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Design of Experiments Approach to Optimisation of a Biomaterial

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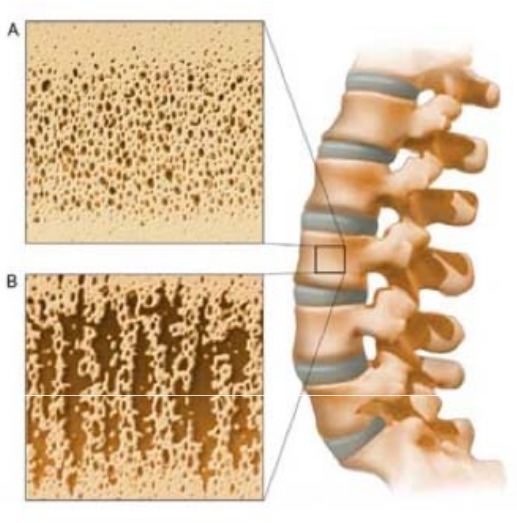
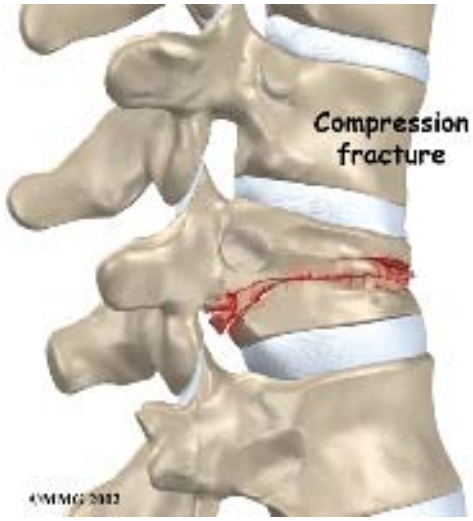
BiomMedD'2010

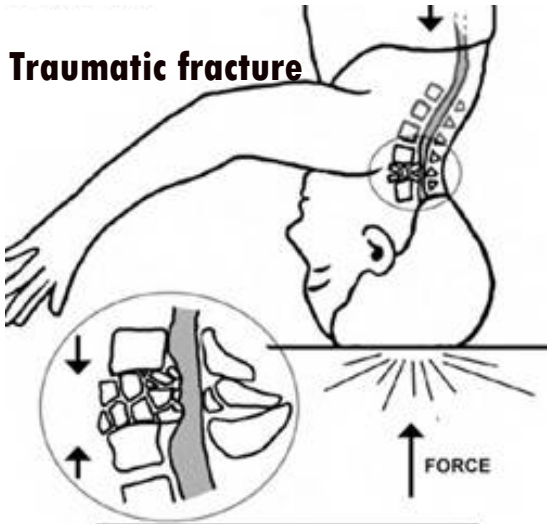
SRB Societatea Română de Biomateriale

young.scientists forum

Diseased or Damaged Bone



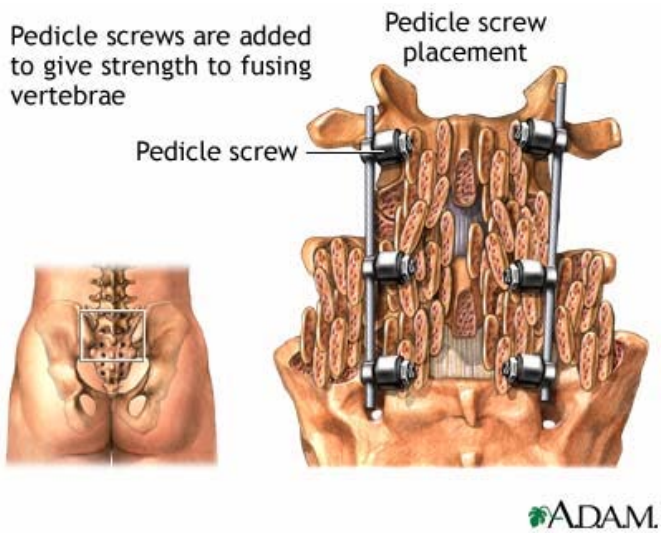




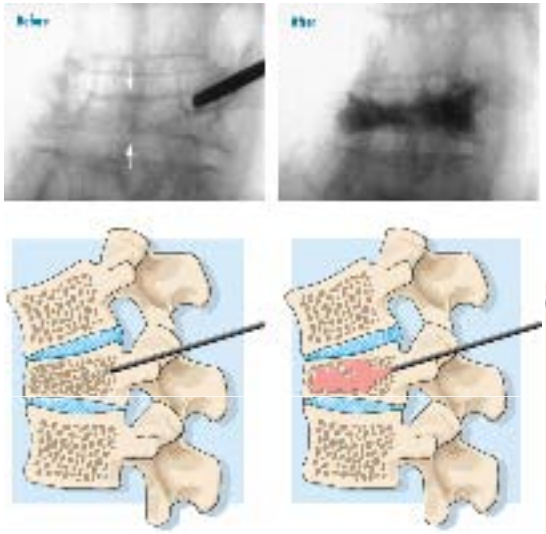
- Rheumatoid arthritis; 3 cases per 10k population per annum in US
- Osteoarthritis; 27m people in the US
- Osteoporosis; 1/3 women and 1/12 men +50yr of age worldwide
- Vertebral fractures worldwide ca. 1.4m, ca. 700k in USA (2009)
- Burst fractures account for ca. 15% of all spinal fractures*

* Denis, F., Spine (8), pp 817-831

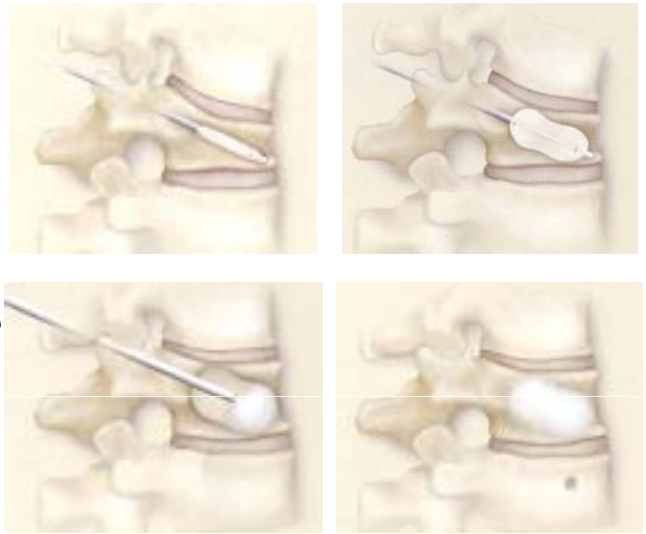
Surgical Intervention



Spinal Fusion



Vertebroplasty

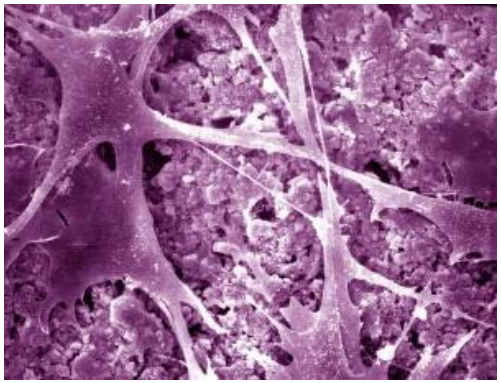


Khyphoplasty

- PMMA based
- Composite based
- Calcium phosphate

Calcium Phosphate Cements

- CPC was developed in 1980, to be bioactive and stimulate bone formation
- Low temperature CPCs are made of precipitated HA, similar in composition to the mineral part of bone
- Two categories of CPCs exist: (1) apatite (PHA) and (2) brushite (DCPD)
- Problems include:
  - » Poor mechanical properties
  - » Limited to non-load bearing cases
  - » Long setting times
  - » Injectability issues



Comp strength	10-50 MPa
Tensile strength	1-10 MPa

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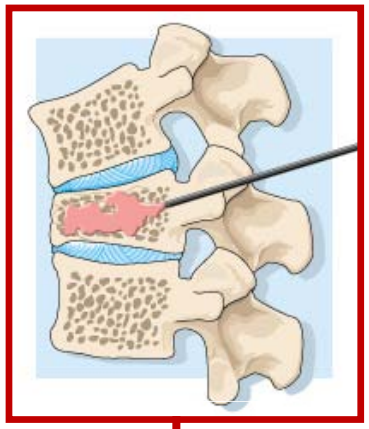
Desirable Properties – Vertebroplasty

	Clinical
Compressive Strength (MPa)	10-30*
Compressive Modulus (MPa)	50-800**



Injectability (%)	100*
Initial Setting Time (Min.)	8*
Final Setting Time (Min.)	15*

**Banse , Sims, Bailey , J Bone Miner Res 20002.

*Jansen, J. Orthop Clin N Am 2005

- Injectable
- Resorbable
- Final Setting Time
- Biocompatibility
- Mechanical Properties
- Cellular Response

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Research Aims

Manufacture and characterise CaP cements to meet surgical requirements

***Stage One*:**
Determine the optimum cement parameters

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Experimental Methodology

Input Factors & Parameters

Weight percentage Na_2HPO_4	Liquid to powder ratio (LPR)	Type of HA	Loading of HA	Time in Ringer's solution
1wt%	0.35mL/g	nano	0 wt%	3days
5wt%	0.50mL/g	micro	3 wt%	7days

Design of Experiments

- Optimum cement properties
- Factors affecting properties
- Interactions between factors

Experimental Methodology-Stage 1

DoE involved a two level factorial design using a ½ fractional factorial

20 random experiments

Vs.

Full experimental study of 1

≈120 experiments

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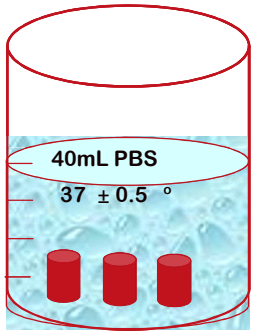
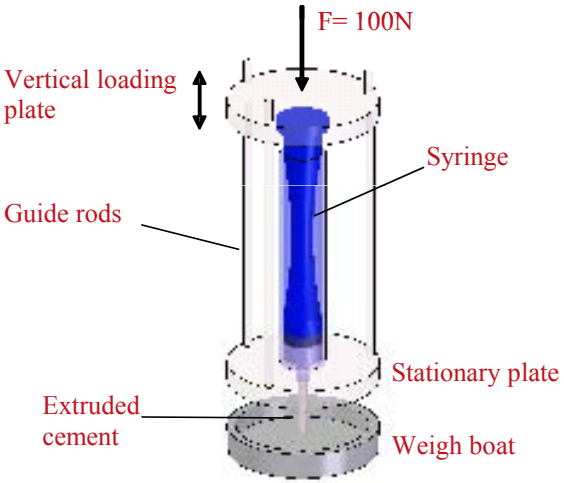
Experimental Methodology

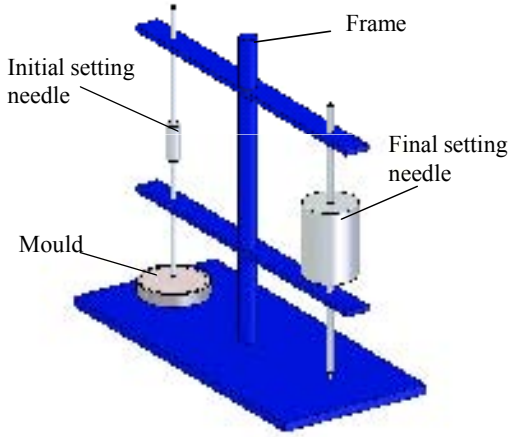
Compressive Properties:
Specimens in Ringer's solution
(ISO 5833: 2002)



Injectability:
4g CPC, constant load applied to syringe of nozzle Ø 2.3mm



Setting Times:
Initial and final setting times using Gillmore Needle (ASTM C266)



O'Hara et al. J Mater Sci: Mater Med 2010; DOI 10.1007/s10856-009-3977-9

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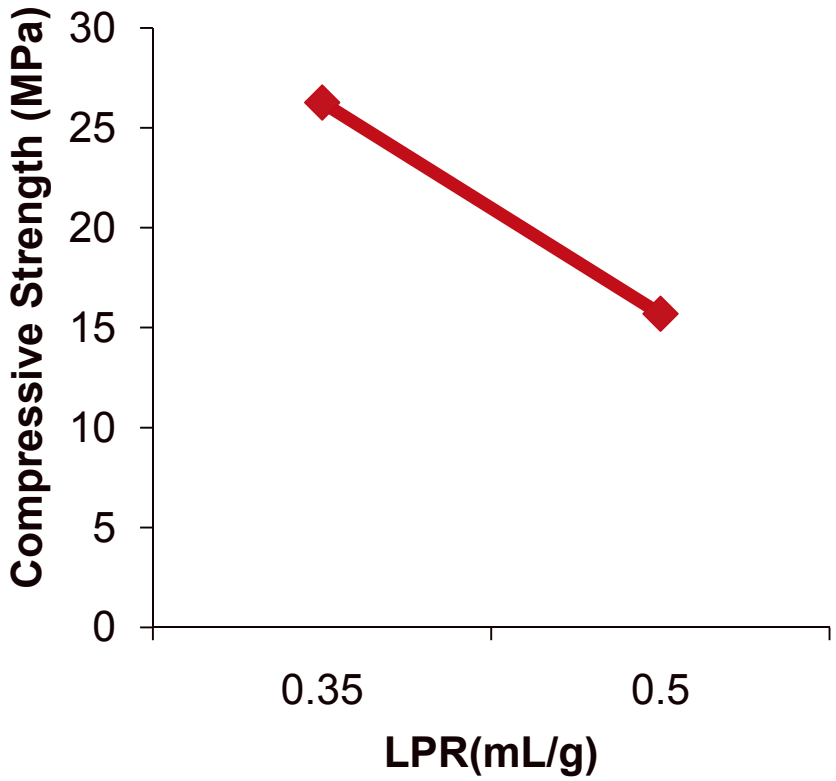
Results : Compressive Strength



Factor	Percentage Contribution
Weight Na_2HPO_4	1.72
LPR	81.92
Type of HA	0.43
Loading of HA	0.22
Time in Ringer's Solution	4.55
Interactions	11.16

- Predominant factor influencing compressive properties was LPR. No strong interactions between factors studied and compressive properties. Overall contributions less ≤10% were deemed not to be significant.

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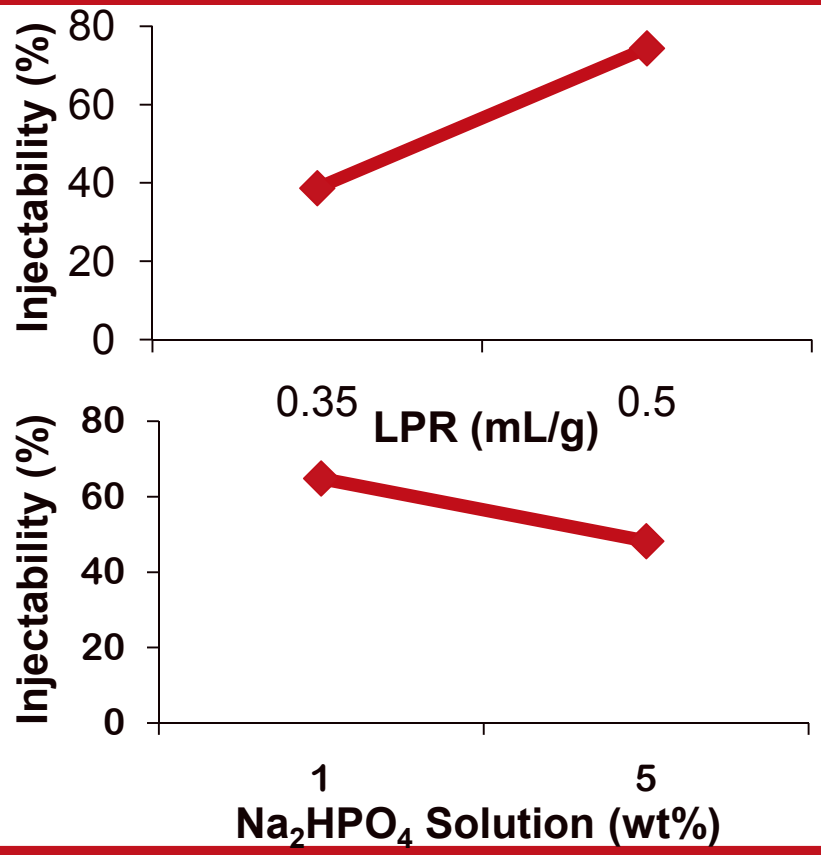
Results: Injectability



Factor	Percentage Contribution
Weight Na_2HPO_4	14.01
LPR	64.50
Type of HA	0.08
Loading of HA	2.71
Time in Ringer's Solution	0.01
Interactions	18.69

- Factors influencing injectability were LPR and %wt Na_2HPO_4. Mild interaction between injection properties studied and LPR and %wt Na_2HPO_4.

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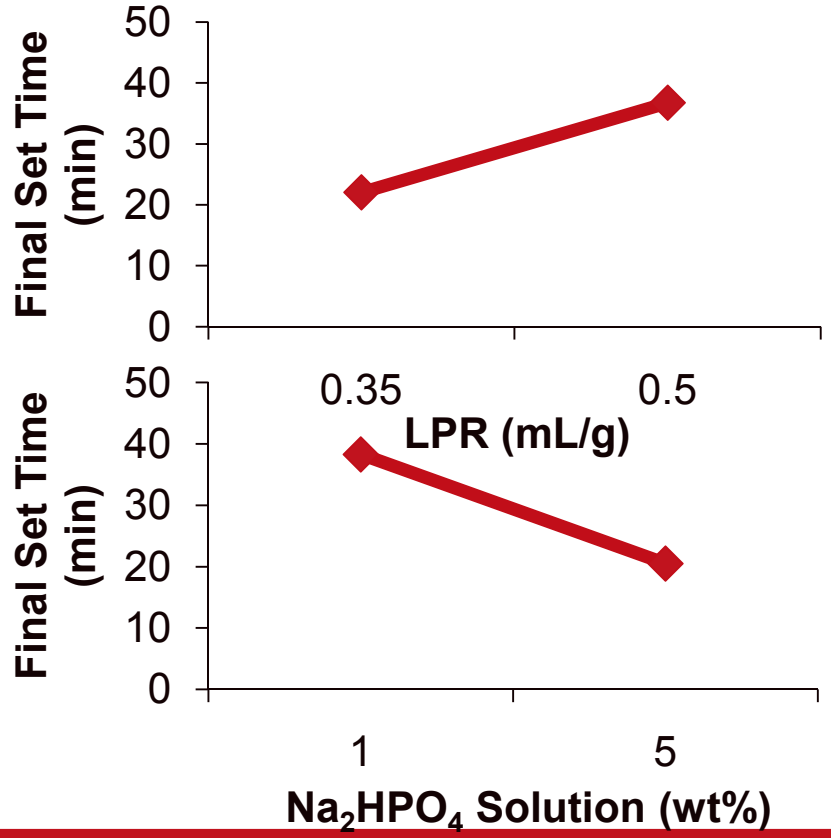
Results: Setting Times



Factor	Percentage Contribution
Weight Na_2HPO_4	50.43
LPR	34.47
Type of HA	0.47
Loading of HA	3.92
Time in Ringer's Solution	0.006
Interactions	10.70

- Factors influencing setting times were LPR and %wt Na_2HPO_4. No interaction demonstrated between LPR, %wt Na_2HPO_4 and setting properties of cement.

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Optimum Calcium Phosphate Cement

Powder Component: 100 % α-TCP

Liquid Component: 5 wt% Na_2HPO_4 at 0.35 mL/g

Testing Time: *7* days in Ringer's Solution

	Predicted	Actual	Clinical
Compressive Strength	26 MPa	30.3 MPa	10-30 MPa
Compressive Modulus	1028 MPa	1010 MPa	50-800 MPa
Injectability	30 %	52.6 %	100%
Initial Setting Time	5 min	10 min	8 min
Final Setting Time	13 min	23 min	15 min

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Acknowledgements

- Engineering Science Physical Research Council
- Queens University Belfast
- University Leeds
- Summit Medical Ltd.
- Smith & Nephew
- CMW Laboratories
- Klinipharm

- Dr Fraser Buchanan
- Dr Susan Clarke
- Professor John Orr
- Rochelle O'Hara
- Iwan Palmer

- Dr Ruth Wilcox
- Professor David Barton
- Sami Tarsuslugil
- Corinne Hanlon