Injectable Mg-doped calcium phosphate cement for controlled BMP2 delivery aiming bone regeneration

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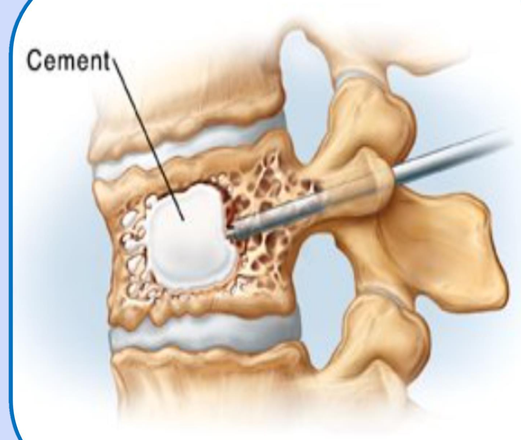
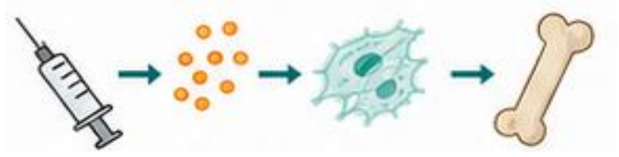


1. INTRODUCTION

- Calcium phosphate cements (CPC) are attractive materials for bone repair because they are biocompatible, osteoconductive, biodegradable, injectable and able to conform to irregular bone defects.
- Clinical translation requires balancing injectability, setting behaviour, mechanical stability and controlled osteoinductive-factor delivery
- BMP2 can enhance bone regeneration, but controlled local delivery is essential

Objective: To develop an injectable Mg-doped CPC capable of controlled BMP2 delivery and enhanced osteogenic response



Injectable CPC → **BMP2 release** → **Stem-cell osteogenic differentiation** → **Bone regeneration**

2. EXPERIMENTAL

Base: β-TCP/TTCP
Mg-doped CCP

- HPMC removal
- Bioactive glass addition
- Gamma irradiation

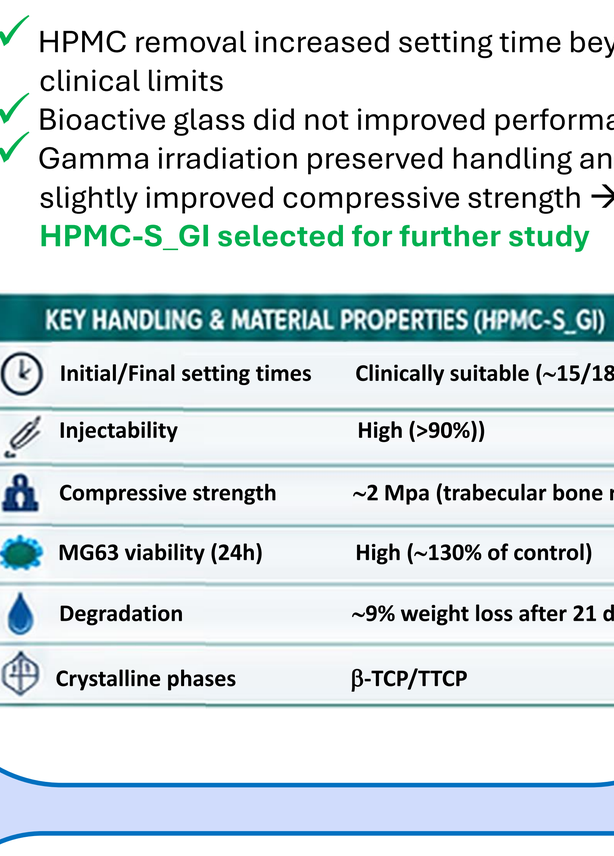
- Setting time
- Injectability
- Compressive strength
- MG63 cytocompatibility

Select for validation
HPMC-S_GI
(HPMC-containing, no BG, gamma irradiated raw materials

- SEM
- XRD
- Degradation
- BMP2 release

- Osteogenuc assays with hBMMSCs
- μ-CT (injection in human trabecular bone)

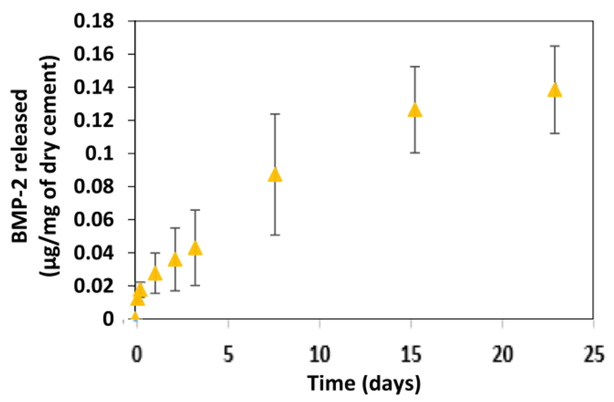
3. FORMULATION SCREENING



- ✓ HPMC removal increased setting time beyond clinical limits
- ✓ Bioactive glass did not improved performance
- ✓ Gamma irradiation preserved handling and slightly improved compressive strength → **HPMC-S_GI selected for further study**

KEY HANDLING & MATERIAL PROPERTIES (HPMC-S_GI)	
Initial/Final setting times	Clinically suitable (~15/18 min)
Injectability	High (>90%))
Compressive strength	~2 Mpa (trabecular bone range)
MG63 viability (24h)	High (~130% of control)
Degradation	~9% weight loss after 21 days
Crystalline phases	β-TCP/TTCP

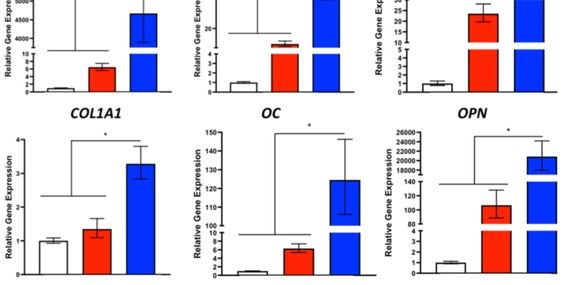
4. CONTROLLED BMP2 RELEASE



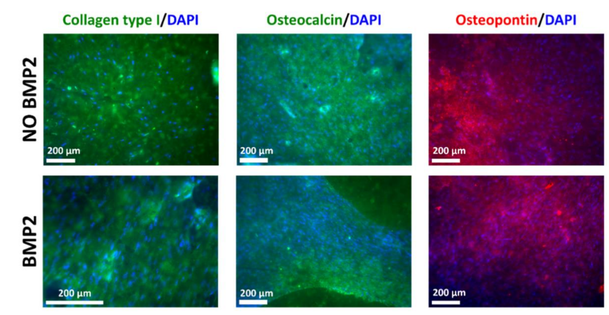
- ✓ Sustained BMP2 release over 3 weeks, reaching ≈0.14 μg BMP2/mg dry cement (~ 32% of the incorporated protein)

5. BIOLOGICAL PERFORMANCE

ALP activity



Immunofluorescence (day 21)

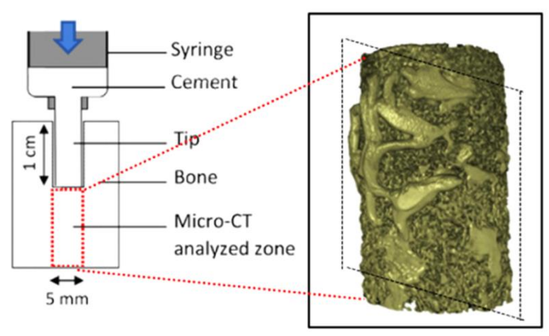


Osteogenic gene expression (qPCR day 21)

Compared with non-loaded controls, BMP2-loaded CPCs promoted:

- ✓ Higher early metabolic activity of hBMSCs
- ✓ Increased cell proliferation
- ✓ Higher ALP activity after 14 and 21 day
- ✓ Stronger expression of bone-related proteins: collagen type I, osteocalcin and osteopontin
- ✓ Upregulation of osteogenic genes including ALP, Runx2, OSX, COL1A1, OC and OPN

6. INJECTABILITY IN BONE



- ✓ μ-CT confirmed effective filling of the injection channel and penetration into surrounding trabecular bone
- ✓ CPC-filled region showed ~60% porosity

7. CONCLUSIONS

- ✓ Injectable Mg-doped CPC with clinically relevant handling properties was successfully optimized
- ✓ Gamma-irradiated **HPMC-S_GI** was selected as the most promising formulation.
- ✓ It combined high injectability, suitable setting time and compressive strength within the trabecular bone range
- ✓ It showed low degradation and sustained BMP2 release over three weeks
- ✓ BMP2 incorporation enhanced hBMSC proliferation and osteogenic differentiation
- ✓ μ/CT confirmed effective penetration of the cement into human trabecular bone

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