Final Report

Evaluation of pre-clinical efficacy of fixture surface osseointegration

(Test number: BMC24_001)

BMC 생체재료개발센터장

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Final Report Statement

Study title	**Evaluation of pre-clinical efficacy of fixture surface osseointegration**
Test sponsor	Name: Cowellmedi Co., Ltd. Address: 48, Hakgam-daero 221beon-gil, Sasang-gu, Busan, Korea Representative: Hyunmyung Choe
Test institution	Name: Biomaterial R&BD Center Address: 77, Yongbong-ro, Buk-gu, Gwangju, Korea
Study director	Name: Yangwon Chae Affiliation: Biomaterial R&BD Center
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Quality assurance	Name: Se Eun Kim Affiliation: Biomaterial R&BD Center
Study personnel	Name: Ji Hye Jeong Name: Min Joo Cho

Title: Evaluation of pre-clinical efficacy of fixture surface osseointegration (**BMC24_001)**

Test Schedule	Date of animal receipt		APR 24, 2024
	Experiment period		AUG 23, 2024
	Sacrifice	8 weeks sacrifice	OCT 18, 2024
	Final report	Interim report	NOV 20, 2024
		Drafted final report	MAR 13, 2025
Approve	Study director: Yangwon Chae (signature)		MAR 13, 2025
	Institutional official: Seong Soo Kang (signature)		MAR 13, 2025
Quality Assurance	Se Eun Kim (signature)		MAR 13, 2025

Approval of Final Report

Study title	**Evaluation of pre-clinical efficacy of fixture surface osseointegration**
Animal welfare	This experiment was approved by the animal experiment ethics committee of Biomaterials R&BD center on the Animal Protection Act (No. 4397 of Law enacted at May 31, 1991, and No. 16977 of Law revised on February 11, 2020) (Approval number: BMC-IACUC-2024-02(01))
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Test institution	Name: Biomaterial R&BD Center Address: 77, Yongbong-ro, Buk-gu, Gwangju, Korea

Approve the final report for this experiment

Cowellmedi Co., Ltd.

Cowellmedi President HYUN MYUNG CHOE
The Pioneers in Dental Implant and E.rhBMP-2

(Signature) (YYYY-MM-DD)

2025-03-27

Hyunmyung Choe
Test sponsor
Cowellmedi Co., Ltd.

Date

Summary

This study was performed to evaluate the biocompatibility and efficacy (osseointegration) of the INNO Implant, a dental implant fixture marketed by Cowellmedi Co., Ltd., in the mandibles of beagle dogs, and to compare its substantial equivalence with other dental implant fixtures available on the market.

For this purpose, all bilateral premolars and first molars of the mandibles of beagle dogs were extracted. After 8 weeks, the BLX (Straumann®, Basel, Switzerland), TS III SA (OSSTEM IMPLANT Co., Ltd., Seoul, Korea), Superline II (Dentium Co., Ltd., Suwon, Korea), and INNO (Cowellmedi Co., Ltd., Busan, Korea) implants were implanted in the recovered alveolar bone. The animals were sacrificed after 8 weeks to evaluate tissue response and osteogenesis through gross examination, dental radiography, micro-computed tomography (micro-CT), and histological analysis.

Gross examination revealed no adverse events, such as inflammation, dehiscence, or implant exposure to surrounding tissues, in most groups during the monitoring period after implantation.

Dental radiographs and micro-CT images indicated that all experimental groups maintained relative stability at the implant site at 8 weeks post-implantation; no alveolar bone loss was observed in most groups. Micro-CT microarchitectural analysis, which assessed percent bone volume, trabecular thickness, trabecular number, and trabecular separation, demonstrated no significant differences between groups at 8 weeks post-implantation.

Histological analysis revealed no inflammation in most groups at 8 weeks post-implantation, confirming that the implants were well maintained in the implanted position. Bone-to-implant contact (BIC) analysis revealed no significant differences between the experimental groups, although a higher tendency was observed in the INNO group compared with the other groups at 8 weeks post-implantation (BLX: 66.5 ± 2.67%, TS III SA: 72.8 ± 3.56%, Superline II: 70.58 ± 4.5%, INNO: 79.32 ± 3.69%). Bone area fraction occupancy (BAFO) analysis also showed no significant differences between the groups, but a higher tendency was noted in the INNO group compared with the other groups at 8 weeks post-implantation (BLX: 66.94 ± 3.26%, TS III SA: 69.46 ± 4.24%, Superline II: 71.51 ± 3.58%, INNO: 73.54 ± 2.64%).

Based on these findings, most groups exhibited no inflammatory reaction between the implant and surrounding tissues; they also showed no dehiscence, implant exposure, or alveolar bone loss throughout the study period. The INNO group did not show any particular difference in bone-to-implant contact (BIC) and bone area fraction occupancy (BAFO) compared to the other dental implant fixtures used in this experiment.

Contents

1. Study purpose

This study aimed to evaluate the biocompatibility and efficacy (osseointegration) of the INNO Implant, a dental implant fixture marketed by Cowellmedi Co., Ltd., in the mandibles of beagle dogs and to compare its substantial equivalence with other dental implant fixtures available on the market.

2. Materials and methods

2.1. Group and test samples

Table 1. Categorizing the groups

Symbols	Groups	Description	n
A	BLX	BLX implantation in beagle mandible	6
B	TS III SA	TS III SA implantation in beagle mandible	6
C	Superline II	Superline II implantation in beagle mandible	6
D	INNO	INNO implantation in beagle mandible	6

Table 2. Experimental animals

Group	Number of animals	Sacrifice time point
8 weeks	4	8 weeks post-implantation

2.2. Test samples

Table 3. Test samples

Symbols	Test samples	Manufacture	Product size	etc.
A	BLX	Straumann®	3.5 Ø x 8 mm	Test sample 1
B	TS III SA	OSSTEM IMPLANT Co., Ltd.	4.0 Ø x 8.5 mm	Test sample 2
C	Superline II	Dentium Co., Ltd.	3.6 Ø x 8 mm	Test sample 3
D	INNO	Cowellmedi Co., Ltd.	3.5 Ø x 8 mm	Test sample 4

2.2.1. Test sample 1

Figure 1. BLX (Straumann®, Basel, Swiss)

- Name: BLX
- Item name: Dental implant
- Model name: 061.3308
- Manufacturer: Straumann®
- Lot No.: AVGW3
- Expiration date: 2028-10-15
- Product size: 3.5 Ø x 8 mm
- Storage condition: store in a dry room temperature below 30℃
- Certification: No.11-1388

2.2.2. Test sample 2

Figure 2. TS III SA (OSSTEM IMPLANT Co., Ltd., Seoul, Korea)

- Name: TS III SA
- Item name: Dental implant
- Model name: TS3S4008S
- Manufacturer: OSSTEM IMPLANT Co., Ltd.
- Lot No.: FTN24C314
- Expiration date: 2031-02-25
- Product size: 4.0 Ø x 8.5 mm
- Storage condition: store in a dry room temperature below 30℃
- Certification: No.09-160

2.2.3. Test sample 3

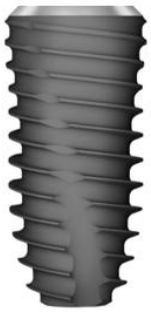


Figure 3. Superline II (Dentium Co., Ltd., Suwon, Korea)

- Name: Superline II
- Item name: Dental implant
- Model name: FXS3608
- Manufacturer: Dentium Co., Ltd.
- Lot No.: 202311010344
- Expiration date: 2031-11-14
- Product size: 3.6 Ø x 8 mm
- Storage condition: store in a dry room temperature below 30℃
- Certification: No.08-637

2.2.4. Test sample 4

Figure 4. INNO (Cowellmedi Co., Ltd., Busan, Korea)

- Name: INNO
- Item name: Dental implant
- Model name: ST3508SM
- Manufacturer: Cowellmedi Co., Ltd.
- Lot No.: 24G080350A
- Expiration date: 2029-07-01
- Product size: 3.5 Ø x 8 mm
- Storage condition: store in a dry room temperature below 30℃
- Certification: No.12-625

2.3. Information on a test system

1	Animal system and species	Beagle (Canine)
2	Produced and purchased by	Dooyeol-Biotech Inc. Address: 14, Yangjacheon-ro 17-gil, Seocho-gu, Seoul, Korea Call: 02-575-6598
3	Reasons for selecting species and systems	Beagle dogs and humans share many bone characteristics, notably similar secondary osteon structure and cortical remodeling. Collagen, cortical bone, and insulin-like growth factors in cancellous bone are similar. Furthermore, the periodontal tissues and bone mineral density of the beagle dog mandible are similar to human bone, and many dental implant trials are conducted in the beagle dog mandible, so the beagle dog mandible model was chosen for this animal study.
4	Animal information on receipt (Sex/number of animals/age/weight range)	Male /4 dogs /12 months /10 ~ 15 kg
5	Animal information on study (Sex/number of animals/age/weight range)	Male /4 dogs /12 months /10 ~ 15 kg
6	Acclimatization	When animals are obtained, only the healthy animals are introduced after confirming the health status of the animals. Only animals without abnormalities, such as weight loss after acclimatization for 7 days after introduction, are used for the test. The animals recover from shipping stress, acclimate to their environment, and regain normal behaviors (eating, drinking, micturition, defecation, etc.) During acclimatization, animals are observed and/or assessed by animal care management and people.
7	Identification of animals and breeding boxes	For animal identification, an animal identification card describing the test number, test period, sex, animal number, test personnel, and principal investigator is attached to the cage. An ear tattoo is used to identify animals.
8	Grouping	Grouping is performed at the end of the acclimatization phase (Day of grouping) in animals without general symptoms and weight gain. Healthy animals are selected on the grouping day.
9	Animal welfare	Study personnel are trained by the institutional veterinarian and study director in observing animal symptoms. This experiment was approved by the animal experiment ethics committee of Biomaterials R&BD Center on the Animal Protection Act (No. 4397 of Law enacted on May 31, 1991, and No. 16977 of Law revised on February 11, 2020) (Approval number: BMC-IACUC-2024-02(01))

2.4. Breeding environment

1	Animal room number	Biomaterial R&BD Center Beagle room 107
2	Breeding box	One animal is bred in a stainless-steel breeding cage (1,000 mm x 1,200 mm x 800 mm).
3	Environmental condition	This experiment is performed in a normal breeding room set at a temperature of 20±3°C, a relative humidity of 50±10%, a ventilation frequency of 10 to 15 times/hour, 12 hours of light/dark cycle, and an illumination condition of 150 to 300 Lux.
4	Animal feed and drink	The animals are fed with 500 g/animal of feed (LAB ANIMAL DIET –38070 Laboratory canine diets, PURINA, Korea) once a day, and the groundwater, which is filtered through a reverse osmosis filtered water sterilizer and then sterilized with ultraviolet light, is provided water tube.

2.5. Study Protocol

2.5.1. Equipment

1) Veterinary inhalation anesthesia machine

- A veterinary inhalation anesthesia machine (9100c NXT, GE healthcare, Chicago, IL, USA) was used to maintain inhalation anesthesia.

Figure 5. Veterinary inhalation anesthesia machine

2) Veterinary patient monitoring device

- A veterinary patient monitoring device (MAX-12HD, MIDMARK, Dayton, OH, USA) was used during anesthesia to continuously monitor the vital signs to maintain a safe depth of anesthesia and respond quickly to emergencies.

Figure 6. Veterinary patient monitoring device

3) Surgical motor

- A surgical motor (Surgic Pro+, NSK, Tokyo, Japan) was used for implantation in the beagle mandibular alveolar bone.
- Use a surgical motor set to 1,200 to 1,400 RPM, 20 to 50 Ncm, and a 20:1 gear ratio.

Figure 7. Surgical motor

4) Dental radiography

- Dental radiographs were taken at 70 kV, 2 mA, 0.12 sec using an radiograph generating unit (CLAROX VX-30, VSI, Cheongju, Korea), and the radiograph films were read using a reading unit (CS7600, Carestream dental, Atlanta, GA, USA).

Figure 8. Dental radiograph generating devices (left) and film reading equipment (right)

5) Micro-computed tomography (micro-CT)

- Micro-CT (SkyScan1273, Bruker corporation, Billerica, MA, USA)
- Filter= Al 1.0 mm, Source Voltage (kV)= 80, Source Current (㎂)= 55, Rotation Stop (deg)= 0.3

Figure 9. Micro-CT

6) EXAKT cutting machine

- Resin-embedded beagle mandibular tissue blocks were cut using an EXAKT cutting machine (DIAMOND BAND SAW EXAKT 300 / CL & CP, EXAKT Advanced Technologies GmbH, Norderstedt, Germany).

Figure 10. EXAKT cutting machine

7) Micro-grinder

- The cut tissue blocks were ground with a micro-grinder (MICRO GRINDER EXAKT 400 CS, EXAKT Advanced Technologies GmbH, Norderstedt, Germany) to produce 5 mm thick tissue sections.

Figure 11. Micro-grinder

8) Leica autostainer XL

- All tissues were stained using a Leica autostainer XL (ST5010, Leica, Wetzlar, Germany).

Figure 12. Leica autostainer XL

9) Optical microscope/digital slide scanner

- Digital images were acquired using an optical microscope/digital slide scanner (Axio Scan.Z1, Zeiss, Jena, Germany).

Figure 13. Optical microscope/digital slide scanner

2.5.2. Study process

1) Anesthesia

- Pre-anesthesia medication: glycopyrrolate (Mobinul Inj, Myungmoon, Seoul, Korea) 0.005 mg/kg, administered via subcutaneous injection, to prevent bradycardia and ptyalism (hypersalivation); famotidine (Gaster Inj, Dong-A, Seoul, Korea) 0.5 mg/kg, administered via intravenous injection (I.V.), to protect the gastrointestinal tract.
- Sedation or induction of anesthesia: medetomidine (Tomidin®, Provet Veterinary Products Ltd., Istanbul, Turkey) 0.005–0.02 mg/kg, administered via intramuscular injection; alfaxalone (Alfaxan Multidose, JUROX Pty. Limited, NSW, Australia) 1.5–2 mg/kg, administered via I.V.
- Maintenance of anesthesia: after endotracheal intubation, a mixture of 2–3% isoflurane (Isoflurane, Hana Pharm, Seoul, Korea) and oxygen was used.
- Pain control and antibiotic administration during surgery: cefazolin (Cefozol Inj, Hankook Korus Pharm, Chuncheon, Korea) 20 mg/kg, administered via I.V.; carprofen (Rimadyl Inj 50, Zoetis, Seoul, Korea) 4.4 mg/kg, administered via I.V.; and tramadol hydrochloride (Tramadol HCl Huons Inj., Huons Co., Seongnam, Korea) 5 mg/kg, administered via I.V.
- Local anesthesia: bupivacaine (Bupivacaine hydrochloride 0.5% injection, Myungmun Pharm, Seoul, Korea) 1 mg/kg, administered at the mandibular and mental foramina.

2) Surgical procedure

- Oral disinfection with 0.1% chlorhexidine under anesthesia, followed by full-mouth ultrasonic scaling and dental radiography to assess tooth condition.
- Extraction of all bilateral premolars and first molars in the mandibles, with post-extraction dental radiography to confirm complete extraction.
- Dental radiography under anesthesia at 8 weeks post-extraction to confirm healing and bone recovery.
- Use of a guide drill to access the mandible and determine the implantation position, followed by a taper drill to prepare the implantation site (1,200 RPM, torque 30 N, gear ratio 20:1).
- Implantation of three implants on the left and right sides of the mandible according to experimental group (40 RPM, torque 40–50 N, gear ratio 20:1).
- Closure of the gingival mucosal flap using 4-0 poliglecaprone 25 sutures (Monocryl, Ethicon Inc., Raritan, NJ, USA) without tension.
- Postoperative dental radiography to confirm implantation.

3) Postoperative care

- A neck collar was placed after surgery to prevent the beagle from scratching the incision. Famotidine (Gaster Tablets, Dong-A, Seoul, Korea) 1 mg/kg, carprofen (Rimadyl Chewable Tablets 25 mg, Zoetis, Seoul, Korea) 4.4 mg/kg, tramadol hydrochloride (Tramadol Retard Tab., Huons Co., Seongnam, Korea) 5 mg/kg, gabapentin (Neurontin Cap 100 mg, Pfizer, Seoul, Korea) 10 mg/kg, and enrofloxacin (Vitril Flavor Tablet, Bayer Korea Ltd., Seoul, Korea) 10 mg/kg were administered orally once daily for 1 week to reduce pain and prevent infection.
- Dry food was soaked in water and provided as soft feed for 2 weeks postoperatively. After feeding, oral food debris was cleaned with water using a 30-cc syringe, followed by the application of 1% zinc (Maxigard 2 fl, Betcom Co., Gwacheon, Korea) orally once daily for 1–2 weeks.

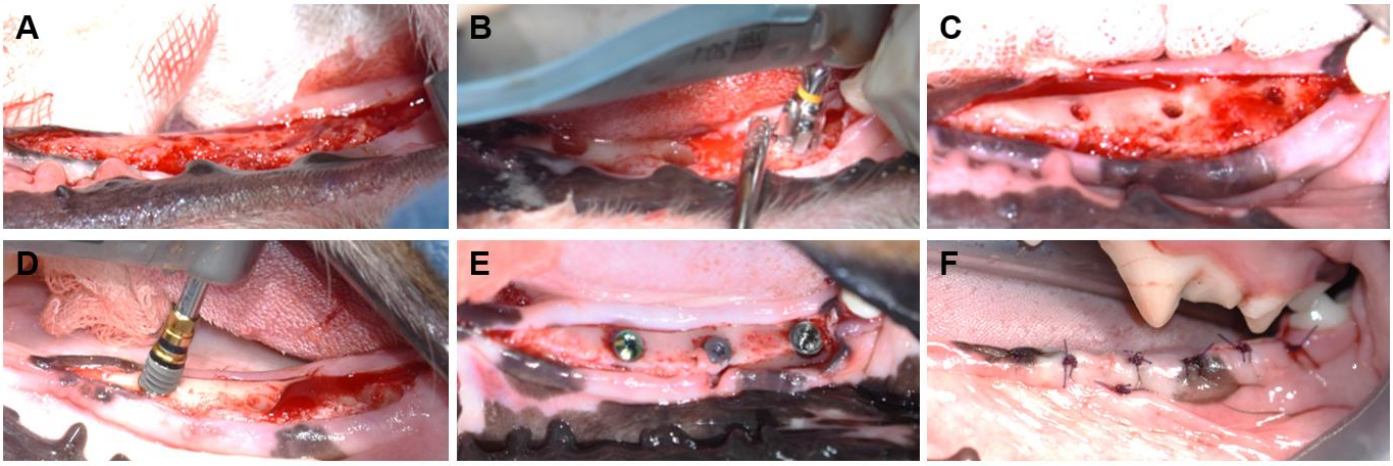
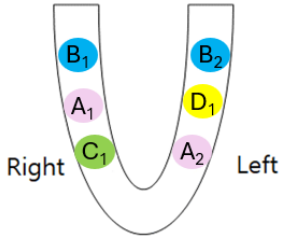
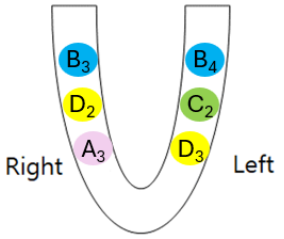
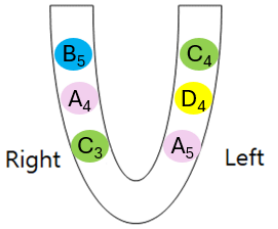
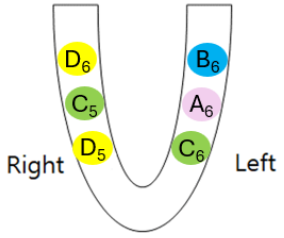


Figure 14. Surgical procedure
A) Mandibular approach, (B) Drilling of the implantation hole, (C) Implantation hole,
(D-E) Implantation, (F) Gingival suturing

Table 4. Sample implantation position

Animals	Position	Right mandible	Left mandible	Implantation position
Beagle 1	Distal	B_1	B_2	
	Middle	A_1	D_1	
	Mesial	C_1	A_2	
Beagle 2	Distal	B_3	B_4	
	Middle	D_2	C_2	
	Mesial	A_3	D_3	
Beagle 3	Distal	B_5	C_3	
	Middle	A_4	D_4	
	Mesial	C_4	A_5	
Beagle 4	Distal	D_5	B_6	
	Middle	C_5	A_6	
	Mesial	D_6	C_6	

2.5.3. Sacrifice and sample collection

1) Interim monitoring

- Gross examination and dental radiographic evaluation were performed immediately after implantation and at 4 and 8 weeks post-implantation.

2) Sacrifice time

- Euthanasia was performed at 8 weeks postoperatively for sample collection.

3) Euthanasia methods and sample collection process

- Deep anesthesia was induced through injectable and inhalation anesthesia as described in the experimental protocol. Euthanasia was confirmed after induction of cardiac arrest by 10–20 mL/body of potassium chloride (J.D.U. Pharmaceutical, Gwacheon, Korea), administered via I.V. The entire bilateral mandibles were collected and fixed in 10% neutral formalin.
- Mandibles obtained at the 8-week sacrifice were evaluated using micro-computed tomography (CT) imaging and tissue staining.

2.6. Evaluation

2.6.1. Gross examination

- Intraoral gross examination was performed at 4 and 8 weeks post-implantation. Photographs were taken concurrently with the gross examination. Animals were assessed for abnormalities, including inflammatory reactions, dehiscence, or implant exposure.

2.6.2. Dental radiography

- Dental radiographs were taken immediately after implantation and at 4 and 8 weeks post-implantation to assess implant stability and alveolar bone loss.

2.6.3. Micro-CT

- At 8 weeks post-implantation, animals were euthanized and mandibles were collected to evaluate bone formation at the implant site using micro-CT. Micro-CT microarchitectural analysis was performed for the quantitative assessment of percent bone volume, trabecular thickness, trabecular number, and trabecular separation.

2.6.4. Histological examination

1) Tissue slide preparation

- Beagle mandibular tissue fixed in 10% neutral formalin was dehydrated with increasing concentrations of alcohol using a tissue processor and embedded in resin (Technovit 7200 VLC, Kulzer GmbH, Hanau, Germany). After resin embedding and ultraviolet light curing, blocks were prepared. Blocks were sectioned using an EXAKT cutting machine (DIAMOND BAND SAW EXAKT 300 / CL & CP, EXAKT Advanced Technologies GmbH, Norderstedt, Germany) and polished with a micro-grinder (MICRO GRINDER EXAKT 400 CS, EXAKT Advanced Technologies GmbH) to obtain 5-mm-thick tissue specimens.

2) Tissue staining

- All tissue specimens were stained with hematoxylin and eosin (H&E) using a Leica autostainer XL (ST5010, Leica, Wetzlar, Germany) to identify cells and assess the inflammatory response. Goldner's trichrome (GT) staining was performed to evaluate new bone formation.

3) Digital image acquisition

- Histomorphometric measurements were obtained using a digital slide scanner (Axio Scan.Z1, Zeiss, Jena, Germany) for digital image acquisition.

4) Histomorphometric measurements

- Digital images acquired with the slide scanner were viewed using CaseViewer software (3DHISTECH Ltd., Budapest, Hungary), and image measurements were performed using ImageJ software (Version 1.41, National Institutes of Health, Bethesda, MD, USA). Microscopic observations were conducted across the entire specimen at 20× magnification; regions selected for histomorphometric analysis were further enlarged for measurement. Histomorphometric assessments included bone-to-implant contact (BIC) and bone area fraction occupancy (BAFO).

Figure 15. Programs for histomorphometric measurements

2.6.5. Statistical analysis

- GraphPad Prism 8.0 software (GraphPad Software, Inc., Boston, MA, USA) was used for statistical analysis.
- The mean and standard deviation of peri-implant bone formation in the experimental groups after implantation were calculated.
- Statistical significance was evaluated using one-way ANOVA and Tukey's post hoc test for comparisons between experimental groups.
- A *p*-value of less than 0.05 was considered statistically significant.
- Samples that developed inflammation and alveolar bone loss during the experiment (B_1, C_1 implants) were excluded from statistical analysis.

3. Result

3.1. Gross examination

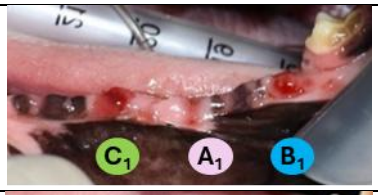
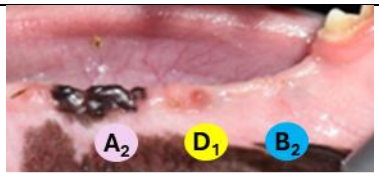
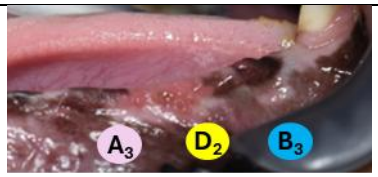
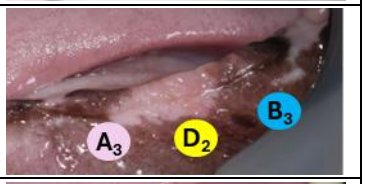
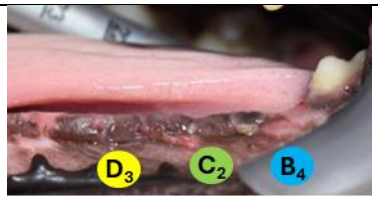
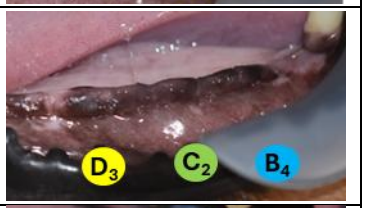
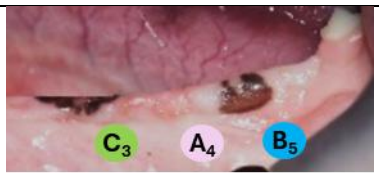
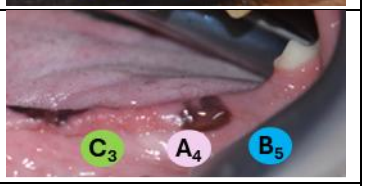
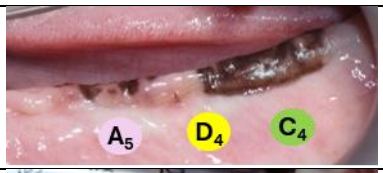
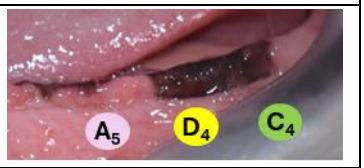
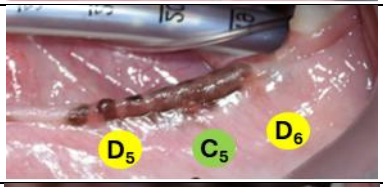
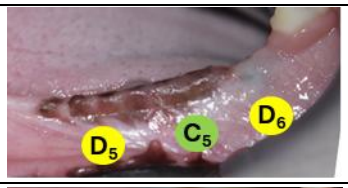
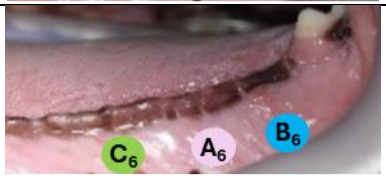
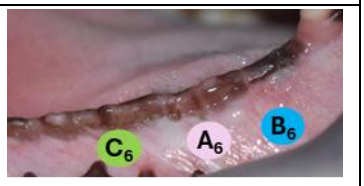
Groups		4 weeks	8 weeks
Beagle 1	Right mandible		
	Left mandible		
Beagle 2	Right mandible		
	Left mandible		
Beagle 3	Right mandible		
	Left mandible		
Beagle 4	Right mandible		
	Left mandible		

Figure 16. Images of gross examination

3.2. Dental radiography

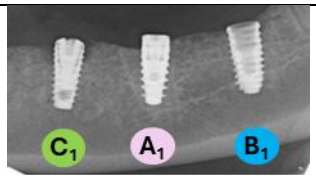
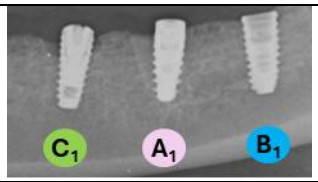
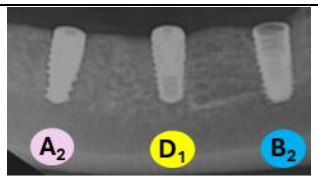
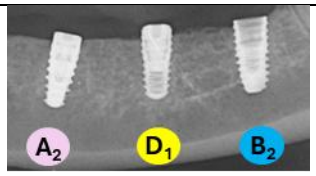
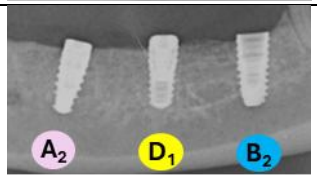
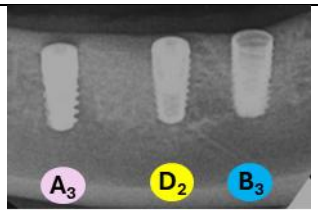
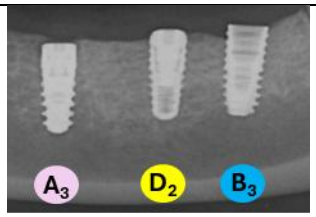
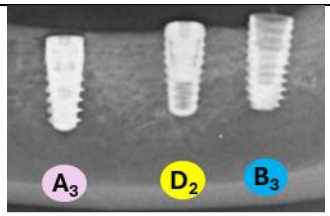
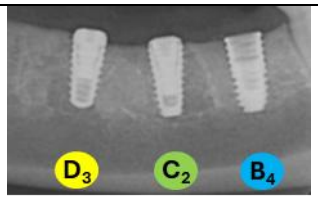
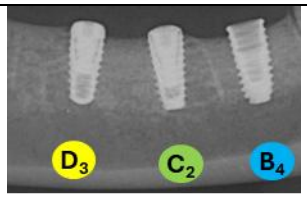
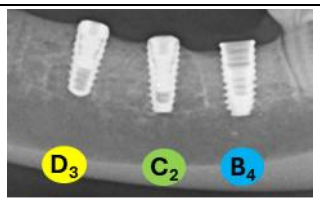
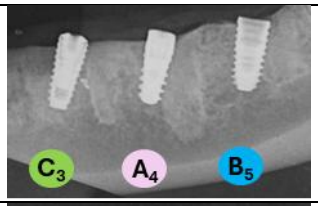
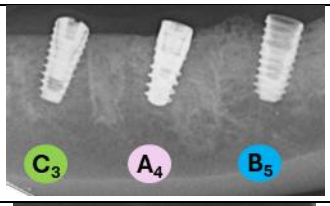
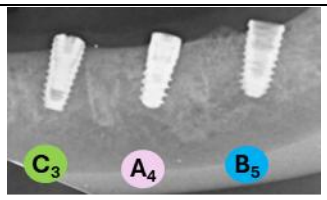
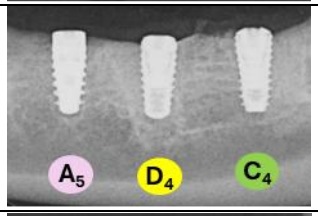
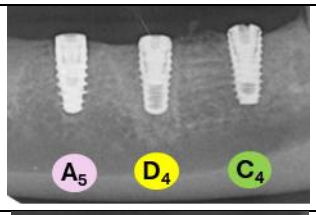
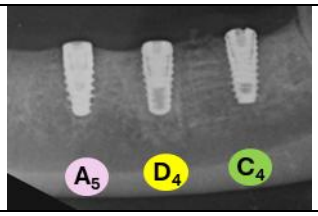
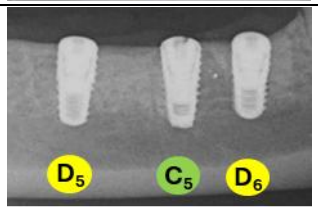
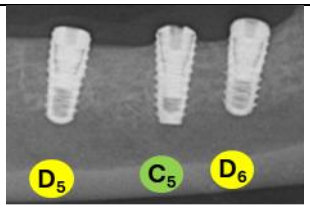
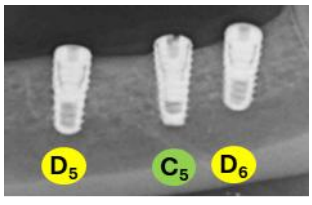
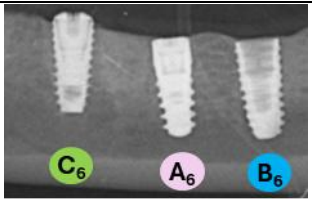
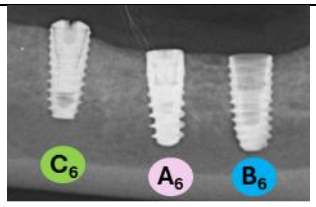
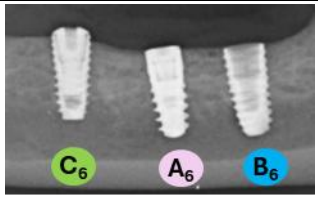
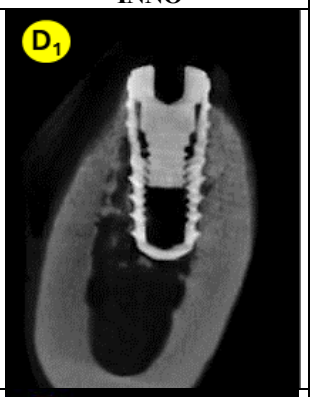
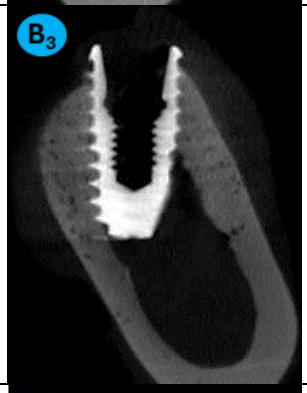
Groups		Immediately after	4 weeks	8 weeks
Beagle 1	Right mandible			
	Left mandible			
Beagle 2	Right mandible			
	Left mandible			
Beagle 3	Right mandible			
	Left mandible			
Beagle 4	Right mandible			
	Left mandible			

Figure 17. Images of dental radiography

3.3. Micro-CT

No.	BLX	TS III SA	Superline II	INNO
1				
2				
3				
4				

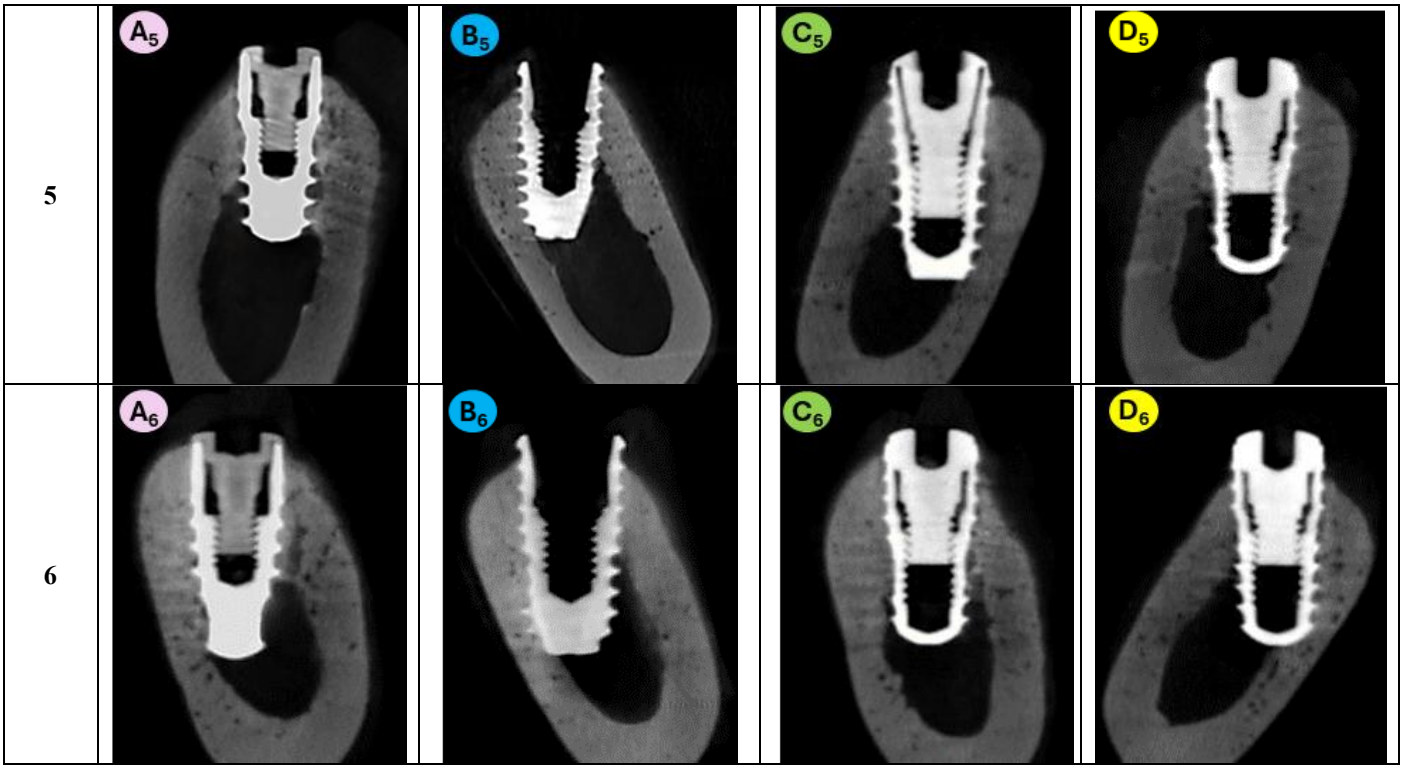
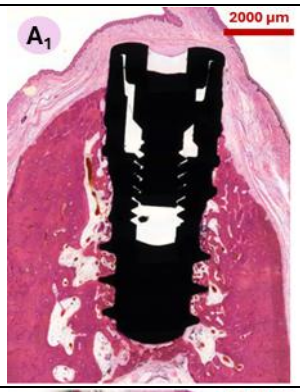
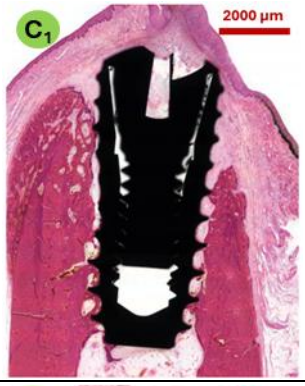
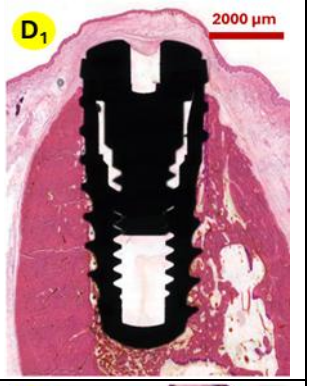
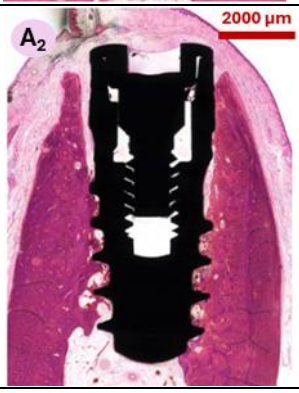
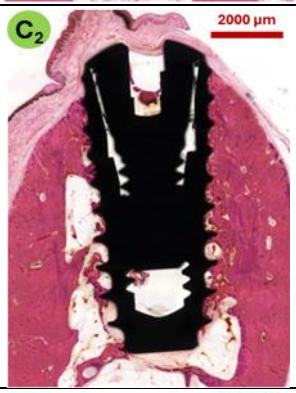
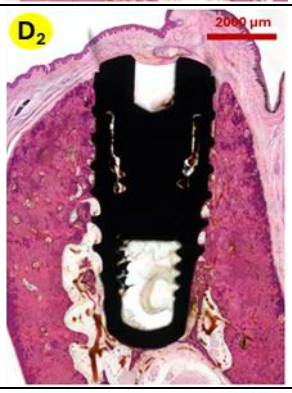
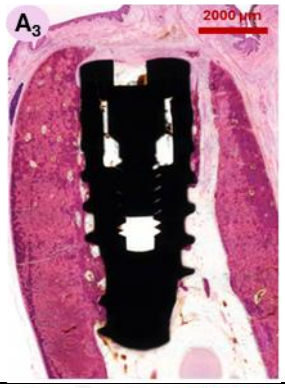
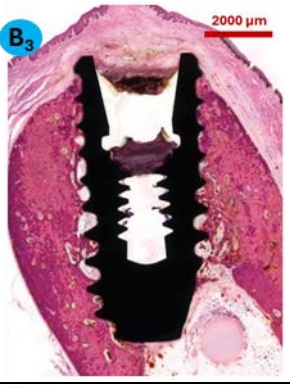
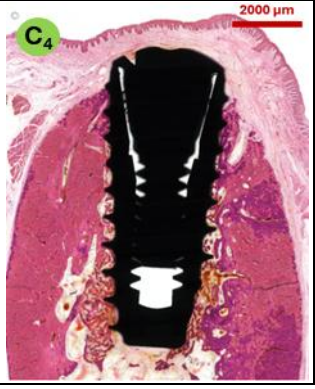


Figure 18. Images of micro-CT

3.4. Histological examination

3.4.1. Hematoxylin and eosin staining images

No.	BLX	TS III SA	Superline II	INNO
1				
2				
3				
4				

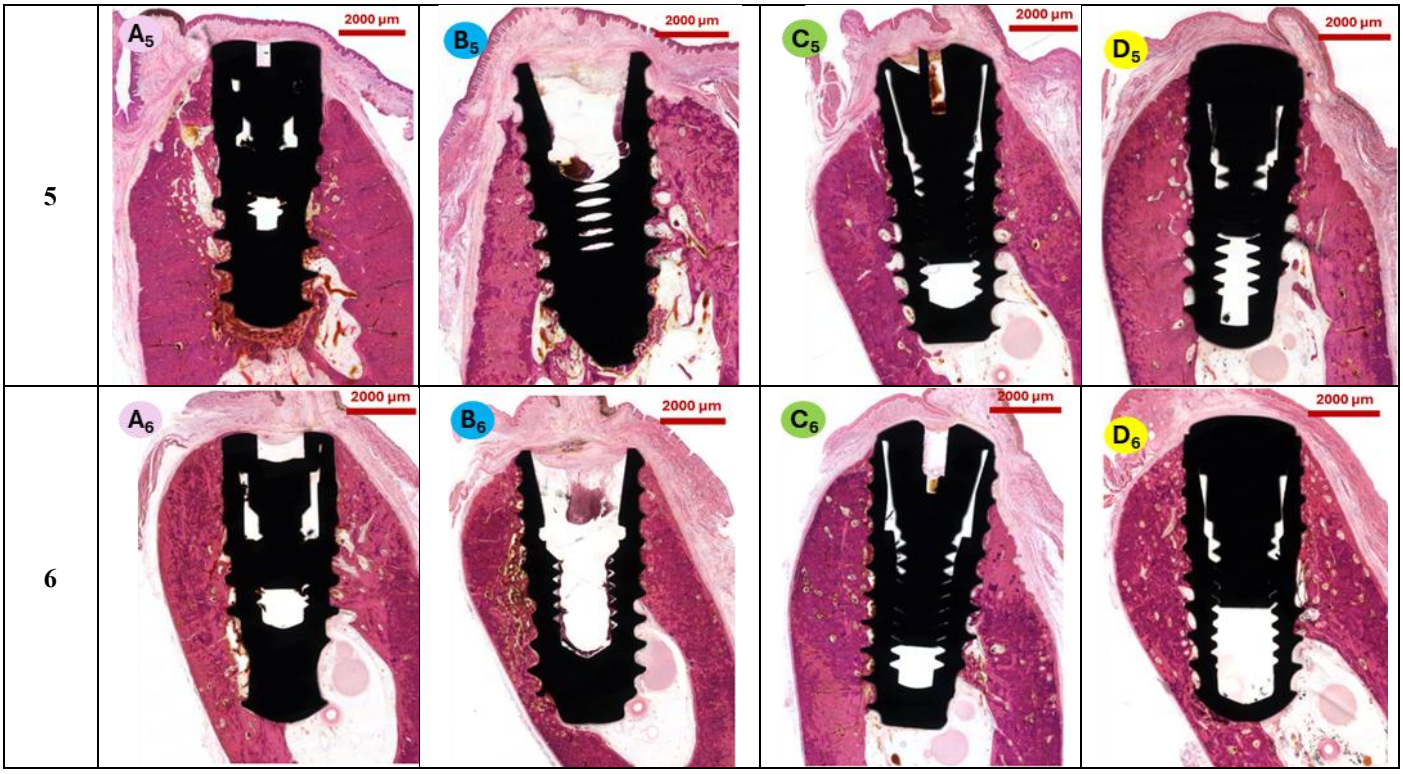
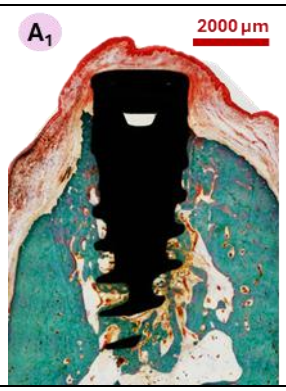
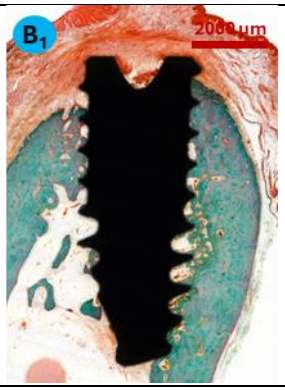
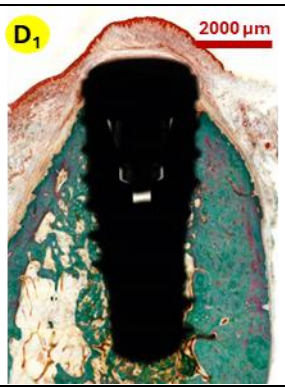
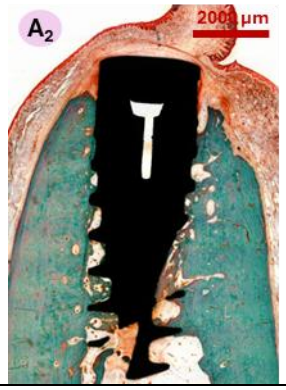
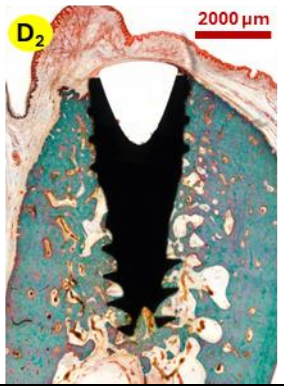
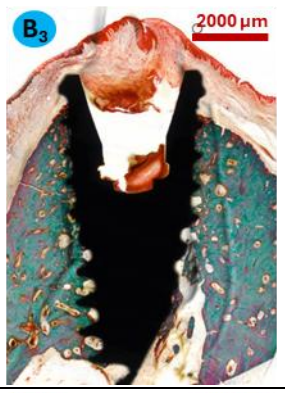
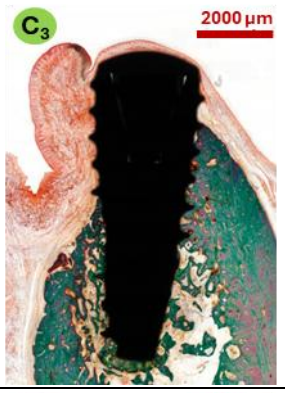
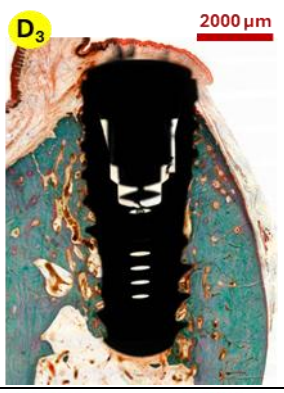
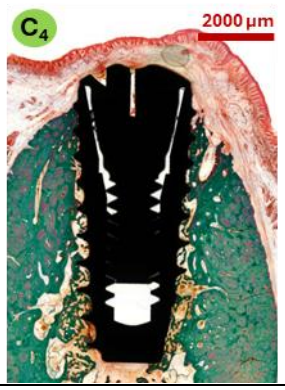
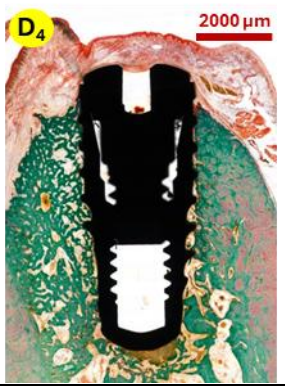


Figure 19. Hematoxylin and eosin staining images

3.4.2. Goldner's trichrome staining images

번호	BLX	TS III SA	Superline II	INNO
1				
2				
3				
4				

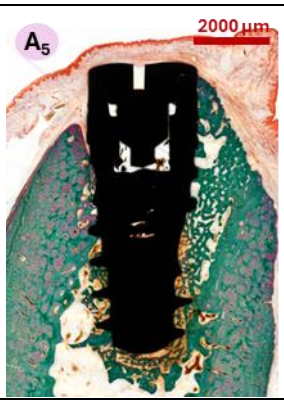
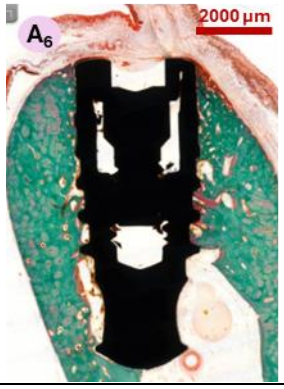
5				
6				

Figure 20. Goldner's trichrome staining images

4. Result analysis

4.1. Gross analysis

At 4 and 8 weeks post-implantation, redness and an inflammatory reaction were observed in the right mandibular mesial gingiva of beagle 1 with a C_1 implant (Superline II, Dentium Co., Ltd., Suwon, Korea) and in the right mandibular distal gingiva of beagle 1 with a B_1 implant (TS III SA, OSSTEM IMPLANT Co., Ltd., Seoul, Korea) upon visual inspection (Figure 21). In all other experimental groups, no inflammatory reaction was observed at the implantation site (Figure 16).

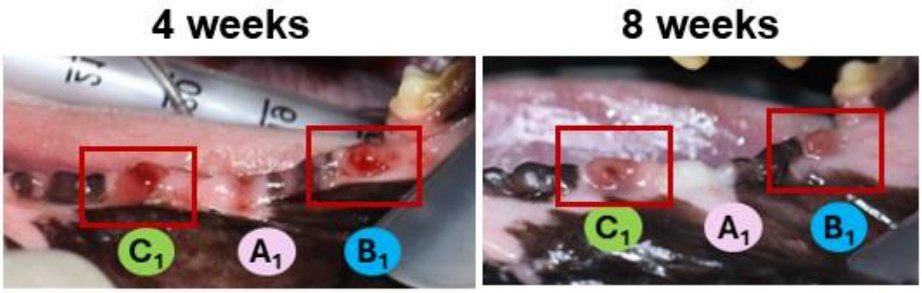


Figure 21. Gross image of the right mandible of beagle 1
Inflammation observed in the right mandibular gingiva (red square)

4.2. Dental radiography analysis

At 4 and 8 weeks post-implantation, slight bone loss was observed in the right mandibular mesial alveolar bone of beagle 1 with C_1 implants (Superline II, Dentium Co., Ltd.) and in the right mandibular distal alveolar bone of beagle 1 with B_1 implants (TS III SA, OSSTEM IMPLANT Co., Ltd.) (Figure 22). In all other experimental groups, the implants remained stable, and no alveolar bone loss was observed around the implants (Figure 17).

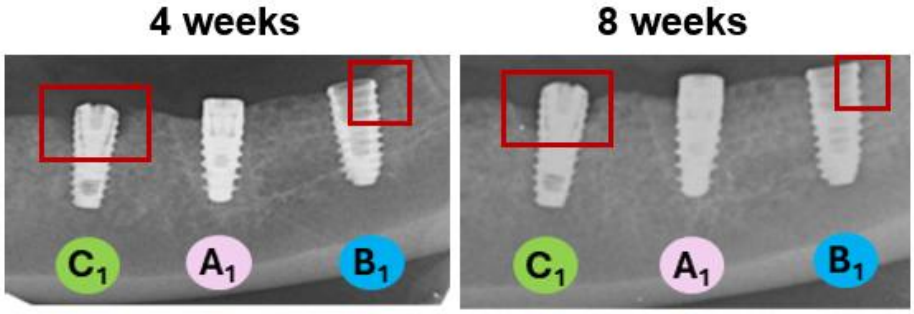


Figure 22. Dental radiographs of the right mandible of beagle 1
Loss of alveolar bone observed around the right mandibular alveolar bone area (red square)

4.3. Micro-CT analysis

4.3.1. Micro-CT analysis

Micro-CT scans taken at 8 weeks post-implantation revealed slight bone loss in the right mandibular mesial alveolar bone of beagle 1 with a C_1 implant (Superline II, Dentium Co., Ltd.) and in the right mandibular distal alveolar bone of beagle 1 with a B_1 implant (TS III SA, OSSTEM IMPLANT Co., Ltd.) (Figure 23). In all other experimental groups, the implants remained stable, and no alveolar bone loss was observed around the implants (Figure 18).

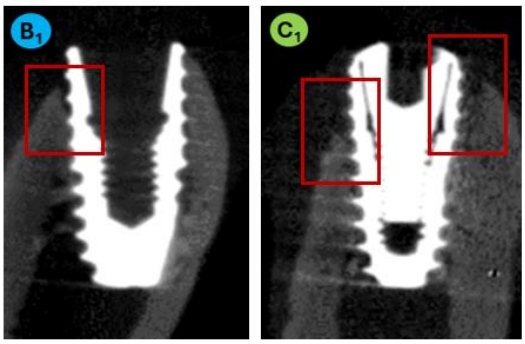


Figure 23. Micro-CT image of the right mandible of beagle 1
Loss of alveolar bone observed around the right mandibular alveolar bone area (red square)

4.3.2. Micro-CT microarchitectural analysis

Table 10. Micro-CT analysis of percent bone volume, trabecular thickness, trabecular number, and trabecular separation between experimental groups

Evaluation	BLX	TS III SA	Superline II	INNO
Percent bone volume (%)	22.77 ± 0.95	22.92 ± 1.24	23.42 ± 1.55	25.04 ± 1.13
Trabecular thickness (mm)	0.54 ± 0.02	0.60 ± 0.01	0.59 ± 0.03	0.55 ± 0.02
Trabecular number (1/mm)	0.42 ± 0.02	0.37 ± 0.01	0.39 ± 0.02	0.45 ± 0.01
Trabecular separation (mm)	1.85 ± 0.03	2.07 ± 0.03	1.90 ± 0.01	1.98 ± 0.02

Data are expressed as mean ± standard error.

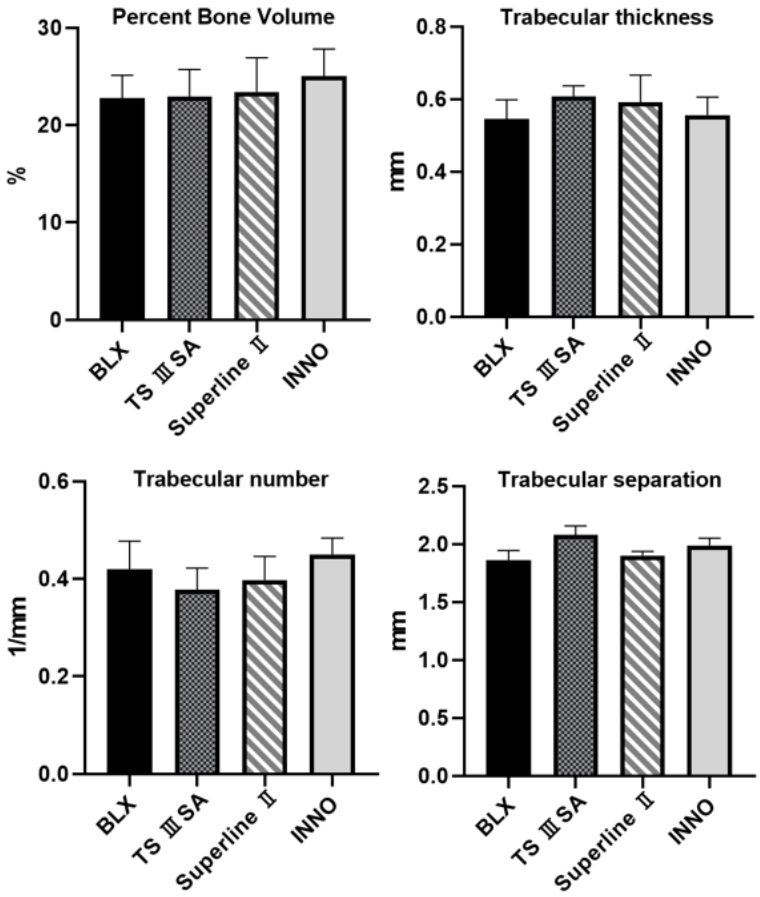


Figure 24. Micro-CT analysis of percent bone volume, trabecular thickness, trabecular number, and trabecular separation between experimental groups

Data are expressed as mean ± standard error.

Micro-CT microarchitectural analysis was performed to quantitatively assess percent bone volume, trabecular thickness, trabecular number, and trabecular separation. No significant differences were observed between the groups (Table 10, Figure 24).

4.4. Histological analysis
4.4.1. Histological analysis

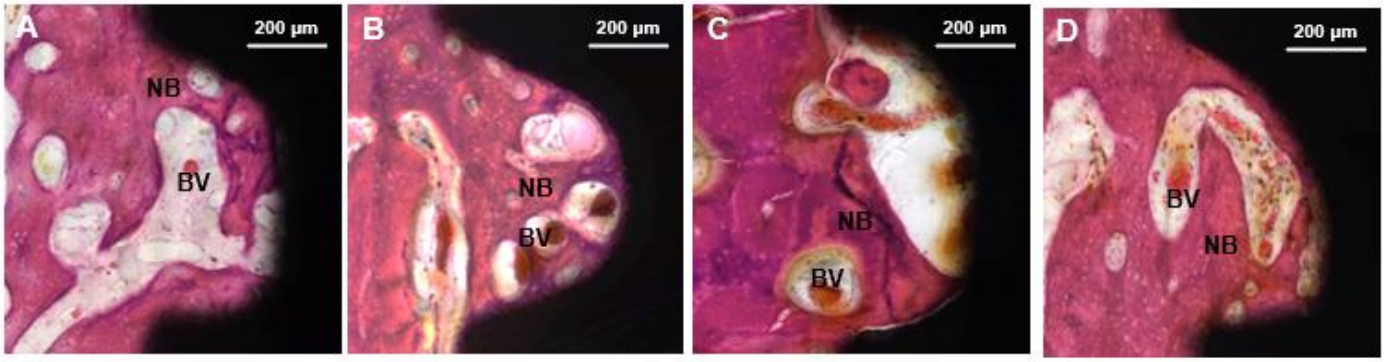


Figure 25. Representative images of histological analysis

(A) BLX implant, (B) TS III SA implant, (C) Superline II implant, (D) INNO implant
NB: new bone, BV: blood vessel

Histological staining at 8 weeks post-implantation confirmed that the implants remained relatively stable in all experimental groups (Figures 19, 20). High-magnification histological analysis showed no presence of specific inflammatory or abnormal cells in any experimental group except for the C_1 implant (Superline II, Dentium Co., Ltd.) and the B_1 implant (TS III SA, OSSTEM IMPLANT Co., Ltd.). New bone (NB) and blood vessels (BV) were observed around the implant threads (Figure 25).

4.4.2. Histomorphometric analysis (BIC, BAFO)

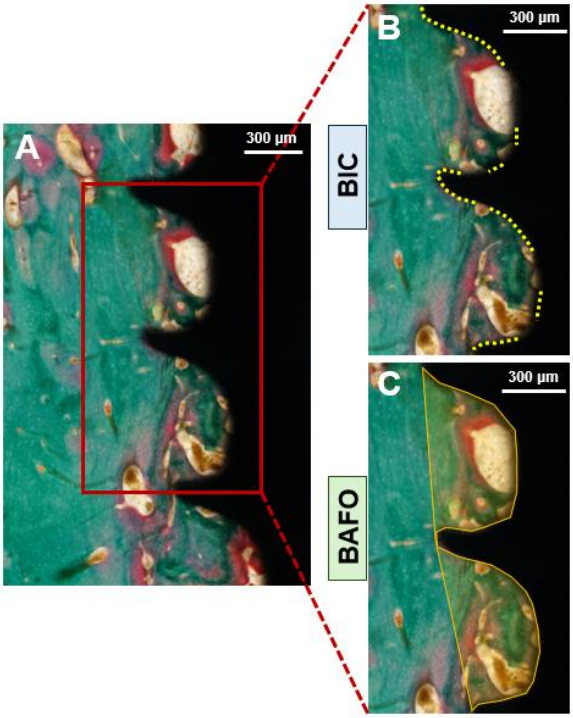


Figure 26. Histomorphometric analysis schematic

(A) Region of interest (ROI) set in the middle of the implant (red square), (B) Example of bone to implant contact (BIC) measurement (yellow dashed line), and (C) Example of bone area fraction occupancy (BAFO) measurement (yellow area)

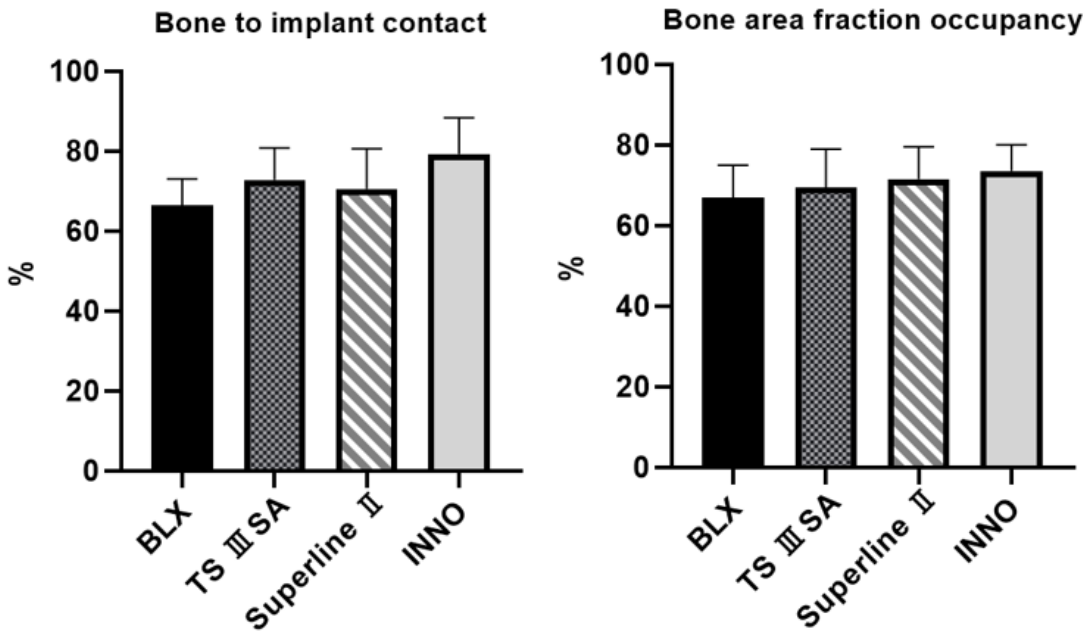


Figure 27. Bone to implant contact (BIC) and bone area fraction occupancy (BAFO) comparison graphs between experimental groups
Data are expressed as mean ± standard error.

The region of interest (ROI) was set at three implant screw thread areas in the middle portion of the implant (Figure 26A). BIC was calculated as the percentage of thread length in contact with bone tissue within the ROI; average values were compared and analyzed (Figure 26B). BAFO was calculated as the percentage of the bone area occupied by new bone tissue relative to the total area between the threads in the ROI; average values were compared and analyzed (Figure 26C). BIC analysis conducted at 8 weeks post-implantation revealed no significant differences between the experimental groups, although a higher tendency was observed in the INNO group compared with the other groups (BLX: 66.5 ± 2.67%, TS III SA: 72.8 ± 3.56%, Superline II: 70.58 ± 4.5%, INNO: 79.32 ± 3.69%). Similarly, BAFO analysis at 8 weeks post-implantation showed no significant differences between the groups, but a higher tendency was noted in the INNO group compared with the other groups (BLX: 66.94 ± 3.26%, TS III SA: 69.46 ± 4.24%, Superline II: 71.51 ± 3.58%, INNO: 73.54 ± 2.64%) (Figure 27).

5. Conclusion

Based on these findings, most groups exhibited no inflammatory reaction between the implant and surrounding tissues; they also showed no dehiscence, implant exposure, or alveolar bone loss throughout the study period. The INNO group did not show any particular difference in bone-to-implant contact (BIC) and bone area fraction occupancy (BAFO) compared to the other dental implant fixtures used in this experiment.

6. References

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