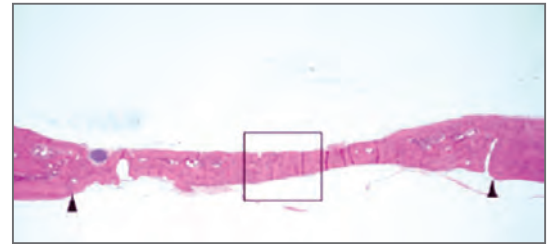
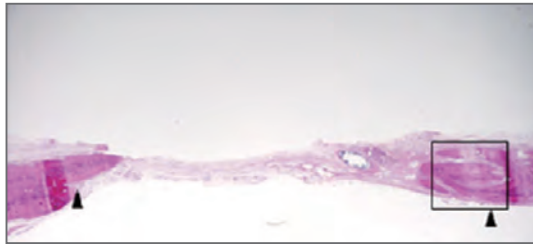
■ Critically Defected Model

Bone Graft Type

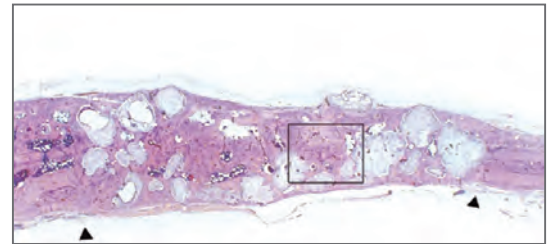
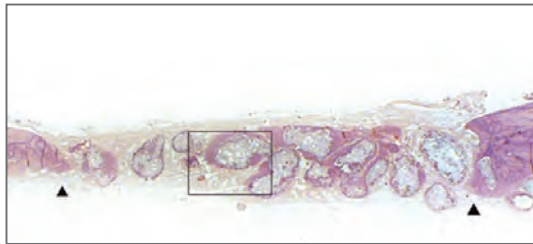
Without rhBMP-2

With rhBMP-2

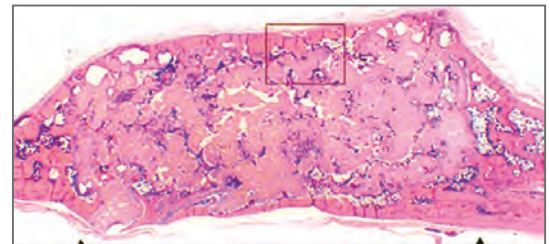
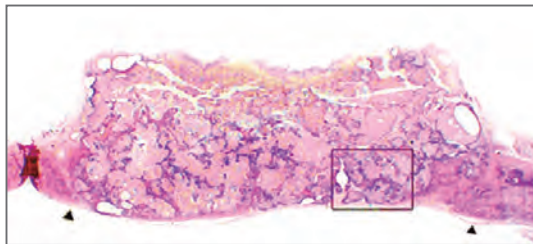
Collagen



Particle Graft

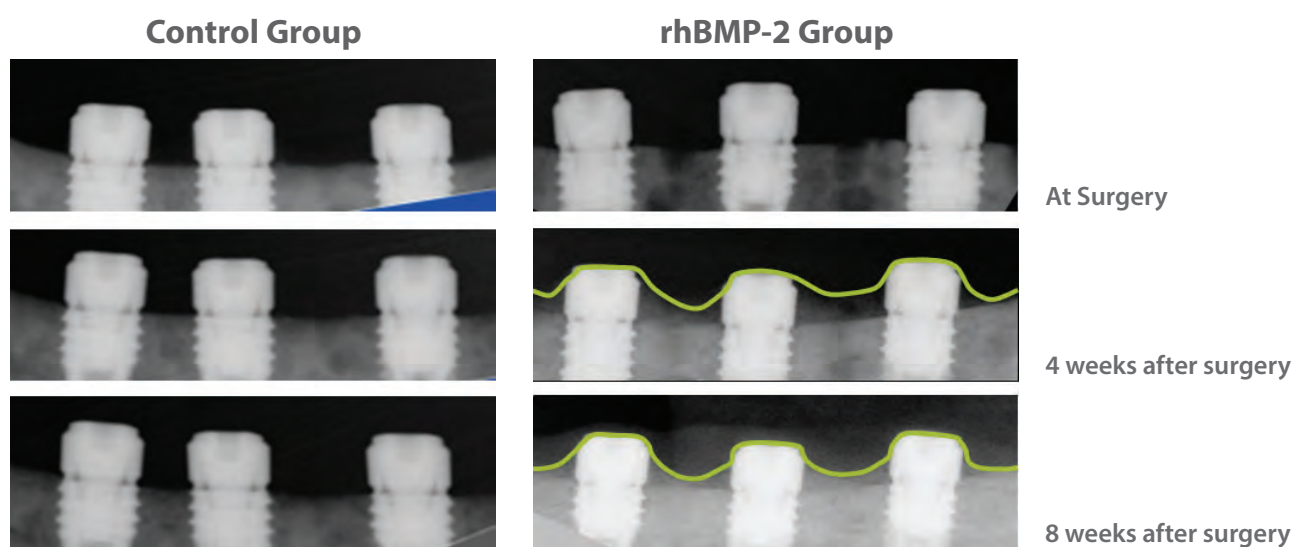


Block Graft

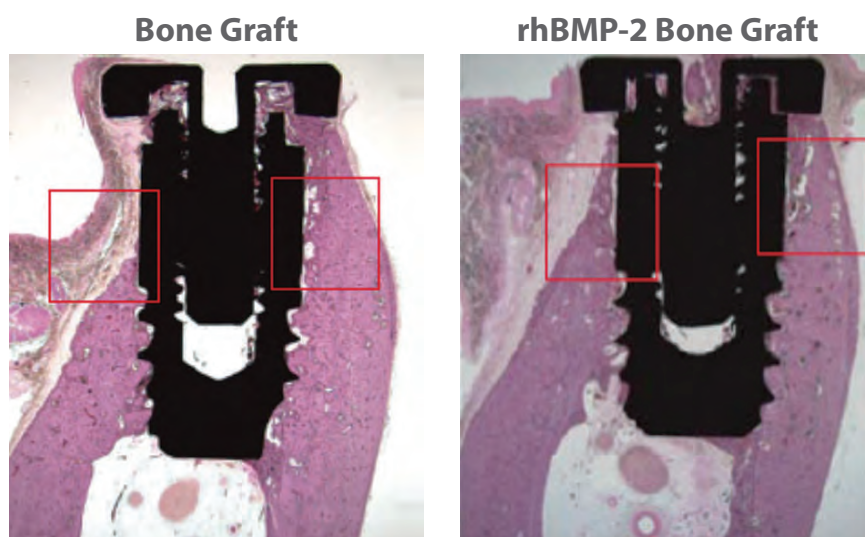


■ rhBMP-2 Coated Implant

Vertical Defect



Dehiscence Defect

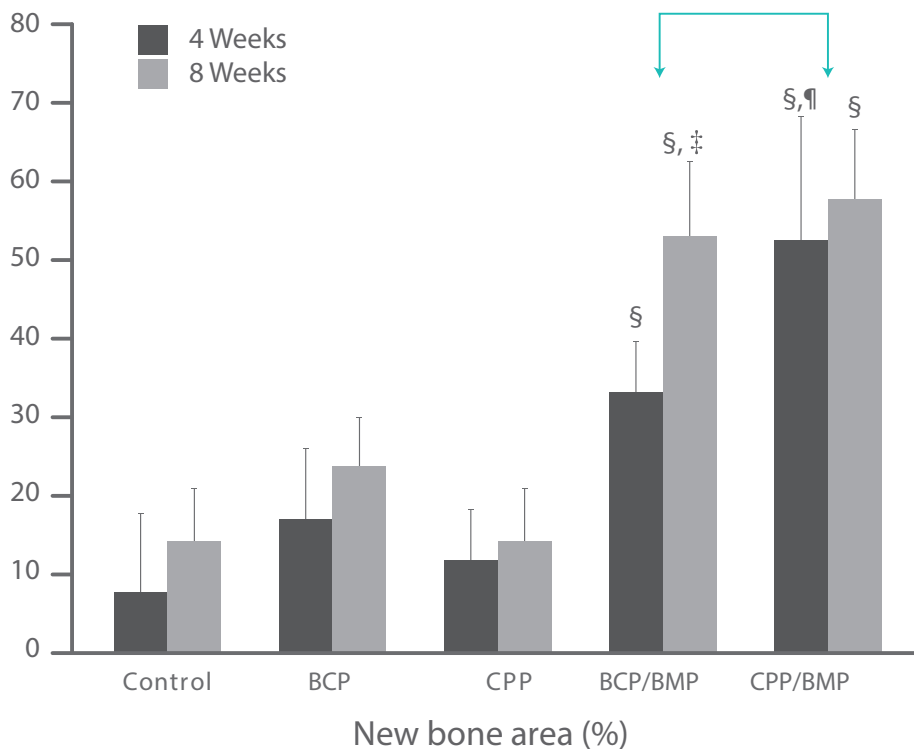
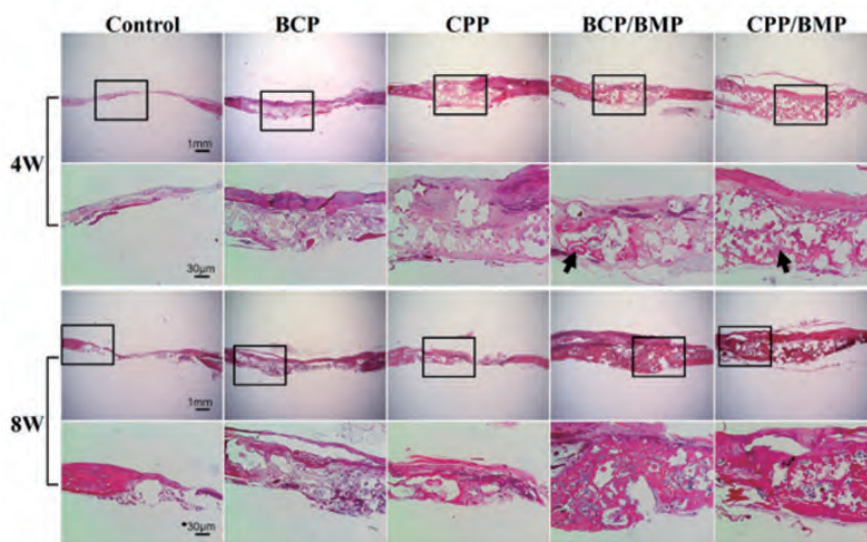


* Bone is safely formed without barrier membrane after rhBMP-2 bone graft, however, when use of general bone graft, barrier membrane is essential

Effectiveness of COWELL BMP

■ Comparison with other materials

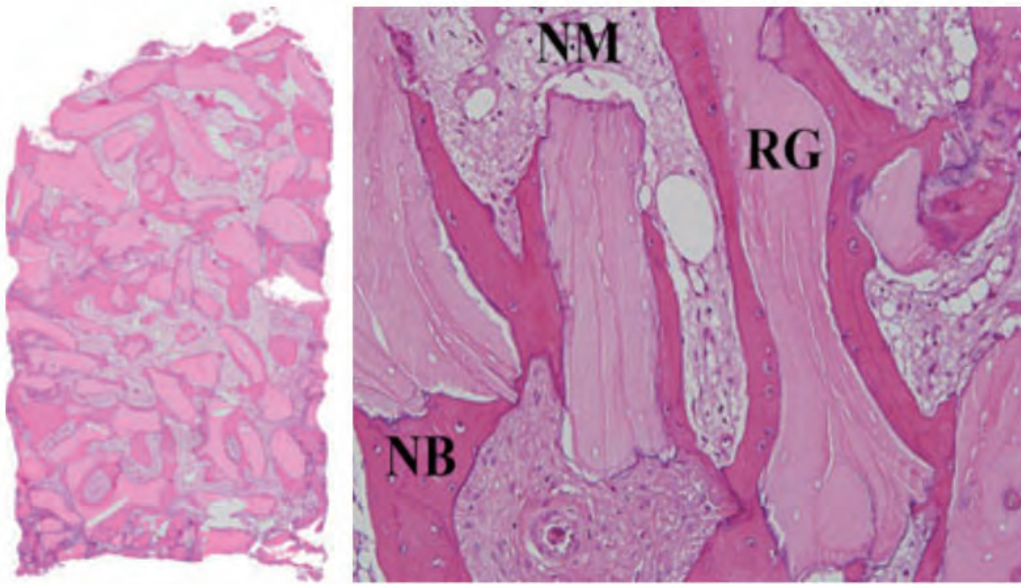
Both Calcium Pyrophosphate, CPP(Ca/P=1) and Biphasic Calcium Phosphate, BCP(Ca/P=1.55) are very effective for early osteoanagenesis. CPP, however, has higher absorption rate than BCP and is slightly more effective for osteoanagenesis.



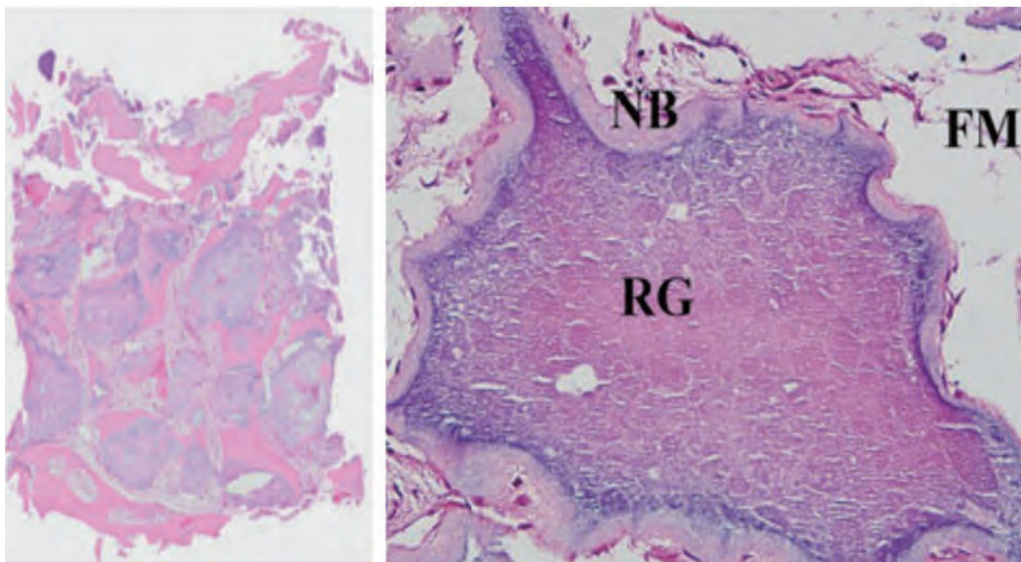
There is no difference in the ratio of new bone generation.

However, Graft B forms hard fibrous tissue between particles and the COWELL BMP fills bone marrow tissue.

The Graft B received site has high resistance against drilling while the COWELL BMP has excellence in bone remodeling by bone.



Control ("Graft B")



COWELL BMP

CLINICAL CASE

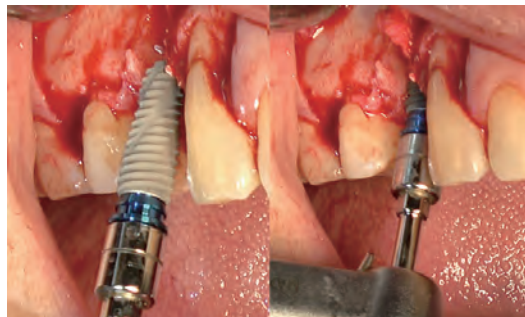
Case 1. Bone Regeneration and Gingival Improvement Using Bone Augmentation using COWELL BMP



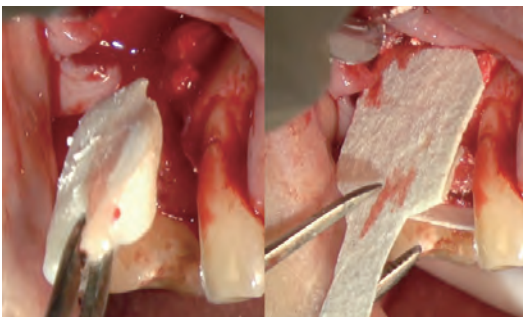
Dr. Claudio Sotomayor Julio,
D.D.S.
Chille



① Pre-operative



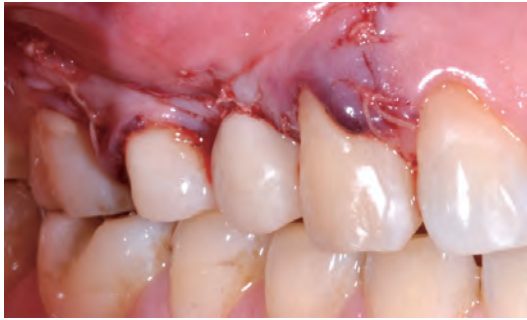
② INNO implant placement



③ 2 layers of membrane placement
with COWELL BMP BCP powder



④ COWELL BMP injection



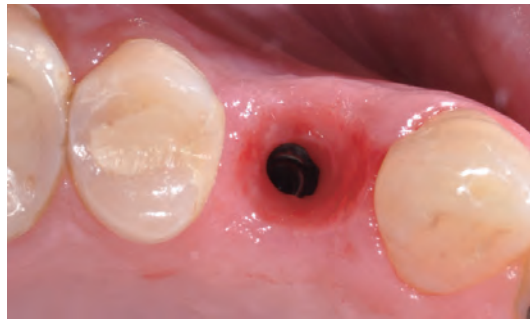
⑤ Post-operative



⑥ 1 month



⑦ 4 months healing period and removal of adhesive provisional tooth



⑧ 2 weeks after connection surgery



⑨ 5 months



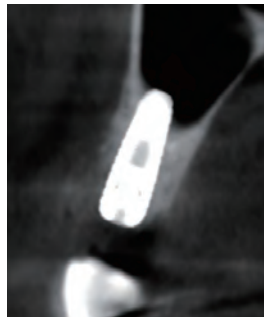
⑩ 5 month after surgery : final rehabilitation



Pre-operation
(18.08.02)



Post-operation
(18.08.02)



4 months
(18.12.03)

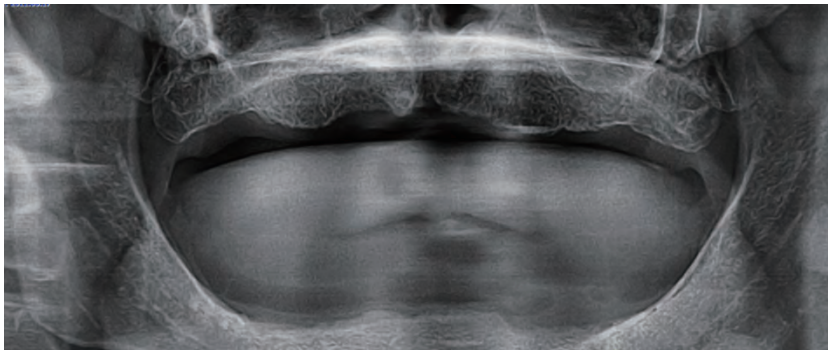


1 year
(19.08.06)

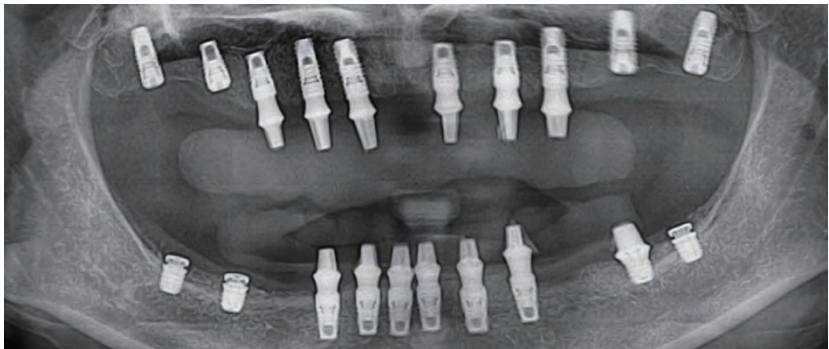
CLINICAL CASE

Case 2.
Bone regeneration in combination of rhBMP-2 and autogenous bone

62 years old, Female



Preoperative
2010. 04. 05



Postoperative
2010. 04. 05



10 months
2011. 02. 25



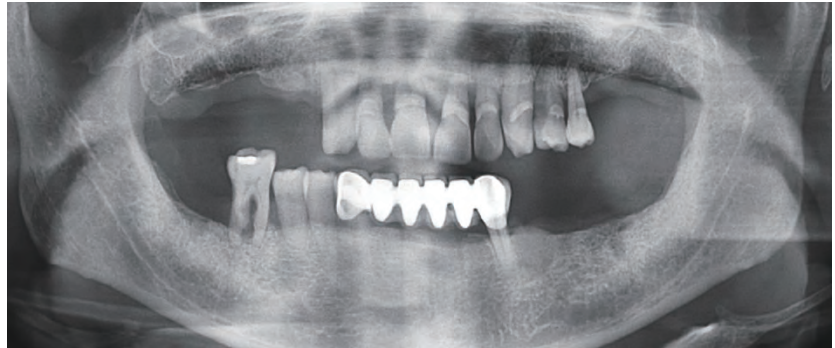
8 years
2019. 01. 18

CLINICAL CASE

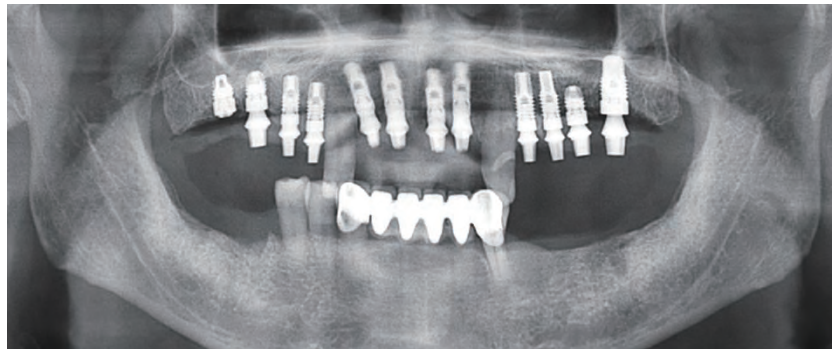
Case 3. Staged implantation in healed ridge and extraction socket

63 years old, Male

Preoperative
2010.04.06



Postoperative
2010.04.30



9 months
2011.01.19



8 years
2019.01.08



Scientific Proofs of COWELL BMP's Effectiveness

1. Analysis of hydrolyzable polyethylene glycol hydrogels and deproteinized bone mineral as delivery systems for glycosylated and non-glycosylated bone morphogenetic protein-2.
Acta Biomater. 2012 Jan;8(1):116-23.
2. Effects of rhBMP-2 Coating Tricalcium Phosphate on Socket Preservation in Dog Extraction Socket.
Tissue Engineering and Regenerative Medicine, Vol. 5, No. 4~6, pp 637-642 (2008)
3. Effects of Polycaprolactone-Tricalcium Phosphate, Recombinant Human Bone Morphogenetic Protein-2 and Dog Mesenchymal Stem Cells on Bone Formation: Pilot Study in Dogs.
Yonsei Med J 50(6): 825-831,(2009)
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