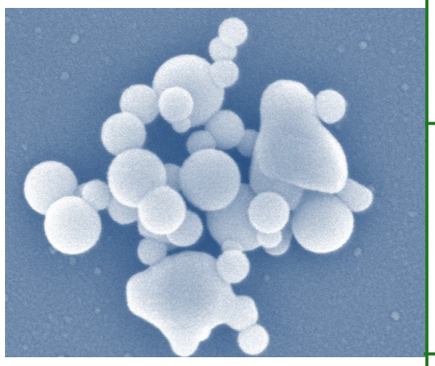


GRIBOI 2011

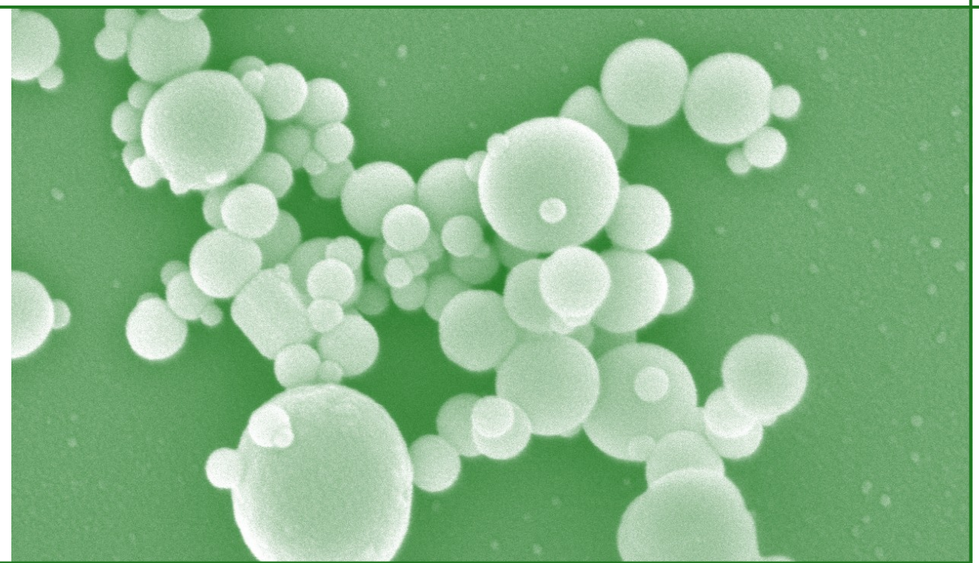
Actes de conférence de la

21st Interdisciplinary Research Conference on Injectable Osteoarticular Biomaterials in Bone Augmentation Procedures

G. Baroud, J. Hirsch, F. McKiernan, M. Bohner

Group de recherche interdisciplinaire sur les biomatériaux ostéo-articulaires injectable (GRIBOI)

The 21st Interdisciplinary Research Conference on Injectable Osteoarticular Biomaterials in Bone Augmentation Procedures



5-7 April 2011, Boston, USA

GRIBOI

G. Baroud
J. Hirsch
F. McKiernan
M. Bohner

The 21st Interdisciplinary Research Conference on Injectable Osteoarticular Biomaterials in Bone Augmentation Procedures

GRIBOI 2011 Conference

5-7 April 2011, Boston

Welcome to the GRIBOI 2011 – Injectable Osteoarticular Biomaterials and Bone Augmentation Procedures Conference.

Building on recent successes in **Torino** (2010), **Fort-de-France** (2009), **Montreal** (2008), **Oxford** (2007), **Berne** (2006), **Baltimore** (2005), **Limoges** (2004) and **Shanghai** (2003) it is our honor and pleasure to welcome you to Boston. Expect GRIBOI 2011 to be an interactive meeting where clinicians, scientists and engineers discuss cutting-edge topics related to the clinical use of bone substitutes and injectable biomaterials in bone augmentation procedures.

GRIBOI, the acronym for "Groupe de Recherche Interdisciplinaire sur les Biomatériaux Ostéo-articulaires Injectables", began in 1989 when a group of French physicians met informally to discuss injectable biomaterials. Now, 22 years later, GRIBOI comes to Boston with strong international representation while retaining the intimate, interdisciplinary collegiality intended by its founders.

The unique strength of the GRIBOI is its ability to gather international experts from apparently disparate clinical and laboratory disciplines to advance the field of bone augmentation by mutual inspiration. The conference format consists of lectures, oral and poster presentations.

This year there will be nine plenary sessions:

(**1**) Aging spine and vertebral compression fractures
(**2**) Image-guided augmentation procedures
(**3**) Evidentiary status of bone augmentation procedures
(**4**) Injectable biomaterials and design
(**5**) VBA and biomechanics
(**6**) Spine biology, VBA and reconstruction
(**7**) Tumor, VBA and Ablation
(**8**) Bone grafting, biology and substitutes
(**9**) Intradiscal injections

We welcome you and wish you a successful GRIBOI 2011.

Prof. **Gamal Baroud**
Chair, GRIBOI 2011

Canada Research Chair
Université de Sherbrooke
Sherbrooke, Qc Canada

Prof. **Joshua Hirsch**
Vice-Chair

Massachusetts General Hospital
Boston, MA, USA

Prof. **Fergus McKiernan**
Vice-Chair

Center for Bone Diseases
Marshfield Clinic, WI, USA

Prof. **Marc Bohner**
Vice-Chair

RMS Foundation
Bettlach, Switzerland

Bienvenue à GRIBOI 2011 – Conférence sur les biomatériaux ostéo-articulaires injectables et sur les méthodes de régénération vertébrale.

Ayant connu de récents succès à **Torino** (2010), **Fort-de-France** (2009), **Montréal** (2008), **Oxford** (2007), **Berne** (2006), **Baltimore** (2005), **Limoges** (2004) et **Shanghai** (2003), c'est un honneur et un plaisir de vous inviter à Boston. Cette année, GRIBOI 2011 vous offre des rencontres interactives où cliniciens, scientifiques et ingénieurs discuterons de sujets avant-gardistes portant sur l'utilisation clinique de substituts osseux et de biomatériaux injectables.

GRIBOI, acronyme de "Groupe de Recherche Interdisciplinaire sur les Biomatériaux Ostéo-articulaires Injectables", a été fondé en 1989 par un groupe de chirurgiens français lors d'une rencontre informelle qui portait sur les biomatériaux injectables. Aujourd'hui, 22 ans plus tard, c'est à Boston que se tiendra cette réunion d'envergure internationale, où une intime et interdisciplinaire collégialité sera de mise à l'intention des fondateurs.

La force exceptionnelle de GRIBOI est sa capacité de réunir des experts internationaux travaillant dans des disciplines distinctes et de leur permettre de profiter des connaissances d'autrui afin de progresser dans le domaine de la régénération osseuse. Le congrès consistera de conférences pléniaires, et de présentations orales.

Cette année, neuf séances sont prévues :

(**1**) Vieillissement de la colonne vertébrale et fractures en compression de vertèbres
(**2**) Régénération osseuse guidée par imagerie
(**3**) Efficacité des méthodes de régénération osseuse
(**4**) Biomatériaux injectables : leur conception et synthèse
(**5**) Vertébroplastie (VBA) et biomécanique
(**6**) Biologie de la colonne vertébrale, VBA et reconstruction
(**7**) Tumeur, VBA et Ablation
(**8**) Greffe osseuse, biologie et substituts osseux
(**9**) Injections intradiscales

Nous vous souhaitons la bienvenue et beaucoup de succès à GRIBOI 2011

Prof. **Gamal Baroud**
Organisateur, GRIBOI 2011
Chair de recherche du Canada
Université de Sherbrooke
Sherbrooke, Qc Canada

Prof. **Joshua Hirsch**
Co-organisateur

Massachusetts General Hospital
Boston, MA, USA

Prof. **Fergus McKiernan**
Co-organisateur

Centre des maladies de l'os, Clinique Marshfield, WI, USA

Prof. **Marc Bohner**
Co-organisateur

Fondation RMS
Bettlach, Switzerland

ADVISORY CONFERENCE MEMBERS

- Stephan Becker, Austria
- Tom Faciszewski, USA
- Kiernan Murphy, Canada
- Peter Munk, Canada
- Bassem Georgy, USA
- James Triffitt, UK
- Michael Liebschner, USA
- Hassan Serhan, USA

INTERNATIONAL FACULTY MEMBERS

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- GianCarlo Anselmetti, Italy
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- Alexis Kelekis, Greece
- Antonio Krueger, Germany
- Sune Larsson, Sweden
- Xiaodong Li, USA
- Luigi Manfré, Italy
- John Mathis, USA
- Robert Mitchell, Canada
- Kieran Murphy, Canada
- Malin Nilson, Sweden
- Robert Pflugmacher, Germany
- Howard Seeherman, USA
- Patrick Sharrock, France
- Thomas Steffen, Canada
- Sean Tutton, USA
- Pierre Weiss, France
- Ruth Wilcox, UK
- Hansen Yuan, USA
- Gregg Zoarski, USA

ACKNOWLEDGEMENT

The organizers are grateful for the support received from

- DePuy Spine
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- Université de Sherbrooke

The convention center is the **VETERANS MEMORIAL CONVENTION CENTER** and it is located at **900 Boylston Street, Boston, MA 02115, USA**

PROGRAM OF GRIBOI 2011

Please note that the GRIBOI participants may be eligible to receive RCPSC MOCOMP credits. The GRIBOI 2011 is expecting CAR accredited.

1st DAY

TUESDAY APRIL 5th 2011

7.00 am- ongoing	Welcoming and Registration
8.00 am – 8.15 am	Opening
KEY LECTURES	*CHAIRMEN – Tom FACISZEWSKI & Peter MUNK*
8.15 am – 8.35 am	Lecture - 1 **Herve DERAMOND,** France EVIDENCE, HISTORY, UPDATE, SOCIOECONOMICS OF VBA IN EUROPE
8.35 am – 8.55 am	Lecture - 2 **Ray BAKER,** President of North American Spine Society (NASS), USA EVIDENCE, STATUS, SOCIOECONOMICS OF VBA IN THE UNITED STATES
8.55 am – 9.30 am	Breakfast / Time for discussion
S E S S I O N 1	***VCF AND AGING SPINE*** *CHAIRMEN – Fergus MCKIERNAN & Richard HALL*
9.30 am – 9.50 am	Lecture - 3 **Mary BOUXSEIN,** USA BIOMECHANICS OF THE AGEING VERTEBRAL BODY
9.50 am – 10.10 am	Lecture - 4 **Patricia DOLAN,** UK BIOMECHANICS OF THE AGEING SPINE
10.10 am – 10.30 am	Lecture - 5

	Fergus MCKIERNAN, USA THE CLINICAL VERTEBRAL FRACTURE EVENT; EPIDEMIOLOGY AND MORBIDITY
	5-minute Break
S E S S I O N 2	***EVIDENTIARY STATUS OF VERTEBRAL AUGMENTATION: 2011*** *CHAIRMEN – Joshua HIRSCH & Gregg ZOARSKI*
10.30 am – 10.50 am	Lecture - 6 **Allan BROOK,** USA ANALYZING THE EVIDENCE ABSENT THE NEJM RCTS
10.50 am – 11.10 am	Lecture - 7 **David KALLMES,** USA ANALYZING THE HIGHEST LEVEL EVIDENCE: TWO BLINDED RCTS FROM THE NEJM
11.10 am – 11.30 am	Lecture - 8 **Christopher BONO,** USA RESOLVING THE DIFFERENCES BETWEEN THE OLD AND THE NEW DATA: ARE THEY REALLY SAYING DIFFERENT THINGS?
11.30 am – 12.15 pm	**Panel Discussion** *Moderators – Joshua HIRSCH & Gregg ZOARSKI* C. BONO, D. KALLMES, A. BROOK
12.15 pm – 12.30 pm	**Concluding Remarks** T. FACISZEWSKI
12.30 pm – 2.00 pm	Lunch / Exhibitors
S E S S I O N 3	***BONE GRAFTING PROCEDURES*** *CHAIRMEN – Christopher BONO, Hansen YUAN & Jean-Michel BOULER*
2.00 pm – 2.20 pm	Lecture – 9 **Sune LARSSON,** Sweden CLINICAL USE OF INJECTABLE CERAMICS IN EXTREMITIES
2.20 pm – 2.40 pm	Lecture – 10 **Marc BOHNER,** Switzerland CERAMIC-BASED BONE GRAFT SUBSTITUTES
2.40 pm – 2.50 pm	Selected Abstract – 1 E. VERRON, B.H. FELLAH, P. JANVIER, H. LE GUEN, R. CAVAGNA, D HOLOPHERNE-DORAN, O. GAUTHIER, J.M. BOULER, France CALCIUM-DEFICIENT APATITE MICROGRANULES AND CEMENTS COMBINED WITH BUPIVACAINE: INFLUENCE ON THE DRUG RELEASE PROFILE
2.50 pm – 3.00 pm	Selected Abstract – 2 A ROSENBERG, N.R. CAMACHO, J. CHANG, K. MURPHY, USA NOVEL BIORESORBABLE CEMENT FOR PERCUTANEOUS VERTEBRAL FRACTURE TREATMENT
3.00 pm – 3.10 pm	Selected Abstract – 3 S. TADIER, O. MARSAN, C. REY, C. COMBES, France SETTING REACTION OF A CALCIUM PHOSPHATE - CALCIUM CARBONATE INJECTABLE CEMENT: A KINETIC STUDY

3.10 pm – 3.15 pm	Featured Poster – 1 A. COUGHLAN, M.R. TOWLER, USA BACTERIAL INHIBITORY COATINGS BASED ON GLASS POLYALKENOATE CEMENT CHEMISTRY
3.15 pm – 3.20 pm	Featured Poster – 2 V. SCHNITZLER, F. FAYON, C. DESPAS, D. MASSIOT, A. WALCARIUS, P. JANVIER, O. GAUTHIER, G. MONTAVON, J.M. BOULER, B. BUJOLI, France ALENDRONATE-DOPED APATITIC CEMENTS AS A POTENTIAL TECHNOLOGY FOR THE PREVENTION OF OSTEOPOROTIC HIP FRACTURES
3.20 pm – 3.25 pm	Featured Poster – 3 A. GOEL, S. KAPOOR, J.M.F. FERREIRA FAST HEALING, STRONG AND RESORBABLE ALKALI-FREE PHOSPHO-SILICATE BIOGLASS GRANULES, SCAFFOLDS AND INJECTABLE COMPOSITES FOR REGENERATIVE MEDICINE
3.25 pm – 4.00 pm	Coffee break / Poster session / Exhibitions
S E S S I O N 4	***DRUG-LOADED GRAFTING*** *CHAIRMEN – Marc BOHNER, Bassem GEORGY & Michael HOFMANN*
4.00 pm – 4.20 pm	Lecture – 11 **Howard SEEHERMAN,** USA ROLE OF MACROPOROSITY IN DELIVERY MODALITIES FOR BMP
4.20 pm – 4.40 pm	Lecture – 12 **Xiaodong LI,** USA SYSTEMIC INHIBITION OF SCLEROSTIN AS AN ANABOLIC APPROACH FOR OSTEOPOROSIS AND FRACTURE HEALING
4.40 pm – 4.50 pm	Selected Abstract – 4 A.W. WREN, N.M. CUMMINS, M.R. TOWLER, USA ALUMINIUM-FREE GLASS POLYALKENOATE SPINAL CEMENTS
4.50 pm – 5.00 pm	Selected Abstract – 5 H. ZHANG, Zh. XIA, S. FRANKLIN, J.T. CZERNUSZKA, UK INJECTABLE POROUS MICROSPHERES FOR CONTROLLED DRUG AND CELL DELIVERY
5.00 pm – 5.10 pm	Selected Abstract – 6 M. STRUNK, S. PARK, T. RICKETTS, J. CHANG, USA RATES OF GROWTH FACTOR RELEASE FROM AN INJECTABLE CARRIER OF AUTOLOGOUS BLOOD AND BONE MARROW
5.10 pm – 5.15 pm	Featured Poster – 4 O. GAUTHIER, France VERTEBROPLASTY USING BISPHOSPHATE-LOADED CALCIUM PHOSPHATE
5.15 pm – 5.20 pm	Featured Poster – 5 J.E. DUMAS, E.M. PRIETO, G. HOLT, J. BIBLE, S.A. GUELCHER, USA LOW POROSITY INJECTABLE BIOCOMPOSITES INCORPORATING RHBMP-2 ENHANCE BONE REMODELING IN A RABBIT FEMORAL PLUG MODEL
5.20 pm – 5.25 pm	Featured Poster – 6 C. MELLIER, B.H. FELLAH, O. GAUTIER, N. ROCHET, B. BUJOLI, P. JANVIER, J.M. BOULER, France

	INFLUENCE OF BLOOD ADDITION ON MECHANICAL, TEXTURAL AND BIOLOGICAL OF CALCIUM PHOSPHATE CEMENT
5.25 pm – 5.30 pm	Featured Poster – 7 G. CAMA, L. DI SILVIO,S. DEB, UK MACROPOROUS BRUSHITE BONE CEMENT
LECTURES	*CHAIRMEN – Michael LIEBSCHNER & Johannes HIERHOLZER*
5.30 pm – 5.45 pm	Lecture – 13 **Gregg ZOARSKI,** USA BIOMECHANICS OF VBA
5.45 pm – 6.00 pm	Lecture – 14 **Michael ADAMS,** UK VERTEBRAL FRACTURE AND AUGMENTATION INFLUENCE LOAD-BEARING BY NEIGHBOURING VERTEBRAE

2nd DAY

WEDNESDAY APRIL 6th 2011

KEY LECTURES	*CHAIRMEN – Stephan BECKER, Peter JARZEM & Bob POSER*
8.00 am – 8.15 am	Lecture – 15 **Rex Peters,** USA MARKET AND REGULATORY BURDENS IN USA
8.15 am – 8.30 am	Lecture – 16 **Hansen YUAN,** USA CONFLICT OF INTEREST, PATIENT SAFETY, AND THE REGULATORY BURDEN OUTSIDE THE UNITED STATES
8.30 am – 8.45 am	Lecture – 17 **Robert MITCHELL,** Canada INTELLECTUAL PROPERTIES IN VBA
8.45 am – 9.00 am	**Panel Discussion** *Moderators – TBD* R. Peter, H. Yuan, R. Mitchell
9.00 am – 9.30 min	Breakfast / Poster session / Exhibitions
SESSION 5	***INDUSTRIAL INNOVATION*** *CHAIRMEN – Gian-Carlo ANSELMETTI, Herve DERAMOND & Kieran MURPHY*
9.30 am – 9.40 am	Lecture – 18 **Gian-Carlo ANSELMETTI,** Italy SPINEALIGN AUGMENTATION SYSTEM
9.40 am – 9.50 am	Lecture – 19 **Sean TUTTON,** USA KIVA AUGMENTATION SYSTEM

9.50 am – 10.00 am	Lecture – 20 TBD, Canada SITE SPECIFIC BONE AUGMENTATION THERAPY FROM UNIGENE
10.00 am – 10.10 am	Lecture – 21 **Johannes HIERHOLZER,** Germany (17) SHIELD KYPHOPLASTY SYSTEM
10.10 am – 10.20 am	Lecture – 22 **Stephan BECKER,** Austria SKELTEX ISV SYSTEM
10.20 am – 10.30 am	**Discussion / Take-away Message**
	5-minute Break
S E S S I O N 6	***TUMOUR SESSION*** *CHAIRMEN – John MATHIS , Allan BROOK & Bassem GEORGY*
10.30 am – 10.45 am	Lecture – 23 **Bassem GEORGY,** USA AUGMENTATION IN MALIGNANT LESIONS; IMAGING, BIOMECHANICS AND APPROACH
10.45 am – 11.00 am	Lecture – 24 **Peter MUNK,** Canada RADIOFREQUENCY ABLATION IN COMBINATION WITH CEMENT INJECTION AND TREATMENT OF MALIGNANT LESIONS
11.00 am – 11.15 am	Lecture – 25 **Gian-Carlo ANSELMETTI,** Italy AUGMENTATION OF CERVICAL MALIGNANT LESIONS
11.15 am – 11.30 am	Lecture – 26 **Ariel HIRSCH,** USA PMMA AND RADIOISOTOPES IN VBA
11.30 am – 11.45 am	Lecture – 27 **Kieran MURPHY,** Canada INNOVATIVE APPROACHES TO TUMOUR AND OLIGOMETASTSTIC DISEASE
11.45 am – 11.50 am	Featured Poster – 8 J. HIERHOLZER, TH. VOGL, R. PFLUGMACHER, M. GOUNIS, A. WAKHLOO, CH. FIEBIG, R. HAMMERSTINGL, Germany REDUCED CEMENT LEAKAGE WITH DIRECTED CEMENT FLOW KYPHOPLASTY
11.50 am – 11.55 am	Featured Poster – 9 J. WOO, P. PEZESHKI, A.J.M. YEE, C.M. WHYNE, M.K. AKENS, E. WON, M. GOFELD, Canada VALIDATION OF A NOVEL BONE TUMOR RF ABLATION SYSTEM –PHYSICS AND ANIMAL DATA
11.55 am – 12.00 pm	Featured Poster – 10 T.S. KANEKO, V. SEHGAL, H.B. SKINNER, M.S. AL-GHAZI, B.H. HOANG, N.S. RAMSINGHANI, J.H. KEYAK, USA RADIOACTIVE BONE CEMENT FOR THE TREATMENT OF VERTEBRAL METASTASES
12.00 pm – 12.05 pm	Featured Poster – 11 M.A. LOPEZ-HEREDIA, X.F. WALBOOMERS, P.C. THÜNE, F.C. ÖNER, J.A.

	JANSEN, Netherland CALCIUM PHOSPHATE CEMENTS FOR LOCAL DELIVERY OF CHEMOTHERAPEUTICS
12.05 pm – 12.30 pm	GRIBOI ASSEMBLY
12.30 pm – 2.00 pm	Lunch / Exhibitors
S E S S I O N 7	***CAVITY-ASSISTED VBA*** *CHAIRMEN – Hansen YUAN, Sune LARSSON & Antonio KRUEGER*
2.00 pm – 2.15 pm	Lecture – 28 **Peter JARZEM,** Canada KYPHOPLASTY IN CANCER PATIENTS
2.15 pm – 2.30 pm	Lecture – 29 **Antonio KRUEGER,** Germany KYPHOPLASTY IN TRAUMA PATIENTS
2.30 pm – 2.45 pm	Lecture – 30 **Natale FRANCAVIGLIA,** Italy KYPHOPLASTY USING CALCIUM-PHOSPHATE CEMENT TRAUMA PATIENTS
2.45 pm – 2.50 pm	Featured Poster – 12 R. CONNOLLY, T. MCGRATH, J. EMERY, USA TREATMENT OF NON-OSTEOPOROTIC BURST-TYPE VERTEBRAL COMPRESSION FRACTURES USING A NEW PEEK IMPLANT IN COMBINATION WITH PMMA CEMENT
2.50 pm – 2.55 pm	Featured Poster – 13 M. DRAGANI, A. OCCHIOCUPO, S. FANTINI, S. MARCIA, Italy NEW OSTEOCONDUCTIVE MATERIAL – CERAMENT - USED IN KYPHOPLASTY: RESULTS AT 1 YEAR
2.55 pm – 3.00 pm	Featured Poster – 14 M. MARQUEZ-MIRANDA, T.S. KANEKO, J.H. KEYAK, USA A NOVEL DEVICE FOR CREATING A VOID DURING VERTEBROPLASTY FOR BONE METASTASES
3.00 pm – 3.05 pm	Featured Poster – 15 B.E. DALTON, A.C. KOHM, R.D. POSER, USA COMPARISON OF RADIOFREQUENCY TARGETED VERTEBRAL AUGMENTATION (RF-TVA) TECHNIQUE VERSUS BALLOON KYPHOPLASTY IN AN EX VIVO VERTEBRAL COMPRESSION FRACTURE MODEL
3.05 pm – 3.10 pm	Featured Poster – 16 M. LORIO, M. FOWLER, D. BEALL, R. EASTLACK, USA SIX MONTH RESULTS FROM A US IDE TRIAL EVALUATING THE OSSEOFIX IMPLANT FOR TREATMENT OF VERTEBRAL COMPRESSION FRACTURES
3.10 pm -3.45 pm	Coffee break / Poster session / Exhibitions
S E S S I O N 8	***BIOMECHANICS IN VBA*** *CHAIRMEN – Hassan SERHAN, Nicholas DUNNE & Patricia DOLAN*
3.45 pm – 4.00 pm	Lecture – 31 **Ruth WILCOX,** UK COMPUTATIONAL MODELLING FOR PRE-CLINICAL EVALUATION OF FUNCTIONAL SPINAL

	INTERVENTIONS: ANALYSIS OF PROPHYLACTIC VERTEBROPLASTY
4.00 pm – 4.15 pm	Lecture – 32 **Michael LIEBSCHNER,** USA EFFICACY OF VERTEBROPLASTY: WHY ARE WE NEGLECTING ITS BIOMECHANICS?
4.15 pm – 4.25 pm	Selected Abstract – 7 M. KINZL, A. BOGER, P.K. ZYSSET, D.H. PAHR, Austria INFLUENCES OF PORE AND BONE VOLUME FRACTION ON THE MECHANICAL PROPERTIES OF STANDARD AND LOW-MODULUS PMMA/BONE BIOPSIES EXTRACTED FROM AUGMENTED VERTEBRAL BODIES
4.25 pm – 4.35 pm	Selected Abstract – 8 A. BRUNO, D. ANDERSON, J. D'AGOSTINO, M. BOUXSEIN, USA HYPERKYPHOSIS INDUCED BY VERTEBRAL FRACTURE INCREASES COMPRESSIVE LOADS ON THE VERTEBRAE MORE THAN KYPHOSIS INDUCED BY DEGENERATIVE CHANGES
4.35 pm – 4.45 pm	Selected Abstract – 9 C. PERSSON, A. LÓPEZ, A. HOESS, M. OTT, H. ENGQVIST, Sweden TOWARDS LOW-MODULUS BONE CEMENTS – THE EFFECT OF A NATURAL OIL IN PMMA
4.45 pm – 4.50 pm	Featured Poster – 17 S. TARSUSLUGIL, R. O'HARA, N. DUNNE, F. BUCHANNAN, J. ORR, D.C. BARTON, R.K. WILCOX, UK OPTIMISATION OF CALCIUM PHOSPHATE CEMENTS TO AUGMENT TRAUMATIC SPINAL FRACTURES USING EXPERIMENTALLY VALIDATED COMPUTATIONAL MODELS
4.50 pm – 4.55 pm	Featured Poster – 18 V. BORSE, A.M. LIDDLE, N. KAPUR, J. TIMOTHY, P.A. MILLNER, R.M. HALL, UK BIPEDICULAR VERSUS UNIPEDICULAR APPROACHES IN VERTEBROPLASTY: EFFECT OF CEMENT VOLUME
	5-min Break
S E S S I O N 8	***BIOMECHANICS IN VBA*** *CHAIRMEN – Mary BOUXSEIN & Ruth WILCOX*
5.00 pm – 5.15 pm	Lecture – 33 N. DUNNE, F. BUCHANAN, R. O'HARA, J. CRAIG, UK EFFECT OF CEMENT VISCOSITY ON MECHANICAL BEHAVIOUR: AN OSTEOPOROTIC BONE MODEL
5.15 pm – 5.25 pm	Selected Abstract – 10 O. HOLUB, V. BORSE, A. LIDDLE, N. KAPUR, R.M. HALL, UK COMPARISON OF FRACTURE PREDICTION IN OSTEOPOROTIC SAMPLES
5.25 pm – 5.35 pm	Selected Abstract – 11 R. LANDGRAF, J. IHLEMANN, S. KOLMEDER, A. LION, Germany THERMOMECHANICAL MODELING APPROACH FOR THE REPRESENTATION OF COUPLED CURING PROCESSES IN ACRYLIC BONE CEMENTS USED IN VERTEBROPLASTY
5.35 pm – 5.40 pm	Featured Poster – 19 A.M. LIDDLE, V.H. BORSE, D.M. SKRZYPIEC, J. TIMOTHY, N. KAPUR, R.M. HALL, UK MINIMISING SUBSIDENCE IN LUMBAR TOTAL DISC REPLACEMENT THROUGH EFFECTIVE CEMENT PLACEMENT

3rd DAY

THURSDAY APRIL 7th 2011

SESSION 9	***NON-SPINAL APPLICATION*** *CHAIRMEN – Peter MUNK & Sean TUTTON*
8.00 am – 8.15 am	Lecture – 34 **John MATHIS,** USA SACROPLASTY
8.15 am – 8.30 am	Lecture – 35 **Alexis KELEKIS,** Greece AUGMENTATION IN THE PELVIS
8.30 am – 8.40 am	Selected Abstract – 12 R. PFLUGMACHER , R. BORNEMANN , T. RANDAU , D.C. WIRTZ, Germany RADIOFREQUENCY (RF) KYPHOPLASTY IN THE TREATMENT OF OSTEOLYTIC VERTEBRAL FRACTURES
8.40 am – 8.50 am	Selected Abstract – 13 J.M. PERSENAIRE, UK SIGNIFICANCE OF FILL PATTERNS OBSERVED WITH TWO DIFFERENT BONE AUGMENTATION MATERIALS USED IN PERCUTANEOUS VERTEBROPLASTY
8.50 am – 8.55 am	Featured Poster – 20 J.F. CAZENEUVE, Y. HASSAN, A. HILANEH, France WHICH IS THE BEST FOR OSTEOPOROTIC VERTEBRAL COMPRESSION FRACTURES: BALLOON KYPHOPLASTY OR CONSERVATIVE THERAPY?
8.55 am – 9.00 am	Featured Poster – 21 P.E. ZOUBOULIS, A. VRIS, A. PANAGOPOULOS, P. SALONIKIDIS, M. TYLLIANAKIS, Greece SAFE AND SUCCESSFUL TREATMENT OF VERTEBRAL COMPRESSION FRACTURES WITH THE OSSEOFIX™ SPINAL FRACTURE REDUCTION SYSTEM: FIRST 2 YEARS OF APPLICATION
9.00 am – 9:30 am	**Breakfast / Poster session / Exhibitors**
SESSION 10	***INTRADISCAL INJECTIONS*** *CHAIRMEN – Stephan BECKER & Thomas STEFFEN*
9.30 am – 9.45 am	Lecture – 36 **Stephan BECKER,** Austria NON-SPINAL FUSION TECHNQIUES: STATUS
9.45 am – 10.00 am	Lecture – 37 **Thomas STEFFEN,** Canada NUCLEOPLASTY – INDICATIONS, SURGICAL CHALLENGES AND RISKS
10.00 am – 10.10 am	Selected Abstract – 14 E. REDERSTORFF, C. VINATIER, S. COLLIEC-JOUAULT, P. PILET, S. LAIB, J. GUICHEUX, P. WEISS, France AN INJECTABLE SELF-SETTING HYDROGEL DOPED WITH AN EXOPOLYSACCHARIDE FROM

	MARINE ORIGIN AS A SYNTHETIC EXTRACELLULAR MATRIX FOR CARTILAGE TISSUE ENGINEERING
10.10 am – 10.20 am	Selected Abstract – 15 M. CLAUSS, H. U. FURUSTRAND, A. BIZZINI, A. TRAMPUZ, T. ILCHMANN, Switzerland THE INFECTED BONE GRAFT IN-VITRO EVALUATION OF STAPHYLOCOCCAL BIOFILM FORMATION ON FRESH (FR), FRESH-FROZEN (FF) OR PROCESSED HUMAN (PH) AND PROCESSED BOVINE (PB) SPONGIOSA
10.20 am – 10.30 am	Selected Abstract – 16 S. AGRAWAL, V.K. SHARMA, S. BATRA, India ROLE OF INJECTABLE BONE GRAFT SUBSTITUTE IN FUNCTIONAL OUTCOME OF DISTAL RADIUS FRACTURES
	5 min Break
S E S S I O N 1 1	***BIOLOGICS AND FUNCTIONALIZATION*** *CHAIRMEN – Jim TRIFFITT & Kerong DAI*
10.35 am – 10.50 am	Lecture – 38 **Kerong DAI,** China A STUDY OF TITANIUM FIBER BALLS COMBINED WITH NANO-SR-HA IN THE BONE DEFECT REPAIR AND VERTEBRAL AUGMENTATION
10.50 am – 11.05 am	Lecture – 39 **Jim TRIFFITT,** UK MESENCHYMAL STEM CELLS
11.05 am – 11.15 am	Selected Abstract – 17 K.B. FONSECA, F.A. CRUZ, A.F. LOURENÇO, P.L. GRANJA, C.C. BARRIAS, Portugal INJECTABLE ALGINATE POLYMERS FOR BONE TISSUE REGENERATION: PHYSICO-CHEMICAL PROPERTIES AND IN VITRO MESENCHYMAL STEM CELL RESPONSE
11.15 am – 11.25 am	Selected Abstract – 18 Zh. XIA, R. LOCKLIN, J.T. TRIFFITT, UK FATE OF HUMAN MESENCHYMAL STEM CELLS IN IMMUNODEFICIENT MICE: DIFFERENTIATION OR TRANSDIFFERENTIATION?
11.25 am – 11.35 am	Selected Abstract – 19 M.T. SOHAIL, Pakistan BONE GRAFT SUBSTITUTE -ANTIBIOTIC IMPREGNATED IN CHRONIC OSTEOMYELITIS
11.35 am – 11.40 am	Featured Poster – 22 H. YUAN, A. WENGER, F.PHILLIPS, S. HOCHSCHULER, U. BERLEMANN, J. MAYER, USA BONEWELDING TECHNOLOGY: ENHANCED BIOMECHANICAL STABILITY FOR PEDICLE SCREWS
S E S S I O N 1 2	***INJECTABLE BIOMATERIALS*** *CHAIRMEN – Marc BOHNER, Christele COMBES & Pierre WEISS*
11.40 am – 11.55 am	Lecture – 40 **Sanjukta DEB,** UK CEMENTS IN ORTHOPAEDIC SURGERY

11.55 am – 12.10 pm	Lecture – 41 P.M.C. Torres, S.M. Olhero, S. Pina**, J.M.F. Ferreira**, Portugal INFLUENCE OF PARTICLE/AGGLOMERATE SIZE OF B–TCP ON ITS REACTIVITY AS COMPONENT FOR BRUSHITE FORMING BONE CEMENTS
12.10 pm – 12.15 pm	Featured Poster – 23 R. O'Hara, F. Buchanan, J. Orr, N. Dunne, UK APPLICATION OF MARINE DERIVED COLLAGEN TO A CALCIUM PHOSPHATE CEMENT SYSTEM FOR SPINAL FRACTURE FIXATION
12.15 pm – 12.20 pm	Featured Poster – 24 G. Wynn-Jones, R.M. Shelton, M.P. Hofmann, UK INJECTABILITY OF PORTLAND CEMENT FOR ORTHOPAEDIC APPLICATION
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LIST OF SELECTED ABSTRACTS

LIST OF SELECTED POSTERS

Key Lectures

Chairmen: Tom FACISZEWSKI & Peter MUNK

Evidence, History, Update, Socioeconomics of VBA in Europe

H. Deramond

Centre Hospitalier Universitaire, Amiens, France

Evidence, Status, Socioeconomics of VBA in the United States

R. Baker

President of the North American Spine Society (NASS), USA

Session 1

VCF AND AGING SPINE

Chairmen: Fergus MCKIERNAN & Richard HALL

Biomechanics of the Ageing Vertebral Body

M. Bouxsein

Department of Orthopedic Surgery, Harvard Medical School, Boston, Massachusetts, USA

Biomechanics of the Ageing Spine

P. Dolan

Centre for Comparative and Clinical Anatomy, University of Bristol, Bristol, UK

The Clinical Vertebral Fracture Event; Epidemiology and Morbidity

F. Mckiernan

Center for Bone Diseases, Marshfield Clinic, Marshfield, Wisconsin, USA

Session 2

EVIDENTIARY STATUS OF VERTEBRAL AUGMENTATION: 2011

Chairmen: Joshua HIRSCH & Gregg ZOARSKI

Analyzing the Evidence absent the NEJM RCTS

A. Brook

Department of Neuroradiology, Montefiore Medical Center, Albert Einstein College of Medicine, Bronx, New York, USA

Analyzing the Highest Level Evidence: Two Blinded RCTS from the NEJM

D. Kallmes

Department of Radiology, Mayo Clinic, Rochester, Minnesota, USA

Resolving the Differences between the Old and the New Data: Are They Really Saying Different things?

C. Bono

Brigham and Women's Hospital, Department of Orthopaedic Surgery, Boston, Massachusetts, USA

Session 3

BONE GRAFTING PROCEDURES

Chairmen: Christopher BONO, Hansen YUAN & Jean-Michel BOULER

Clinical Use of Injectable Ceramics in Extremities

S. Larsson

Department of Orthopaedic Surgery, Uppsala University, Uppsala, Sweden

Ceramic-Based Bone Graft Substitutes

M. Bohner

RMS Foundation, Bischmattstrasse 12, 2544 Bettlach, Switzerland

Calcium-deficient apatite microgranules and cements combined with bupivacaine: influence on the drug release profile.

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University of Nantes, France : [1]INSERM UMR 791 LIOAD,[2]CNRS, UMR 6230, CEISAM, [3]Preclinical Investigation and Research Center, ONIRIS College of Veterinary Medicine

X Biomaterials	☐ Biomechanics	☐ Clinical	X Innovation

INTRODUCTION: One of the major complications following bone recovery for orthopaedic or dental reconstructive surgery is the subsequent development of pain that could jeopardize the global success of the procedure. In this clinical context, we were interested to develop an innovative bioactive bone substitute that delivers *in situ* bupivacaine, a local anesthetic largely used in the management of postoperative pain. The local administration of active agents has numerous advantages compared with systemic treatments in terms of therapeutic efficiency and tolerance. Firstly, we have validated our local delivery by using granules of calcium deficient apatite (CDA) as vehicle of bupivacaine (1). Despite interesting analgesia effects on postoperative pain after implantation in rates, we decided to improve the formulation of this combined device. Because of their excellent biocompatibility and their nonexothermic behavior, we have incorporated bupivacaine in apatitic cement by following the same protocol of our previous association. After characterizing this combined cement, we performed a complete safety and efficiency study.

METHODS: Apatite materials (granules and cement) were loaded with different rates of bupivacaine (0, 4, 8 and 16% w/w) according to a process of ethanolic impregnation and were sterilized by gamma irradiation. Physico-chemical characterizations assays were performed such as XRD, infrared spectroscopy, compression strength assay, injectability test. The *in vitro* release profiles were determined from incubation of apatite (granules and cement) in physiological solution at determined times during 2 weeks.
Wistar male rats were implanted in distal femur with 50mg of granules of CDA associated respectively with 0, 1%, 4% and 16% of bupivacaine (N=10). Analgesia was measured using electronic Von Frey monofilament electronic version, inflammatory response and neurological score. Twelve rabbits were implanted for eight weeks with cement loaded with 0, 8% and 16% of bupivacaine in both proximal femurs (controlateral vs combined cement). Plasmatic dosages of bupivacaine were performed from blood samples at different times following implantation (HPLC coupled with UV detector). Tissue toxicity was evaluated by histological analysis conducted on all implanted (treated and control) femurs. Macroporosity and bone reconstruction were quantitatively determined by using SEM analysis.

RESULTS: The release profile of bupivacaine obtained from granules of CDA showed that 80% of bupivacaine was released within five hours. Despite this burst release, we observed from implantations in rats a dose dependant analgesic effect during the first post-operative day. In contrast to CDA granules, apatitic cement loaded with bupivacaine allowed to extend the release of bupivacaine until at least 96 postoperative hours (Fig 1). Physico-chemical analysis confirms that cement was composed by CDA after setting time and had good injectability properties. Plasmatic dosages indicated absence of systemic passage of bupivacaine after implantation of combined cement. Furthermore, histological analysis of implants showed an excellent biocompatibility of each biomaterial whatever doses used of bupivacaine. Considering the anti-inflammatory properties of bupivacaine, we decided to study the impact of bupivacaine release in terms of bone interface after implantation. Quantitative analysis of implants revealed no difference between control cement vs cement loaded with bupivacaine.

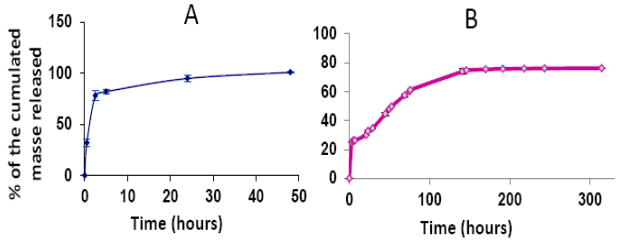

Fig 1: Release profiles of bupivacaine from apatite biomaterials (A) granules, (B) cement.

CONCLUSIONS: Given the potential analgesic effect observed with granules of CDA loaded with bupivacaine, we decided to improve the formulation of CDA for biomechanical and clinical reasons. In this attempt, we have developed injectable cement combined with bupivacaine. This combined cement allowed to extend the release of bupivacaine until at least 96 postoperative hours which is more appropriate to clinical exigencies. Furthermore, our safety study strongly suggested absence of systemic and local toxicities. Additional **e**xperiments in dogs are in progress to evaluate analgesia effect after removal of iliac crest.
This combined device system has been shown to provide a release of local anaesthetic adapted to prevent or limit postoperative pain relative to bone surgery. This innovative approach could be integrated in the global management of pain after specific prosthetic (hip or knee).

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ACKNOWLEDGEMENTS: GRAFTYS SA, Aix en Provence, France

Novel Bioresorbable Cement for Percutaneous Vertebral Fracture Treatment.

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☒ Biomaterials	☐ Biomechanics	☐ Clinical	☐ Innovation

INTRODUCTION

PMMA is the gold standard for treatment of painful vertebral fractures by Percutaneous Vertebroplasty (PVP) and Kyphoplasty techniques, but significant drawbacks are associated with its use. Promising alternatives, resorbable calcium phosphate cements (CPC), are biocompatible, biomimetic and have extensive clinical history. Additionally, these CPCs can be used as delivery vehicles for bioactive molecules to accelerate healing and treat osteoporosis. However, CPC use has been limited due to reports of cardiovascular deterioration. This effect has been associated with cement extravisation leading to pulmonary embolism stimulating thrombosis. In order to minimize these risks, a new class of composite CPCs have been developed with enhanced viscosity, cohesiveness and improved radiographic visualization. Unlike CPCs discussed in the literature, these composite CPCs resist leakage and do not initiate a thrombotic response.

METHODS

Nano-crystalline calcium phosphate (CaP) was prepared from amorphous CaP combined with dicalcium phosphate dehydrate or Brushite. Cellulose based viscosity modifier (CMC: Hercules) and non-ionic iodine based contrast agents (Isovue: Bracco Diagnostics, Omipaque: GE Healthcare) were also obtained. Composite CPCs were formulated by varying CMC concentration (from 5 to 10 w/w %) and molecular weight and the concentration and type of contrast agent. PMMA optimized for Vertebroplasty (Vertefix: Cook) was used as a control. Liquid and powder components of each formulation were mixed by using a liquid to powder ratio (L/P) range of 0.4-0.6 ml/g.

A cadaver model was used to assess the ability of these CPCs to resist extravisation. After mixing, the resulting pastes were immediately transferred into 1cc syringes and injected through 11 gauge, 4 inch vertebroplasty needles (Cook Inc.). Needles were placed transpedicularly into human cadaveric vertebral (L2, L3, L4, L5, T10, T11, T12). Each formulation was injected into a separate vertebra. Two osteoporotic cadavers were used for a total of 13 injections. The PMMA control was injected in one vertebra in each cadaver. Injection was performed under high resolution fluoroscopy. Test samples were injected until indication of cement leakage was observed or 5cc were delivered, whichever came first. Test samples were evaluated and graded for ease of injection (1-east to 4-difficult), extent of leakage (1-none, 2-minor after over filling, 3-many small leaks, 4-catastrophic leakage), and cement dispersion (1- cohesive ball with well defined edges, 2-ball with cloudy edges, 3-finger-like spreading radially outward). After completion of all injections, the entire spine was imaged using CT to confirm fluoroscopic observations of leakage and dispersion.

To asses thrombotic response two models were used an in-vitro Partial Thromboplastin Time (PTT) assay and in in-vivo swine model. For the PTT assay citrated human plasma was exposed successively to the test articles, calcium chloride and partial thromboplastin (extracted from rabbit brain cepalin). Time to clot was recorded for each test article and controls. For the swine model the animals were anesthetized and monitored continuously for arterial and venous blood pressure, cardiac output and heart rate while 3cc of either CPC or control was delivered as a single bolus into the jugular vein.

RESULTS

CPC combination biomaterials were easy to inject and visualize under fluoroscopy. Individual formulations were resistant to leakage and exhibited symmetrical, well defined flow characteristics. Conversely, the PMMA controls exhibited finger-like protrusions indicative of poor resistance to leakage. From an initial 13 formulations, 8 (62%) could be injected easily, 100% were resistant to leakage and exhibited symmetrical and well defined flow characteristics. It was observed that cement injection force, leakage and dispersion were related to: CPC formulations design, CMC molecular weight, ratio and nature and concentration of contrast agents. None of the CPCs tested exhibited PTT shorter than that observed for PMMA. Neither CPC or PMMA initiated thrombosis or significant cardiovascular distress in the swine model.

CONCLUSIONS

This new class of modified CPCs were easy to inject and visualize. Many formulations exhibited improved resistance to leakage and dispersion relative to PMMA. Injection force, leakage and dispersion were related to CPC formulation and can be controlled for optimal performance. Additionally, these CPCs do not exhibit a tendency to initiate thrombosis.

Setting reaction of a calcium phosphate - calcium carbonate injectable cement: a kinetic study

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☒ Biomaterials	☐ Biomechanics	☐ Clinical	☐ Innovation

INTRODUCTION: Calcium phosphate bone cements have the interesting property that they harden *in-situ*. Hence they can be injected as a paste using minimally invasive surgery techniques. However, these techniques require the characteristics of the cement to be accurately controlled. Especially, reaction rate and setting time are two key factors that must be under control to fit surgeons' needs: the cement shouldn't set too quickly, to provide enough time to be mixed and injected, but quick enough to supply early mechanical properties [1]. The comprehension of mechanisms leading to setting and hardening of such a cement is therefore of uttermost value to optimize cement composition and properties.
This study focuses on the kinetics of a calcium carbonate-calcium phosphate cement setting reaction. Complementary characterisation techniques will be used to thoroughly analyse the processes involved during cement setting and to further understand their relation to mechanical properties.

METHODS: Cements have been prepared by mixing deionised water as the liquid phase (L) with the solid phase (S) composed of equal mass of $CaCO_3$-vaterite and dicalcium phosphate dihydrate (DCPD). Setting reaction of the cement paste has been studied by FTIR spectroscopy: 1) in real time by Horizontal Attenuated Total Reflexion (HATR) mode and 2) at fixed times by conventional transmission mode.
1) Real time method: the as-prepared cement paste was placed on a ZnSe crystal to acquire HATR FTIR spectra (Nicolet 5700 spectrometer, ThermoElectron) at 37°C in an atmosphere saturated with water. Phosphate and carbonate FTIR band decomposition was performed using Origin® software to collect semi-quantitative data for cement setting kinetics.
2) Static method: pieces of cement were soaked into liquid nitrogen to stop the setting reaction at different times after mixing L with S, freeze-dried and analysed by FTIR-spectroscopy, X-ray diffraction and SEM (LEO 435VP, samples silver plated before observation).
To perform pH-measurements during the first 4 hours of the setting reaction, cement paste has been placed into an oven with controlled hygrometry (37°C, 95% RH).

RESULTS: Real-time monitoring of the reaction by HATR FTIR spectroscopy highlights that vaterite and DCPD dissolve; precipitation of carbonated apatite is responsible for the setting of the cement. It also clearly shows the decrease of υ2 phosphate bands attributed to DCPD and the rise of apatite absorption bands (υ3 PO_4 at 1018 cm^{-1}, υ1 PO_4 at 954 cm^{-1}). This is confirmed by the pH of the paste which shrinks during the 1st hour of reaction due to DCPD dissolution and reaches a plateau afterwards. During the whole setting process, pH is in the range 7.5-6.3, i.e. close to the physiological pH.
Moreover, using real-time and humid conditions, HATR FTIR spectroscopy has permitted to ascertain the presence of non-apatitic phosphate and carbonate environments associated to the formation of a hydrated layer at the surface of apatite crystals during setting [2].
SEM observations realised at different times illustrate the evolution of reactive powders and cement microstructures. Interestingly, we can notice that apatite nucleates and grows preferentially on vaterite lentils than on DCPD platelets (fig. 1) which is unexpected considering previous studies showing that CO_3^{2-} tends to hinder the precipitation of calcium phosphates [3].

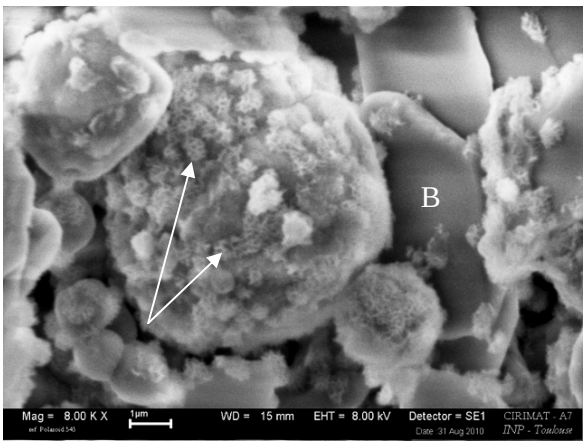

Fig. 1: Cement observation 90 min after mixing L+S (arrows highlight where apatite grows; "B" points out the smooth surface of a DCPD platelet with only very few apatite nuclei; the bar represents 1µm).

CONCLUSIONS: We proposed a methodology which enables to follow the cement setting reaction using HATR FTIR spectroscopy at 37°C. This technique offers additional advantages over the transmission mode as analysis of the cement paste can be performed continuously, in real time and in humid conditions, which allows preservation of the hydrated layer suggested to be involved in biomimetic apatite cement setting, consolidation, and bioactivity [2]. FTIR and pH measurements indicate that during the setting reaction, DCPD and vaterite dissolve, leading to the formation of carbonated apatite analogous to bone mineral. Interestingly, it appeared that nucleation of apatite responsible for the cement setting occurs preferentially on vaterite particles, which was rather unexpected.

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Bacterial Inhibitory Coatings based on Glass Polyalkenoate Cement Chemistry.

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INTRODUCTION: Glass polyalkenoate cements (GPCs) are injectable adhesives that are used in both dental and ear, nose and throat (ENT) applications (1). They are formed by the aqueous reaction of an ion leachable glass with polyacrylic acid (PAA) (1). GPCs act as a reservoir, absorbing the active ion from an external source and releasing it over time. Both the zinc ion (Zn^{2+}) (2) and silver ion (Ag^{+}) (3) are known to be antibacterial. The authors have developed novel GPCs based on a Ag-Zn-Si glass and report herein how these materials release active ions *in vitro* and *in vivo* models for the purpose of inhibiting bacterial growth.

EXPERIMENTAL METHODS: Two Ag-Zn-Si glasses (Table 1) were produced and characterized by conventional techniques.

Table 1: Glass Compositions (mol%)

Glass	SiO_2	ZnO	Ag_2O	Na_2O
A	56.04	32.98	0.11	10.87
B	56.04	32.76	0.33	10.87

Two GPCs were formed from the glasses, by mixing with PAA (Mw, 210,000) and analytical water. (Table 2)

Table 2: Cement compositions

Cement	Glass (g)	Acid (g)	Water (ml)
A	0.5	0.2	0.2
B	0.5	0.2	0.25

The antibacterial activity of the cements were assessed by *in vivo* and *in vitro* tests. The spread plate method was undertaken using two bacteria, *S. aureus* and *P. aeruginosa*. *In vivo* testing involved injecting *G. mellonella* (larvae of wax moth) with 20µl of *S. aureus.* After 20min, the *G. mellonella* were injected with aqueous solutions of cement extract (20µl), to determine their viability. Cement elutions were developed by immersing cements in analytical water for 1, 7 and 30 days.

RESULTS: Working (Wt) and setting (St) times of the two GPCs were determined by ISO standard methodologies (Table 3).

Table 3: Wt and St of cement

Cement	Wt	St
A	4min12	16h07
B	5min22	16h15

Table 3 shows that the Wt were 4mins12 and 5mins 22 respectively and that the St were below 24h. Table 4 shows the results of *in vitro* testing.

Table 4: *In vitro* results of cement

Cement	*S. aureus*	*P. aeruginosa*
A	0.73±0.3	4.6±1.1
B	4.6±1.3	10.3±0.6

Table 4 shows inhibition zones of 4.6mm (*S. aureus*) and 10.3mm (*P. aeruginosa*) were observed for the two bacteria, indicating that the cements are antibacterial. As cement B showed a greater antibacterial effect, it was the only cement selected for the *in vivo* evaluation.

Figure 1 shows the *in vivo* results.

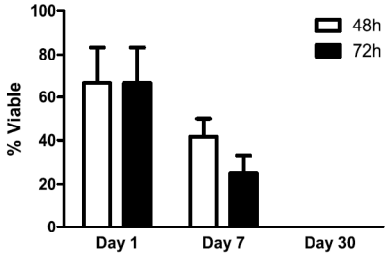

Figure 1: 1, 7 & 30 day elutes % survival at 48h & 72h

The *in vivo* results showed that 1 and 7 day solutions of the cement, injected into *G. mellonella* infected with *S. aureus*, provided a 40-66% viability rate for the animal model.

The results of this project indicate that these novel cements formed from Ag-Zn-silicate glasses are injectable and have suitable properties to serve as antibacterial agents, adhesives or cements for a range of clinical applications.

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Alendronate-doped Apatitic Cements as a Potential Technology for the Prevention of Osteoporotic Hip Fractures

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☒ Biomaterials	☐ Biomechanics	☐ Clinical	☒ Innovation

INTRODUCTION: The integration of drugs and devices is a growing force in the medical industry. The incorporation of pharmaceutical products not only promises to expand the therapeutic scope of device technology but to design a new combination products whose therapeutic value results from both the structural attributes of the device and the intrinsic activity of the drug. In this context, a new calcium phosphate cement-based (CPC) medical device was developed, capable of providing mechanical reinforcement and delivering a bisphosphonate (BP) antiresorptive drug locally.

METHODS: The optimized CPC formulation had the following composition for the solid phase: α-TCP ($Ca_3(PO_4)_2$, 78 wt%), DCPD ($CaHPO_4.2H_2O$, 5 wt%), MCPM ($Ca(H_2PO_4)_2.H_2O$, 5 wt%), 0.67wt% alendronate-doped CDA ($Ca_{10-x}[\ ]_x(HPO_4)y(PO_4)_{6-y}(OH)_{2-z}[\ ]_z$, 10 wt%) prepared as reported previously[1], hydroxypropyl methyl cellulose [HPMC] (2 wt%). The liquid phase consists in a 5 wt% Na_2HPO_4 solution, with a liquid/powder ratio of 0.5 mL g^{-1}.

RESULTS: Our purpose was to combine a generic BP (alendronate) to an injectable CPC, for the prevention of the osteoporotic fracture. Indeed, cement augmentation of the proximal femur by minimally invasive surgery (femoroplasty) may increase mechanical stability and reduce fracture risk as the primary effect, in addition to the ancillary action of the BP itself. While BPs behave as setting retardants, we have examined whether alendronate can be incorporated in a CPC cement, without affecting the properties of the curing and cured cement. Not surprisingly, the alendronate doping increased the setting time at 20°C regardless and independent of the five methods used for its incorporation, while this trend became more and more significant as the BP-loading increased. However, the retarding effect of the BP on the setting time was found to be limited when combined to CDA. Accordingly, an optimized CPC formulation[2] (see experimental method) was thus obtained, showing a short cohesion time along with setting times appropriate for pre-clinical uses (initial setting time (37°C): 5-7 min.; final setting time (37°C): 15-18 min.). Simulation of the BP release under conditions close to an *in-vivo* situation showed the absence of "flash release". Considering the phosphate concentration encountered in blood (1 mmol.L^{-1}) and the amount of alendronate loaded in the cement used for the pre-clinical evaluation of this system, 0.057 wt% with respect to the solid phase, the alendronate release was found to be constant since it was directly driven by the alendronate /CDA interaction present within the cement (Figure 1).

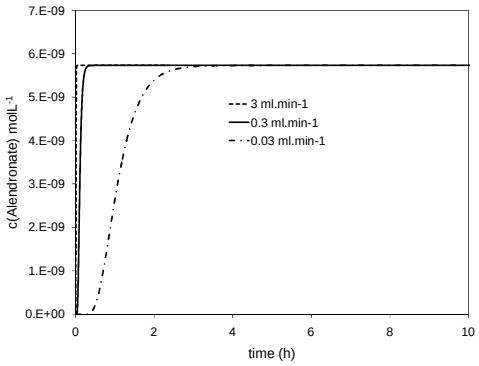

Fig. 1: Modeling of the alendronate concentration released from cement blocks versus time, for a 0.03-3 mL.min^{-1} percolation flux range, and the following conditions: elution = 1 mmol.L^{-1} phosphate buffer, alendronate loading in the cement block = 0.057 wt% with respect to the solid phase.

CONCLUSIONS: A novel and efficient route was designed for introducing a bisphosphonate in a CPC while keeping the main properties of the cement suitable for practical application as a drug delivery system, implantable by minimally invasive surgery. This result was made possible through the original use of (i) high frequency impedance measurements for in situ monitoring of the cement setting reaction (ii) solid state NMR experiments for the investigation of the BP/calcium phosphate interactions (iii) BP adsorption / desorption studies on cement blocks, under continuous flow conditions using a coupled chemistry / transport model, to predict the release profile of the drug under simulated in vivo conditions. *In vivo* investigation of the cement properties showed promising results, showing the ability of the Alendronate-loaded cement to resorb while promoting new bone formation.

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Fast healing, strong and resorbable alkali-free phospho-silicate bioglass granules, scaffolds and injectable composites for regenerative medicine

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☒ Biomaterials	☐ Biomechanics	☐ Clinical	☒ Innovation

INTRODUCTION: Bioactive glasses are a class of biomaterials which elicit a special response on their surface when in contact with biological fluids, leading to strong bonding to living tissues. In the field of bone tissue engineering (TE), bioactivity is defined as the ability of the material to bond to bone tissue *via* the formation of a bone-like HA layer on its surface. Due to a number of attractive properties for use in TE and regeneration, for example: enhanced angiogenesis and up-regulation of specific genes that control the osteoblast cell cycle, there is increasing effort in the use of bioactive glasses in TE applications [1].
Since the discovery of 45S5 Bioglass® [2], many artificial biomaterials based on, or inspired by, Hench's glasses have been developed and successfully employed in clinical applications for repairing and replacing parts of the human body [3]. The high dissolution rate of 45S5 glass due to its high alkali content causes fast resorption that negatively affects the balance of natural bone remodelation and in particular the physiologically vital process of angiogenesis, thus leading to gap formation between the tissue and the implant material. The alkali oxides used to lower the melting temperature might reduce the usefulness of the glass *in vivo*, making the bioactive glasses susceptible to water uptake by osmosis resulting in swelling and cracking of polymer matrix embedding them in composites and increase their degradation rate. High levels of alkalis degrade the sintering ability by increasing the crystallization tendency of glasses, rendering them useless for producing bioactive porous scaffolds. For example, the manufacture of porous scaffolds from the 45S5 Bioglass® is problematic owing to its poor sintering ability and a readily crystallization trend that turns this glass into an inert material with poor mechanical strength [4].

METHODS: A series of glass compositions in the system Diopside – Fluorapatite – Tricalcium phosphate were prepared by the melt-quenching technique from high-purity powders of SiO_2 (purity >99.5%), $CaCO_3$ (>99.5%), $MgCO_3$ (BDH Chemicals Ltd., UK, purity >99.0%), $NH_4H_2PO_4$ (Sigma Aldrich, Germany, >99.0%) and CaF_2 (Sigma Aldrich, Germany, 325 mesh,>99.9%). The glasses were fully characterized concerning the structure, *in vitro* bioactivity and degradation analysis, and thermal behaviour. Injectable composites were prepared by mixing glass particles with UV-curing resins. The suitability of the new bioglasses for bone regeneration was evaluated with *in vivo* using chinchila as animal model.

RESULTS: The ^{29}Si MAS-NMR spectra depict the dominance of Q^2 (Si) structural units for all the glasses, a feature that favours bioactivity. Fig. 1 compares the biomineralization activities of some novel composition with that of 45S5 Bioglass® after 12 h of immersion in SBF. Calcite was the only crystalline phase formed at the surface of 45S5 Bioglass®, while peaks of HA could be observed in the novel bioglasses, being particularly strong in the case of TCP-20 composition.

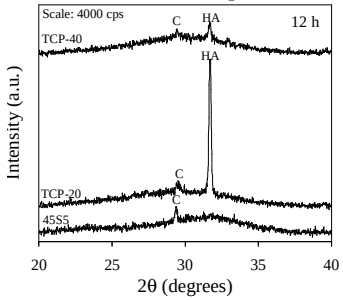

Fig. 1: Comparison of biomineralization activity in SBF

The degradation of bioglasses evaluated in Tris HCl (pH: 7.25) solution along 5 days, according to ISO 10993, showed that 45S5 Bioglass® presented much higher weight loss (3.67%) and final pH (9.68) in comparison to a weight loss of 1.6% and final pH of 8.36 exhibited by the novel bioglasses TCP-20 and TCP-40. Lower degradation rate mean stronger adherence of deposited HA layer, while smaller pH changes enhance viability and cell proliferation. Full densification was achieved for the novel bioglasses before the onset of crystallization, resulting in strong mechanical properties after sintering. *In vivo* tests revealed that bone defects were almost entirely (90-95%) filled after 2-3 months post operation.

CONCLUSIONS: In comparison to the 45S5 Bioglass®, the novel bioglasses are less soluble and degradable, more bioactive, exhibit excellent sintering ability and enable the fabrication of strong porous scaffolds for tissue engineering and bone regeneration.

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Session 4

DRUG-LOADED GRAFTING

Chairmen: Marc BOHNER, Bassem GEORGY & Michael HOFMANN

Role of Macroporosity in Delivery Modalities for BMP

H. Seeherman

Musculoskeletal Therapies, Wyeth Discovery Research, Cambridge, Massachusetts, USA

Systemic Inhibition of Sclerostin as an Anabolic Approach for Osteoporosis and Fracture Healing

X. LI

Metabolic Disorders, Amgen Inc., Thousand Oaks, California, USA

ALUMINIUM-FREE GLASS POLYALKENOATE SPINAL CEMENTS.

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INTRODUCTION:

Glass polyalkenoate cements (GPCs) are prepared by the reaction of an ion-leachable glass with an aqueous solution of polyacrylic acid (PAA)[1]. Conventional GPCs are based on calcium alumino-silicate glass, however aluminium (Al) has been implicated in the pathogenesis of degenerative brain diseases. The authors have previously shown that GPCs can be formulated from Al-free calcium zinc-silicate glasses where the Al has been replaced with zinc (Zn)[1]. These materials are currently being evaluated as injectable bone cements.

This work determines the effect of adding Titanium (Ti) to existing novel GPCs as Ti is used in the fabrication of many implantable materials due to a number of attributes including high strength, corrosion resistance and excellent biocompatibility[2].

EXPERIMENTAL METHODS:

A novel glass series was developed containing four different glasses;

	BT 101	TW-X	TW-Y	TW-Z
SiO_2	0.480	0.464	0.448	0.430
TiO_2	0.000	0.016	0.032	0.050
ZnO	0.360	0.360	0.360	0.360
CaO	0.120	0.120	0.120	0.120
SrO	0.040	0.040	0.040	0.040

Reagents were ball milled and fired in a platinum crucible (1480°C, 1Hr). The melt was quenched in water and the resulting frit was dried, ground & sieved (<45μm). GPCs were produced by mixing the glass in a 2:1.5 (powder: liquid) ratio, with 50wt% E9 (80,800) & E11 (210,000) PAA. Working (T_w) & Setting (T_s) time were conducted in accordance with ISO9917[3]. Biaxial flexural (σ_f) testing was in accordance with a publication by Williams *et al* [4] and cell culture testing was performed according to ISO10993[5] with both cement discs and 100µl water extracts.

RESULTS:

Figure 1 Shows the T_w and T_s of each cement in the series.

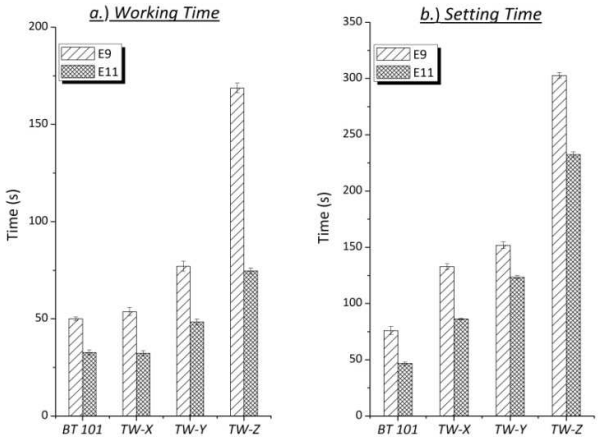

Figure 1. Working (T_w) and Setting time (T_s) of each cement.

Figure 1. Considering BT101 and TW-Z with E9 & E11 PAA the T_w increased from 50 to 169s and 32 to 74s respectively. The T_s also increased with E9 & E11 from 76 to 303s and 47 to 232s respectively.

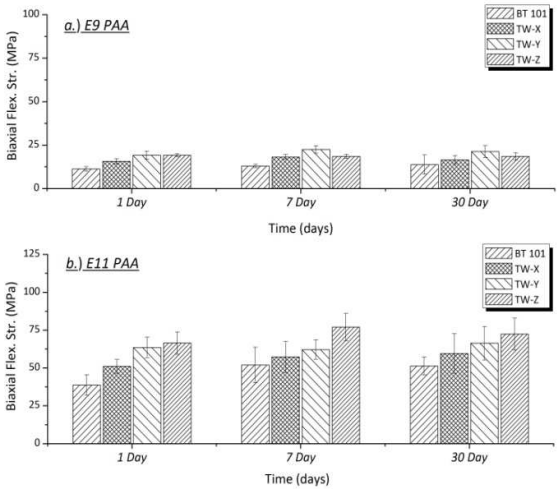

Figure 2. Biaxial Flexural strength of cement series.

Figure 2 Shows the σ_f strength of each cement. E9 cements strengths increased from 11 to 19 MPa, and E11 cements from 25 to 72 MPa for BT101 to TW-Z respectively. No significant increase in strength was observed with respect to maturation between cements.

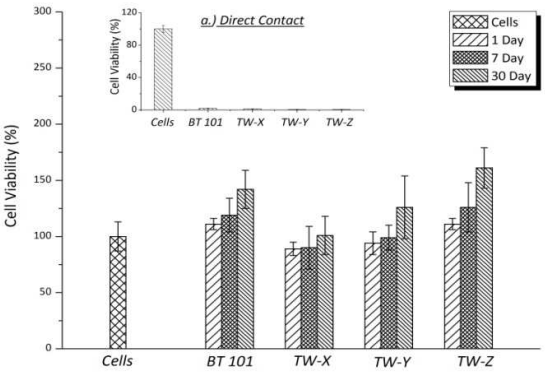

Figure 3. *In vitro* cytotoxicity testing for each cement.

Figure 3 Shows direct contact (discs) and indirect (extracts) cell culture testing. Direct cement exposure resulted in greatly decreasing the cell count in each case to a viability of less than 5%. Testing of extracts resulted in an increase in cell viability, particularly with TW-Z (161%) after 30 days.

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Injectable porous microspheres for controlled drug and cell delivery

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INTRODUCTION: Porous microspheres (MP) are potentially ideal injectable materials for drug and cell delivery, because their interconnected porous structure can provide easier nutrient transport, large surface area and higher buoyancy to improve cell adhesion and growth[1-3]. The present work aimed to fabricate porous poly(lactic-co-glycolic acid) (PLGA) MP using gas foaming double emulsion method with certain surface treatments. Compared with nonporous MP, porous MP and heparin coated porous MP improved mouse bone marrow stem cell (MSC) attachment and proliferation.

METHODS: NH_4HCO_3 solution (W_1) was homogenized in dichloromethane and PLGA (O), and then re-emulsified in PVA solution (W_2). The skin layers of MP were washed away with different treatments to get open porous. Heparin coating was achieved by dipping MP into poly(ethyleneimmine) and heparin solution. MSC metabolic activity was evaluated by Alamar Blue. Surface morphology of MP was observed by SEM. Data was evaluated by one way analysis of variance (ANOVA) with Fisher's test and $p<0.05$ was considered as statistically significant.

RESULTS: There are gas bubbles and pores on the optical microscopy images of PLGA droplets (Fig 1.a-b) during the external solvent evaporation. Hardened MP had well distributed pores on the surface covered by a skin layer (Fig 1.c), compared with normal nonporous MP (80-250μm) fabricated without NH_4HCO_3 (Fig 1.d).

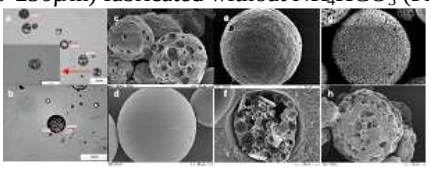

Fig. 1: Optical micrographs of unhardened PLGA droplets after (a) 5min and (b) 3h during the solvent evaporation, and SEM images of (c) partially covered porous, (d) non-porous (e) covered porous MP and (f) their cross areas, (g) rough particles and (h) porous sponge

At the same condition, the surface pores could be entirely covered if the O:W_2 ratio was increased (Fig 1.e). The cross area image (Fig 1.f) confirmed that there were interconnected holes (6-12μm) inside the MP which were totally covered. Deceasing the O:W_2 made the MP become big rough particles and lose the surface morphology along with the well distributed pores (Fig 1.f). Even if increasing NH_4HCO_3 concentration to 4%, the gas bubbles still could not break the skin layer and all surface pores were covered. The skin layer (thinner than 2μm) could be washed away by NaOH solution without changing MP structure. The surface open pore size and ratio increased with increasing NaOH concentration from 0 to 2mg/ml and Fig 2.a-e). However, the sphere structure would be destroyed if ethanol was added to the NaOH (Fig 2.f-g). The acetone solution made the MP adhere to each other (Fig 2.h).

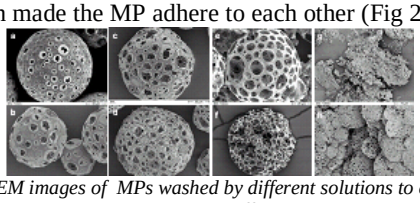

Fig. 2: SEM images of MPs washed by different solutions to clear the skin layer: (a-e) NaOH solution with different concentration from (a) 0, (b) 0.5, (c) 1, (d) 1.5, (e) 2 mg/ml; (f) 4.5 mg/ml NaOH in 10% ethanol, (g) 2 mg/ml NaOH in 50% ethanol, and (h) 25% acetone.

Although nonporous MP were bigger in diameter, porous MP and heparin coated porous MP had higher MSC attachment efficiency and proliferation rate after 3 day culture (Fig 3).

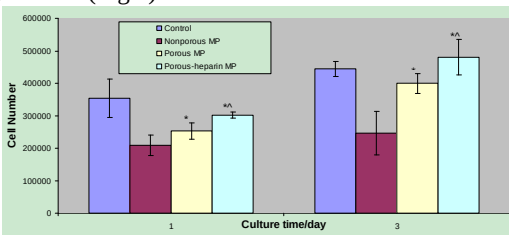

*Fig. 3: MSC proliferations after 1 and 3 day culture on MP (*significant increase compared with Nonporous; ^ significant increase compared with Nonporous and Porous MP $p< 0.05$)*

Only a few of MSC were still attached to the nonporous MP after 3 day culture, while there were more MSC attached on the surface and even inside of the porous MP. The heparin coating on MP further improved the cell attachments (Fig 4).

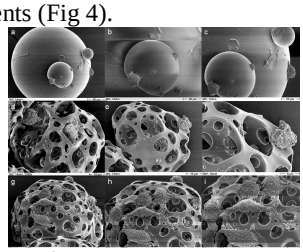

Fig. 4: SEM images of MSC on (a-c) Non-porous (d-f) Porous and (g-i) Heparin-porous MP after 3 days

CONCLUSIONS: Open porous MP can be fabricated and they attract more MSC to the surface and inside than non-porous MP. Their cell delivery properties could be further enhanced by heparin coating. This heparin coated porous MP will have potential to be used as injectable scaffolds for cell delivery and controlled growth factor-related protein release due to the strong protein affinity of heparin [4].

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RATES OF GROWTH FACTOR RELEASE FROM AN INJECTABLE CARRIER OF AUTOLOGOUS BLOOD AND BONE MARROW

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INTRODUCTION:

Venous blood, plasma, platelet concentrate, bone marrow aspirate, and bone marrow concentrate, are excellent sources of platelets, white blood cells, and stromal cells which contain potent mitogens that are known to augment bone repair (i.e. TGF-β, PDGF, VEGF, IGF, and BSP) [1,2]. Growth factors promote tissue repair and influence the reactivity of vascular and other blood cells in angiogenesis and inflammation. Growth factors attached to platelets or fibrin may result in enhanced activity over recombinant proteins[3]. BMP's, which are also released under conditions of low pH by the de-granulation of platelets during clot formation, are thought to be responsible for promoting the initial stages of bone repair[4]. These sources are autologous, and readily available at the point of care for the treatment of wounds, and for the repair of bone and tissue damage[4,5].

In order for growth factors (GF's) to be available to facilitate healing, cells must be lysed, and their contents sustained within the injury site for the duration necessary to affect the critical stages of healing. The use of a delivery vehicles or carrier can extend the retention of GF's to enable sustained release over time. In the case of skeletal tissue repair or augmentation, the vehicle for delivery of autologous GF's, must meet the additional challenge of sharing the mechanical load imparted by surrounding tissue and muscle. The delivery vehicle must maintain the integrity of the repair, while still allowing access of the host repair mechanisms. An ideal carrier for blood and bone marrow would offer the proper mechanical strength, ease of handling, and retention of growth factors. In the present study, different types of carriers such as an injectable, settable composite porous nanocrystalline calcium phosphate (NCCP) bone substitute material (CarriGen), a collagen sponge, and a composite β-TCP/collagen foam are compared as delivery vehicles for bone marrow aspirate and bone marrow concentrate. A comparison is made based on the retention and release of growth factors and mechanical stability of the carrier.

METHODS:

Collection and preparation of bone marrow

Bone marrow aspirate was obtained through the Harvard CBR/Immune Disease Institute (Boston, MA). BMA was concentrated using the Harvesttech SmarPReP 2 BMAC centrifugation system. Total nuclear count of WBC's increased from 24 x 10^3/μl (BMA) to 88 x 10^3/μl (BMC) after concentration. Platelet count increased from 88 x 10^3/μl to 487 x 10^3/μl after concentration.

Sample preparation and *in-vitro* culture

In-vitro culture of the materials (n = 6 wells/treatment) was performed at the Tissue Engineering Resource Center (Tufts University Medford, MA). Collagen based materials were cut into approximately 0.5 cc cubes. 0.5cc of either BMA or BMC was added to the material (w/ thrombin) and gently kneaded in and allowed to clot. The CarriGen (ETEX Corporation) powder was mixed (1:1) with either BMA or BMC (w/ thrombin) in a silicone mixing bulb, then delivered to the culture wells (0.5cc total/well) using a 3 cc syringe. 0.5cc BMC/well (w/ thrombin) was incubated without a carrier at pH = 7.4, and at pH = 5.4 as a control for the release of GF's. The samples were incubated in media at 37°C (5% CO_2). for 14 days. The surrounding incubation media was analyzed by ELISA for BMP-2, TGF-β1, and PDGF-αβ at 1, 4, 7, and 14 days. Recovery of free GF's was determined using BMC spiked with either 0, 5, or 10ng/ml GF's (BMP-2 - Tufts, TGF-β1 & PDGF-αβ - R&D Systems). Changes in gross sample morphology were followed over time with an emphasis on retention of bone marrow and integrity of the sample shape.

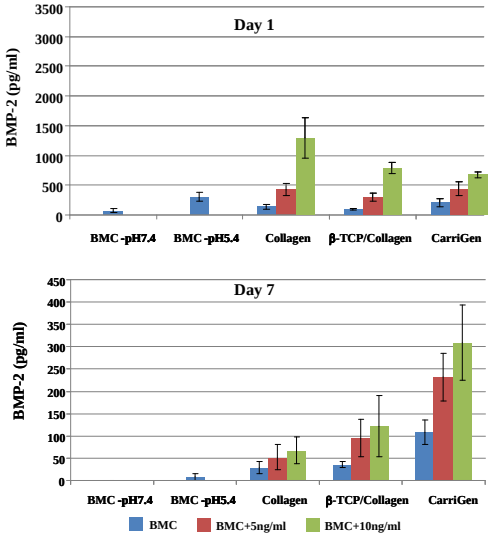
RESULTS:

Gross observations and mechanical strength

The collagen sponge and β-TCP/collagen foam carriers, mixed with BMA or BMC were soft initially and were not able to retain their shape when compressed, although the latter was slightly more resistant to compression. The CarriGen material mixed with BMA or BMC, hardened to a compression resistant form, which maintained its shape throughout the experiments. Both the collagen sponge and β-TCP/collagen foam disintegrated into granules within the 14 day incubation period.

GF retention and release

Figure 1. BMP-2 levels at 1 and 7 days incubation



The collagen sponge-BMA and β-TCP/collagen foam-BMA released PDGF at levels 20% higher than the BMA clot, while CarriGen-BMA released levels 300% higher than the clot at 14days. TGF-β was not detectable in the clot, or either of the collagen-BMA carriers at 14 days. TGF-β release was detectable in the CarriGen-BMA samples at 30% of initial levels at 14 days. BMP-2 levels of all the control and carriers were similar on day 1, however increased by 800% in the CarriGen-BMA samples when compared with the clot and collagen-BMA carriers at days 4, 7, and 14. Enhanced release of BMP's from cells may be caused by the setting reaction of the CarriGen carrier. Spiked levels of growth factors were also significantly higher in CarriGen-BMC after 7 days incubation when compared to the collagen-BMC and β-TCP/collagen-BMC samples (Figure 1).

Conclusions:

This study demonstrates that growth factor release can be sustained for extended durations when BMA, BMC, or GF's are mixed with the injectable, hard setting, porous calcium phosphate carrier (CarriGen) as compared to similar mixtures with a pure collagen sponge, or a β-TCP/collagen foam carrier. CarriGen's ability to retain growth factors may be additionally enhanced by it's favorable mechanical strength over the sponge or foam type carriers.

Acknowledgments:

This study was funded by ETEX Corporation.

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Vertebroplasty using bisphosphonate-loaded calcium phosphate cement in a standardized vertebral body bone defect on an osteoporotic sheep model

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☒ Biomaterials	☐ Biomechanics	☐ Clinical	☒ Innovation

INTRODUCTION: Calcium phosphate (CaP) and PMMA bone cements have been both proposed for bone reinforcement of vertebral bodies through vertebroplasty procedure. CaP cements can be loaded with different active molecules that could be released locally to promote bone augmentation and/or prevent further bone resorption. The present study reported the use of a bisphosphonate-loaded CaP bone cement on a vertebroplasty animal model in sheep.

MATERIALS AND METHODS: A vertebroplasty modelization was developed on 12 adult female sheep, according to European Community guidelines for the care and use of laboratory animals (DE 86/ 609/CEE). Six animals were first ovariectomized to induce osteoporosis over a 6-month period, six were kept intact as control animals.

For surgical procedures, general anesthesia was induced using an intravenous injection of ketamine and propofol and prolonged with isoflurane in oxygen through an endotracheal tube. With the animal in right lateral recumbency, a left paralumbar incision was performed from the caudal aspect of the last rib to the iliac crest to allow a retroperitoneal approach to the lumbar vertebral bodies. A standardized bone defect, preserving the end plates, (8 mm high x 10 mm deep x 20 mm long) was created into the L3 and L4 vertebral bodies with appropriate burs, mimicking a two level vertebroplasty procedure.

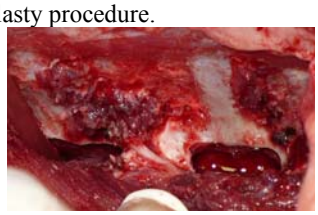

Fig.1. Standardized bone defects into L3 and L4 vertebral bodies.

During drilling, bone debris was removed by saline irrigation. Bone defects were then randomly filled with a CaP bone cement loaded with alendronate[1] or with Graftys® QUICKSET cement. The resulting cements exhibit a global porosity of about 70%, with a macroporosity (pore diameter>100 µm) of 8 to 10%. Three months after implantation, animals were euthanatized and lumbar segments from L1 to L5 were harvested and submitted to XRay imaging. Each implanted vertebral body was analyzed with micro-computed tomography (microCT) and then embedded with PMMA and prepared for histological analysis on non-decalcified sections and histomorphometric analysis with backscattered scanning electron microscopy (SEM). Trabecular bone density of the implanted vertebral bodies, bone-cement interfaces, cement degradation and newly-formed bone apposition was compared in ovariectomized and control sheep.

RESULTS: Specimens from all the animals were studied. Three months after implantation, the injected cements were still present into all implantation sites. MicroCT confirmed bone loss in ovariectomized animals. A new bone apposition was observed at the cement surface that exhibited peripheral resorption and remodeling that appeared more intense with the alendronate–loaded cement.

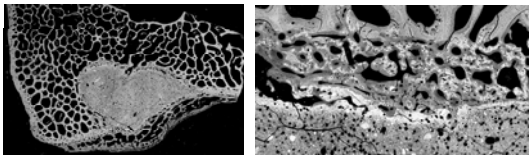

Fig. 2: Backscattered SEM images showing vertebral body bone filling with CaP bone cement and the reactive bone-cement interface after alendronate local release.

The cements we used have a mechanical compressive strength after complete hardening in biologic conditions that reaches 24 MPa, through a very low exothermic reaction. A recent study in dogs using a similar model[2], did not show any significant difference in vertebral body height and compressive strength between PMMA and CaP cements.

CONCLUSIONS: The injection of CaP cement may be an effective method to treat vertebral body bone defects and such alendronate-doped apatitic cement could appear a potential technological approach for the prevention of osteoporotic vertebral compression fractures.

REFERENCES: [1]Schnitzler V, et al. Acta Biomater 2011;7:759-70. [2]Turner TM, et al. Spine Journal 2008;8:482-87.

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Low Porosity Injectable Biocomposites Incorporating rhBMP-2 Enhance Bone Remodeling in a Rabbit Femoral Plug Model

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Introduction: The limited supply and poor mechanical properties of autograft bone have prompted a search for alternatives. A variety of synthetic injectable biomaterials have been tested, but they typically lack the osteogenic properties of autograft. To address the clinical need for alternatives to autograft bone for the treatment of bone defects, we are developing injectable low-porosity biocomposites comprising mineralized allograft bone particles in a biodegradable polyurethane (PUR) matrix. The interactions between the filler surface and the polymeric matrix were varied to reinforce the composites. Recombinant human bone morphogenetic protein-2 (rhBMP-2) was added to some formulations to enhance the osteogenic properties of low porosity injectable composites. The effects of rhBMP-2 dose on new bone formation at 6 and 12 weeks were investigated in a rabbit model.

Experimental Methods: The biocomposite comprised a lysine triisocyanate-polyethylene glycol prepolymer, polyester polyol, allograft bone particles (AMBP), amine catalyst, and rhBMP-2. The filler content of the biocomposite was maintained at 70 wt%. To study the bone-PUR interactions, the surface of the allograft bone was either demineralized (SD) or protected with 4-methoxyphenyl isothiocyanate (PROT), and the compressive mechanical properties of the corresponding composites were compared. Two doses of rhBMP-2 were used: 110 and 440 ug/ml. The cure time was approximately 10 minutes. Bilateral defects (6 mm diameter by 11 mm in depth) were drilled in the metaphysis of the distal femurs of NZW rabbits, and biocomposites were injected into the defects. A uCT40 system was used to acquire images of the femurs. Histological ground sections were stained with Sanderson's rapid bone stain counterstained with Van Gieson.

Results: Biocomposites exhibited compressive strengths (27.2-33.2MPa) comparable to trabecular bone. No significant differences between the mechanical properties of AMBP and SD were identified, while the PROT samples had mechanical properties three times lower than the AMBP composites. This suggests that AMBP reinforced the material by creating chemical bonds between the bone particles and the matrix. Histological sections of the biocomposites without rhBMP-2 after 6 and 12 weeks of implantation revealed extensive cellular infiltration and new bone formation, and uCT images (Figure 1) showed extensive remodeling with negligible resorption gaps. These observations contrast with a previous study where compression-molded materials (79 wt% filler) showed substantial resorption after 6 weeks.[1] Incorporation of 110 ug/ml rhBMP-2 enhanced new bone formation relative to the biocomposite without rhBMP-2, as evidenced by the presence of less AMBP and more new bone. Interestingly, the majority of biocomposites incorporating the 440 ug/ml dose of rhBMP-2 showed comparable remodeling to the low dose, but approximately 30% of the high dose biocomposites displayed extensive areas of osteoclast-mediated resorption at 6 or 12 weeks. Similar observations have been reported for doses of rhBMP-2 exceeding by a factor of 3 the recommended dose delivered on an ACS sponge in a sheep femoral condyle plug model.[2] However, in our study the high dose was the recommended dose for rabbits, suggesting that the release mechanism of rhBMP-2 from the biocomposite may reduce the minimum effective dose required to enhance bone healing. These observations suggest that injectable low-porosity allograft bone/polyurethane biocomposites may be a promising approach for developing weight-bearing, biologically active biomaterials that maintain sufficient mechanical strength while remodeling to form new bone.

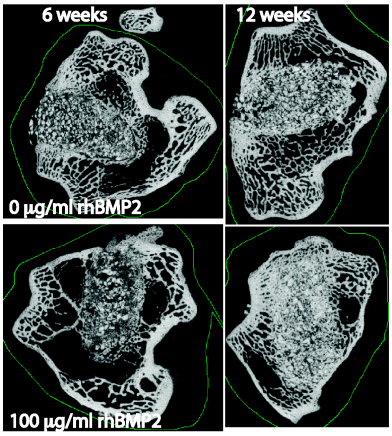

Figure 1. µCT images of allograft/PUR biocomposites carrying rhBMP-2 injected into 6x11 mm plug defects in the femoral condyle of NZW rabbits.

Acknowledgments: This work was supported by the Center for MIlitary Biomaterials Research (DOD/W81WXH-04-2-0031), NSF (DMR-0847711), and Medtronic.

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Influence of blood addition on mechanical, textural and biological of calcium phosphate cement

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☒ Biomaterials	☐ Biomechanics	☐ Clinical	☒ Innovation

INTRODUCTION: Calcium phosphates cements (CPCs) are used as bone substitutes because of their similarity to the mineral phase of bone. But these CPCs present some drawbacks: they can be considered as fragile materials and they usually present limited osteoconductive properties. This explains why they still are dedicated to fill small bone defects in non-load bearing conditions. A recent study [1] has shown that combining blood to CaP micro-particles could bring interesting textural and biological features to the considered. The purpose of this study was to investigate how blood addition can interfere with setting processes and final properties of two types of apatitic CPCs, one presenting a shorter setting time (SST) and the other one a longer setting time (LST).

MATERIALS & METHODS: Two cement formulations (SST and LST) containing mainly α-TCP were studied. The used liquid phases were either a Na_2HPO_4 solution or blood freshly taken from sheep. The chemical transformation of α-TCP to apatite was followed using X-ray diffraction and infrared spectrometry. Three different parameters were compared: setting time (using Gilmore's needle apparatus), injectability and compressive strength. Eventually, a preliminary *in vivo* study in sheep vertebral bodies was conducted to evaluate the biological response of blood-combined SST cement.

RESULTS: α-TCP was transformed into poorly crystalline apatite in all tested samples after 72 hours of incubation in a saline solution. For blood/LST cement, both adhesion properties and time of workability were significantly increased. Compressive strength tests showed a typical ductile material behavior (fig 1.A). Regarding to blood/SST cement (fig 1.B) only a slight increase of both properties and time of workability was observed. After 12 weeks of implantation we could observe an excellent bone/implant osteocoalescent interface.

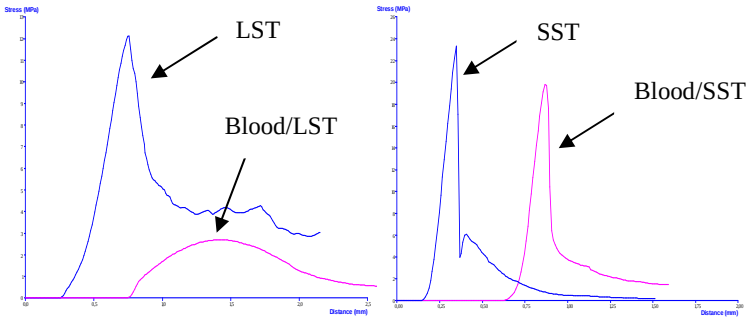

Fig. 1: Comparative compressive strength tests for CPC and blood/CPC (A) LST, (B) SST.

CONCLUSIONS: This study showed that adding blood can have different effects on CPCs properties assuming that they present different setting features. In vivo, it is known that fibrinogen present in the blood usually polymerize into fibrin within 12 minutes approximately. Our hypothesis is as following: when CPC setting time is longer than 12 minutes, significant modifications, possibly due to the fibrin polymerization, of textural and mechanical properties can be observed. On the other hand, for quicker setting times, those properties are only governed by apatite crystallization which suggests that fibrinogen is not able to polymerize into fibrin in that case. Assuming that biological properties do not seem to be jeopardized by blood addition, it seems we have found a very simple way to modulated stiffness and plasticity of apatitic CPCs which could extend potential applications of these injectable biomaterials.

REFERENCES: Balaguer et al., *Tissue Eng Part A.* (2010) **16**: 3495-505

ACKNOWLEDGEMENTS: This work was partially funded by ANR BRB (Tecsan Program 2010-2011) and supported by Graftys SA, Aix en Provence – France.

Macroporous brushite bone cement

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x☐ Biomaterials	☐ Biomechanics	☐ Clinical	☐ Innovation

INTRODUCTION: Brushite ($CaHPO_4 \cdot 2H_2O$) is a metastable calcium phosphate cement which can form under physiological conditions. Recently brushite cements have been of interest as potential bone substitutes due to their resorbability in comparison to apatite cements. The use of water soluble porogens in the base formulation of the cement allows the creation of micro and macro porous structures that facilitate cellular infiltration, thus enhancing bone growth. However, the porosity decreases the mechanical properties which may cause premature implant failure. The aim of the current work was to create a porous cement with optimized properties that facilitates bone growth. The effect of concentration of the porogen on the mechanical properties is reported, with preliminary *in vitro* data on adhesion of cells on the micro and macro porous cements.

METHODS: Brushite bone cements were produced by manual mixing of a solid phase made of equimolar quantities of β-tricalcium phosphate (β-TCP: $Ca_3(PO_4)_2$ assay ≥96% (Fluka Germany), Monocalcium phosphate monohydrate (MCPM: $Ca(H_2PO_4)_2 \cdot H_20$, assay min. 98%) (Sharlau, Spain) and mannitol single crystals in volume fractions between 0 and 15 vol.%, with a liquid phase consisting of sodium citrate solution. A 3:1 powder: liquid ratio was maintained for all the formulations. Water- soluble mannitol crystals were used as a porogen and obtained from re-crystallization using a saturated solution of commercial mannitol. The crystals obtained were of acicular shape and were sieved to keep the diameter in the range of 250-500 μm. The cement samples containing the porogen was allowed to harden and then immersed in deionized water, to remove the porogen. The confirmation of a brushite phase was achieved by means of X-ray diffraction. Compressive test of brushite samples were carried out using cylindrical shape specimens (16mm in length x 8mm in diameter), using a servo-hydraulic machine at a loading rate of 1mm/min starting from a preload of 20N. To estimate the percolation threshold of the macropores contained in the samples, some of them were charged with graphite rods similar in size and shape to the mannitol crystals and the electric conductivity between electrodes fixed to the base was measured by ohmmeter.Cell viability and adhesion on the different samples was assessed using various in vitro cell culture methods such as MTT and alamarBlue.

RESULTS: The X-ray diffraction measurement showed a >95% degree of conversion into brushite phase (Fig. 1). As expected, the compressive strength and modulus decreased with increasing amounts of porogen as shown in Table 1. MTT tests showing metabolic activity of HOS (Fig.2) cells that were exposed to cement elution fluids for 24 and 48 h indicated no statistically significant difference between the experimental and control groups (Kruskal-wallis One Way Anova of variance on Rank(P=0.519).

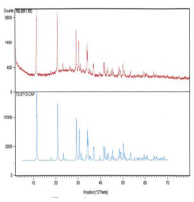

Fig. 1:XRD of brushite(top) with reference brushite

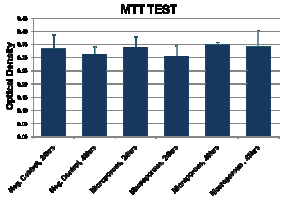

Fig.2: MTT showing metabolic activity of HOS cells on elution fluids at 24 & 48 h.

% v/v mannitol	<σc> (MPa)	Stand.Dev. σc (MPa)	<E> (GPa)	Stand.Dev. E (GPa)
0	32.6	0,8	4.2	0.3
5	24	1.1	2.8	0.6
10	20.4	1.7	2.6	0.4
15	17.5	1.6	2.5	0.2

Table I. Mechanical properties of macroporous cements

CONCLUSIONS: It is seen that the compressive strength of the cement with the highest volume fraction of porogen (15 vol.%), is on average 17MPa, superior to that of cancellous bone (2-12 MPa)* and the introduction of macroporous in the cement tends to reduce its mechanical properties according to a law of the type:$Y=Y_o(1-f_p)^k$ where, Y represents the considered property (σ_c or E) and Y_0 the corresponding value for a non-porous cement; f_p is the volume fraction of macropores and k is a constant exponent expected to depend on the shape and distribution of macropores. The results of the fit are shown in the logarithmic plot of Fig. 2?, where the estimate slopes of the straight lines represent the estimate values of exponent k, respectively $k_\sigma \cong 3.7$ for the compressive strength and $k_E \cong 3$ for the elastic modulus. According to this equation, for a given porosity σ_c can be enhanced by reducing exponent k_σ or by increasing $\sigma_{co.}$ The electric percolation threshold, i.e. the value of porosity corresponding to a rise of electric conductivity by at least one or more orders of magnitude, turned out to be about 30%vol. Unlike electric conductivity which demands at least a conductive path across the pores, osteoconductivity may be effective even with closed pores, because the dissolution process of brushite is expected to be able to open the pore walls. This argument suggests that a good osteoconductive brushite cement might have a porosity somewhat lower than the electric threshold (say 15-20% instead of 30%), with an improvement of mechanical strength. The scaffolds were observed to be non-toxic, promote cell adhesion and spreading on the scaffold surfaces.

Lectures

Chairmen: Michael LIEBSCHNER & Johannes HIERHOLZER

Biomechanics of VBA

G. Zoarski

Section of Neuroradiology, Department of Diagnostic Radiology, University of Maryland School of Medicine, Baltimore, Maryland, USA

Vertebral Fracture and Augmentation Influence Load-Bearing by Neighbouring Vertebrae

M.A. Adams

Centre for Comparative and Clinical Anatomy, University of Bristol, Bristol, UK.

Abstract is included, page 28.

Vertebral fracture and augmentation influence load-bearing by neighbouring vertebrae.

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☐ Biomaterials	☒ Biomechanics	☐ Clinical	☐ Innovation

INTRODUCTION: Fracture of an osteoporotic vertebral body reduces vertebral stiffness, and decompresses the nucleus in the adjacent intervertebral disc. This leads to high compressive stresses acting on the annulus and neural arch (1). Altered load-sharing at the fractured level is suspected to influence loading of neighbouring vertebrae, increasing the risk of a fracture "cascade". Vertebroplasty has been shown to normalise load-bearing by fractured vertebrae (1) but it may increase the risk of adjacent level fracture (2). The aim of this study was to determine the effects of fracture and subsequent vertebroplasty on the loading of neighbouring (non-augmented) vertebrae.

METHODS: 28 three-vertebra cadaver spine specimens (aged 67-92 yrs) were loaded on a materials testing machine to induce fracture. Specimens underwent vertebroplasty, either with PMMA or with a resin (Cortoss), and consolidation was allowed for 1hr under a constant load of 1.0 kN. In 17 specimens, fracture occurred in the uppermost or lowermost vertebra, leaving two adjacent vertebrae and the intervening ('unaffected') disc intact. The distribution of compressive "stress" was measured in both intervertebral discs, by pulling a needle-mounted pressure transducer through each one while the spine specimen was loaded at 1 kN (3). "Stress profiles" were obtained at each stage of the experiment, in simulated flexed and extended postures. They indicated the average intradiscal pressure (IDP) in the nucleus, and the size of stress concentrations in the anterior (SP_A) and posterior (SP_P) annulus (Fig. 1). Compressive load-bearing by anterior (F_A) and posterior (F_P) halves of the vertebral body, and by the neural arch (F_N), were determined by integration of the stress profiles (4).

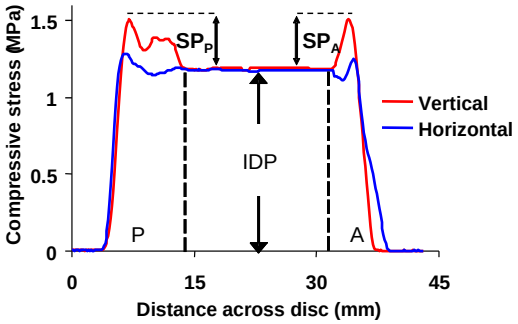

Figure 1. "Stress profiles" from a lumbar disc.

RESULTS: No differences were found between PMMA and Cortoss, so data were pooled for all 17 'unaffected' discs. As expected, fracture caused major changes in the adjacent disc, which were largely reversed by vertebroplasty. Importantly, similar but generally less-marked changes were also observed in the 'unaffected' disc which lay between non-fractured vertebrae (Table 1). Evidently, these intact vertebrae were adversely affected by the neighbouring fracture, and they received some benefit from vertebroplasty.

	Pre-fracture	Post-fracture	Post-VP	Post-Creep	ANOVA
IDP(flexi)	0.89 (0.43)	0.77 (0.42)	0.80 (0.49	0.76 (0.44)	0.037
IDP(ext)	0.93 (0.38)	0.69** (0.49)	0.75*+ (0.52)	0.72** (0.46)	<0.001
SP_A(flex)	1.60 (1.81)	0.82* (1.31)	1.02* (1.16)	1.30 (1.52)	0.011
SP_P(flex)	0.24 (0.37)	0.76* (0.85)	0.39 (0.53)	0.39 (0.52)	0.01
F_A(flex)	55.21 (20.88)	35.50** (14.59)	44.30*+ (15.75)	47.39+ (20.06)	<0.001
F_A(ext)	36.24 (16.33)	27.36** (15.59)	31.94 (12.84)	30.52* (12.38)	0.009
F_N(flex)	16.56 (16.43)	30.72** (15.39)	25.86 (19.75)	24.12 (18.94)	0.01
F_N(ext)	21.88 (18.15)	37.12** (24.29)	33.51* (22.14)	37.11** (21.52)	0.001

*: $p<0.05$, **: $p<0.01$ compared with pre-fracture;
+: $p<0.05$ compared with post-fracture
(VP = vertebroplasty)

Table 1. Mean (SD) data in flexion (flex) and extension (ext) for 17 discs lying between non-fractured vertebrae.

CONCLUSIONS: Vertebral fracture decompresses the adjacent intervertebral disc and profoundly influences the manner in which it applies compresssive load to the next vertebral body in the spine. Vertebroplasty substantially reverses these changes. Smaller but nevertheless significant changes were also observed in the next intervertebral disc along, so both fracture and vertebroplasty exert their effects on at least two vertebrae removed from the fracture site. By restoring normal load-sharing towards pre-fracture values, vertebroplasty may help reduce the risk of a spinal fracture cascade.

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4. Pollintine P et al (2004). Neural arch load-bearing in old and degenerated spines. J Biomech 37:197-204.

ACKNOWLEDGEMENTS: This work was funded by Action Medical Research. Vertebroplasty materials were provided by Stryker UK and by Orthovita.

Atraumatic vertebral deformity arising from an accelerated "creep" mechanism.

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[1] *Department of Life Sciences, University of Roehampton, London, U.K.*
[2] *Centre for Comparative and Clinical Anatomy, University of Bristol, Bristol, U.K.*

☐ Biomaterials	X Biomechanics	☐ Clinical	☐ Innovation

INTRODUCTION: Vertebral deformities often occur in patients who recall no trauma, and display no evident fracture on radiographs. We have shown that old human vertebrae can deform by a gradual "creep" mechanism (1), and we now hypothesise that creep is greatly accelerated following minor damage.

METHODS: Forty-five thoracolumbar spine motion segments were tested from cadavers aged 42-92 yrs. Vertebral body areal BMD was measured using DXA. Each specimen was compressed at 1 kN for 30 min (Fig 1), while creep deformation of each vertebral body was measured using an optical MacReflex system. After 30 min recovery, each specimen was subjected to a controlled overload event which caused minor damage to one of its vertebrae, and the creep test was repeated.

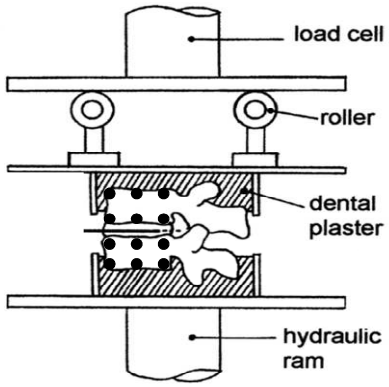

Fig. 1: Motion segment subjected to compressive loading. Roller height could be adjusted to allow the specimen to be loaded in pure compression (as shown) or in flexion (height of the left roller increased). Black circles indicate reflective markers on each vertebra.

RESULTS: Vertebral body creep (Fig 2) was measurable in specimens with areal BMD < 0.5 g/cm^2. Creep was greater anteriorly than posteriorly ($p<0.001$) so that vertebrae developed an anterior wedge deformity. Compressive overload reduced specimen height by 2.24 mm (STD 0.77 mm), and increased vertebral body creep by 800% (anteriorly), 1000% (centrally) and 600% (posteriorly) as shown in Figure 3. In 34 vertebrae with complete before-and-after data, anterior wedging occuring during the 1st creep test averaged 0.07° (STD 0.17°), and in the 2nd test (after damage) it averaged 0.79° (STD 1.03°). The increase was highly significant ($P<0.001$). Vertebral body wedging during the 2nd creep test was proportional to the severity of damage, as quantified by specimen height loss ($r^2=0.51$, $p<0.001$, $n = 34$).

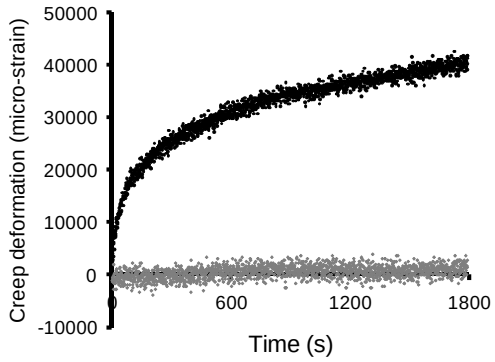

Fig. 2: Typical 'creep' curves for the anterior region of an L3 vertebral body. Initial elastic deformations have been omitted. Creep is shown for the undamaged vertebra (lower) and after minor vertebral damage (upper). Note that creep appears continuous, even in the damaged vertebra, and that the rate of creep falls with time. Data are shown before smoothing.

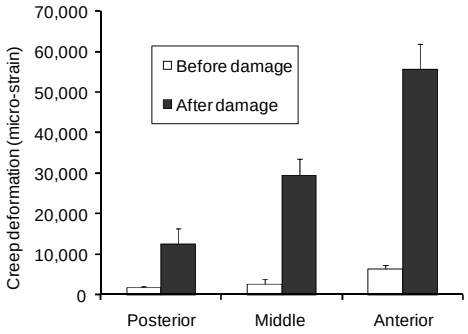

Fig. 3: Creep deformations increased after minor vertebral damage (all regions $P<0.001$) especially in the anterior vertebral body. Error bars indicate SEM.

CONCLUSIONS: Creep in old vertebrae increases greatly if the vertebra sustains even minor damage. The "minor" damage reproduced here is barely discernible on radiographs (2), and immediately increases anterior wedging of the vertebra by an average 0.95°. This is similar to the 0.79° anterior wedging caused here by creep. Our hypothesis is supported. We conclude that 'atraumatic' vertebral deformity can be created by a mechanism involving minor injuries and creep.

REFERENCES:

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2. Jiang et al. (2010). Vertebral fractures in the elderly may not always be 'osteoporotic'. Bone 47 111-6.

ACKNOWLEDGEMENTS: This work was funded by Action Medical Research in the UK.

Key Lectures

Chairmen: Stephan BECKER, Peter JARZEM & Bob POSER

Market and Regulatory Burdens in USA

R. Peters, USA

Entrepreneur and Early Stage CEO

Conflict of Interest, Patient Safety, and the Regulatory Burden Outside the United States

H. Yuan

Professor Emeritus of Orthopedic and Neurosurgery, State University of New York, Upstate Medical University, Syracuse, New York, USA

Intellectual Properties in VBA

R. Mitchell

Patent Agent and Retired Partner at Ogilvy Renault, Canada

Session 5

INDUSTRIAL INNOVATION

Chairmen: Gian-Carlo ANSELMETTI, Herve DERAMOND & Kieran MURPHY

Spinealign Augmentation System

G.C. Anselmetti

Istituto per la Ricerca e Cura del Cancro, Candiolo (Torino) – Italy

Kiva Augmentation System

S. Tutton

Departments of Vascular Surgery and Interventional Radiology, Medical College of Wisconsin, Milwaukee, Wisconsin, USA

Site Specific Bone Augmentation Therapy from Unigene

N. Mehta[2], J. Carlson[1], M. Kim[1], Q. Zhang[1], J. Gilligan[2], K. Murphy[3], A. Vignery[1]

[1]Yale University School of Medicine, New Haven, CT. [2]Unigene Laboratories, Inc., Boonton, NJ. [3]Department of Medical Imaging, University of Toronto, Toronto, Ontario, Canada

Abstract is included, page 37.

Shield Kyphoplasty System

J. Hierholzer

Klinikum Ernst von Bergmann GmbH, Potsdam, Germany

Abstract is included, page 38.

Skeltex ISV System

S. Becker

IMSART, Vienna, Austria

Rapid Site-Specific Bone Growth by a Combination of Bone Marrow Ablation, Bone Compatible Cement and PTH Therapy

Nozer Mehta[2], Jodi Carlson[1], Michael Kim[1], Qing Zhang[1], James Gilligan[2], Kieran Murphy[3], Agnès Vignery[1]
[1]Yale University School of Medicine, New Haven, CT; [2]Unigene Laboratories, Inc., Boonton, NJ;[3] Department of Medical Imaging, University of Toronto, Toronto, Ontario, Canada

x Biomaterials	☐ Biomechanics	☐ Clinical	x Innovation

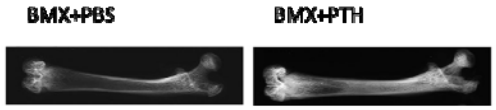
INTRODUCTION: After mechanical bone marrow ablation (BMX), a distinct sequence of events takes place: clot formation, capillary infiltration of the marrow cavity, migration of mesenchymal precursor cells, differentiation of osteoblasts, and formation of cancellous bone. This intramembranous bone formation is distinct from fracture repair in which woven bone replaces regenerated cartilage during endochondral bone formation. The bone-formation phase following irrigation of the bone marrow is completed by day 7 at which time osteoclasts differentiate in synchrony and resorb the newly formed bone to re-create the marrow cavity for bone marrow cell repopulation. This transient induction of bone formation in response to marrow ablation has previously been used as an *in vivo* model to discover new genes, and to investigate the role of known genes, in the process of bone formation. We hypothesized that administration of anabolic hormones such as PTH following marrow ablation could promote and sustain bone formation. We also hypothesized that the formation of newly formed bone could be enhanced in the presence of a bone compatible cement and further, the new bone could be preserved by alendronate, which inhibits osteoclastic bone resorption.

METHODS: Fisher 344 male rats averaging 200 g (Charles River, Kingston, NY) were subjected to femoral marrow ablation as we previously described (Tissue Eng. 14:237, 2008). The marrow cavity of the left femur was flushed with saline and a pipe cleaner was used to remove marrow cells and debris. Control animals were subjected to sham operations in which the femurs were not subjected to bone marrow ablation. A recombinant analog of human PTH (PTH(1-34)NH2; 40 ug/kg/day, Unigene Laboratories, Inc., Boonton, NJ) was injected on the day of surgery and continued for 21 or 84 consecutive days, after which time the animals were euthanized. Alendronate (Sigma, 28 µg/Kg) was injected twice weekly. The marrow femoral cavity of some rats was filled with calcium phosphate based biomatrices (cements) and treated with PBS or PTH for 3 months,. The rats received two i.p. injections of calcein (10 µg/g body weight; Merck, Darmstadt, Germany) on days 8 and 1 before sacrifice. Bone radiography, bone densitometry, computed tomography (micro CT), biomechanical testing, three-point bending test, histology, microscopy, biochemical parameters and statistical analysis were carried out by standard techniques

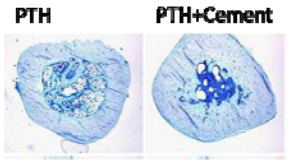
RESULTS and CONCLUSION:
Ablation of bone marrow cells from the femur of rats followed by daily injections of PTH for 21days results in a dramatic increase in bone growth as measured by X-rays (Figure 1). Longer term treatment with PTH for 3 months following bone marrow ablation also results in a dramatic increase in cortical thickness. (Figure 2A). The femoral shafts from PTH-treated BMX rats demonstrated a 43% increase in cortical thickness when compared with controls, and 30% when compared with BMX alone. This 43% increase resulted for the most part from a 35% reduction in endosteal circumference. Marrow ablation alone led to an 8% increase in periosteal circumference. Our results thus demonstrate that BMX induces periosteal bone formation, and potentiates endosteal bone formation induced by PTH.The thickness attained far exceeds that achievable by treatment with PTH alone. It is therefore the combination of the treatments, resulting in increased cortical thickness, which is novel.

- Calcium phosphate cements placed in the marrow cavity of ablated rat femurs and treated with PTH for 3 months promotes the formation of new bone that persists for extended times in the marrow cavity (Figure 2B).

  This technology may potentially be useful for preferential site-directed bone growth in areas of high bone loss, for fracture repair, and for reinforcing the implantation of prosthetic devices.



Bone marrow ablation of rat femur followed by treatment with PTH or vehicle for 21 days. PTH treated femur displays increased bone growth in marrow cavity



Bio-compatible calcium phosphate cement injected into rat femur results in increased cortical bone growth following BMX and PTH treatment

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Comparison of Directed Cement Flow Kyphoplasty and Vertebroplasty in a Prospective, Controlled, Randomized Trial

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☐ Biomaterials	☐ Biomechanics	☐ Clinical	☒ Innovation

INTRODUCTION: A cement directing kyphoplasty system has been developed to provide directional control of cement flow during treatment of painful vertebral compression fractures. This system uses specialized instrumentation to create a central cavity in the vertebral body and insert an implant that directs cement flow. The goal is to place cement on both sides of the sagittal midline, focussing cement flow towards the anterior, superior, and inferior directions, while restricting posterior flow to minimize leakage into the basivertebral vein and spinal canal.

METHODS: A randomized, controlled multi-center clinical study comparing the Shield Kyphoplasty System (SKS, Soteira Inc., Natick, MA) and percutaneous vertebroplasty (PVP) was performed. Patients were randomized 2:1 to receive treatment with SKS or PVP, respectively (SKS=49 pts/65 levels), PVP=28 pts/39 levels). All patients were ≥50 years old with 1-3 painful osteoporotic vertebral compression fractures between T4 and L5.

Pain was assessed pre-operatively using a 10-point visual analog scale (VAS). Patients were randomized into one of the two groups and the SKS or PVP surgical procedure was performed. Post-operative assessment took place within 24 hours and included evaluation of VAS pain scores, A/P and lateral radiographs, and CT scans. Follow up visits occurred at 3 months and one year. Radiographs (A/P and lateral) and CT scans were obtained at 3 months and radiographs were obtained at 12 months. Changes in anterior vertebral body height were determined from the difference between the post-op and 3 month CT heights for 21 levels (n=11 for SKS and n=10 for PVP) from a single site to insure consistency in image quality.

RESULTS: Cement flow in the SKS group was reproducibly directed towards the anterior, superior and inferior regions of the vertebral body (Fig. 1). In contrast, the cement in the PVP group flowed randomly. Pain relief was achieved immediately for both SKS and PVP and pain scores remained stable throughout the 12 month follow up period (Fig 2). The decrease in the post-treatment VAS scores was statistically significant for both treatment groups at every follow up interval ($p<0.0001$ for all comparisons). The mean change in vertebral body height between treatment and 3 months was -4.00% (±8.52) and -9.49% (±8.28) for SKS and PVP, respectively. Levels treated with SKS experienced a smaller decrease in height with time, as compared to levels treated with PVP, although this was not statistically significant (t-test, p=0.1513).

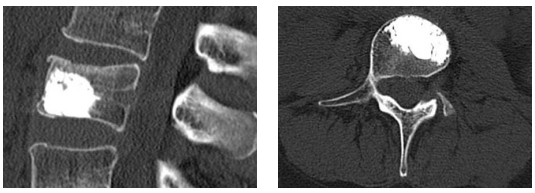

Fig. 1: Sagittal (left) and axial (right) CT images of the cement mantle created by the Shield implant.

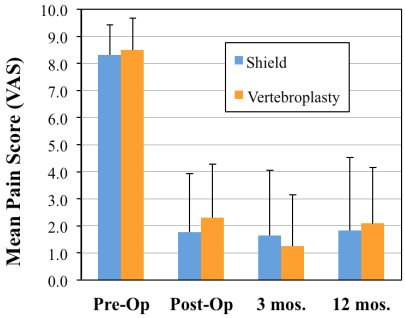

Fig. 2: Comparison of VAS pain scores.

Examination of 12-month radiographs indicated that 2 adjacent level fractures (3.1%) developed in the SKS group and 3 (7.9%) in the PVP group. In comparison, Lee et al. (1) reported 7.4% and 10.2% of adjacent level fracture rates for prospective studies of PVP and balloon kyphoplasty, respectively.

CONCLUSIONS: Directed cement flow kyphoplasty provides controlled and reproducible cement delivery into the anterior, superior and inferior regions of the vertebral body. Pain relief for SKS is equivalent to PVP and is sustained long term. Adjacent level fracture rates for SKS are lower than published rates for PVP and balloon kyphoplasty. Finally, SKS allows post-operative vertebral body height to be maintained by providing a well-interdigitated cement mantle that stabilizes the vertebral body and provides overall biomechanical reinforcement.

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ACKNOWLEDGEMENTS: Funding for this study was provided by Soteira, Inc., Natick, MA, USA

Session 6

TUMOUR SESSION

Chairmen: John MATHIS , Allan BROOK & Bassem GEORGY

Augmentation in Malignant Lesions; Imaging, Biomechanics and Approach.

B. Georgy

University of California, San Diego San Diego, California, USA

Radiofrequency ablation in combination with cement injection and treatment of malignant lesions

P. Munk

Vancouver General Hospital and the University of British Columbia, Canada

Abstract is included, page 43-44.

Augmentation of Cervical Malignant Lesions

G.C. Anselmetti

Istituto per la Ricerca e Cura del Cancro, Candiolo (Torino) – Italy

PMMA and Radioisotopes in VBA

A. Hirsch

Department of Radiation Oncology, Massachusetts General Hospital, Harvard Medical School, USA

Innovative Approaches to Tumour and Oligometaststic Disease

K. Murphy

University of Toronto, Toronto, Ontario, Canada

ABSTRACT FOR THE BOSTON MEETING OF GRIBOI (2011)

Radiofrequency ablation in combination with cement injection and treatment of malignant lesions.

Peter L Munk
Vancouver General Hospital and the University of British Columbia
Vancouver, BC, Canada

This lecture will provide an overview of the potential role of radiofrequency ablation combined with cement augmentation in the treatment of patients with painful malignant lesions of the skeleton.

It is well established that injection of cement in many instances will provide pain relief in patients with metastatic lesions from epithelial malignancies or myeloma. Other investigators have shown that radiofrequency ablation is also quite effective in the treatment of selected lesions. A small body of literature has appeared suggesting that there may be synergistic effect if both are used although direct randomized comparative trials are not available. Although pain relief may be obtained with radiofrequency ablation alone in the case of lytic lesions, concern about structural integrity especially in weight-bearing of bone such as the vertebral column or acetabulum exists. Although pain may initially be relieved, this does not prevent pathologic fracture or collapse from occurring which not only may cause pain in itself but results in mechanical compromise of large joints and nerve root impingement and/or paralysis in the spine. In these instances, augmentation with cement may prove beneficial. Other potential advantages of performing thrombal ablation are

1. Creation of a virtual cavity for cement producing desiccation within tumor.
2. Rendering a large portion of the tumor nonviable following thermal ablation thereby potentially decreasing the risk of further metastasization of tumor on injection of cement. These advantages remain conjectural.

In our practice, particularly patients with lytic destructive lesions of bone undergo radiofrequency ablation under either fluoroscopic or CT-guidance. Attention must be paid to avoid ablation of crucial structures such as nerves. Radiofrequency ablation is usually down coaxially through an introducer needle and after ablation is performed the needle can then be advanced and cement injected. At present, our group has performed a total of 74 combined radiofrequency ablation and cementoplasty procedures (44 vertebra, 22 acetabulum, 4 sacrum, 4 other locations). 100% technical success was achieved. The mean pre-procedural pain is measured on a visual analog scale

was 7.2 out of 10 and decreased to 3.4 out of 10 post-procedure. Single complication of resolving transient thermal sciatic neural damage was experienced.

IMPRESSION: Combined radiofrequency ablation and cementoplasty may be helpful in further augmenting the effect of these treatments in the palliative management of patient's with painful neoplastic lesions of bone.

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JVIR 2009:7;903-11

Reduced Cement Leakage with Directed Cement Flow Kyphoplasty

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☐ Biomaterials	☐ Biomechanics	☐ Clinical	☒ Innovation

INTRODUCTION: In vertebroplasty procedures, the clinician has limited control over the direction of cement flow, which frequently results in unanticipated cement leakage and the risk of clinical complications. In contrast, balloon kyphoplasty restricts cement flow to the prepared cavity, limiting leakage and also limiting biomechanical stabilization of the surrounding bone. This leaves the vertebral body vulnerable to continued collapse over time (1). Directed cement flow kyphoplasty is a unique approach which provides controlled cement delivery while minimizing posterior flow, reducing the risk of leakage into the basivertebral vein and spinal canal.

METHODS: A prospective, randomized, controlled multi-center clinical study comparing the Shield Kyphoplasty System (SKS, Soteira Inc., Natick, MA) and percutaneous vertebroplasty (PVP) was performed. Patients were randomized 2:1 to receive treatment with SKS or PVP, respectively (SKS=49 pts/65 levels, PVP=28 pts/39 levels). All patients were ≥50 years old with 1-3 painful osteoporotic vertebral compression fractures between T4 and L5. The SKS procedure included creation of a central cavity using a unipedicular approach with specialized curving instrumentation, insertion of a self-expanding cement directing implant and cement injection. Holes on the anterior surface of the cement directing implant guided cement flow toward the anterior, superior and inferior regions of the vertebral body. The PVP procedure was performed according to the standard technique practiced by the investigator.

Cement leakage was evaluated from post-operative CT images. Leaks were rigorously identified without regard to cement volume. Multiple leaks were counted and categorized separately. Leaks were classified according to location using the scheme shown (Fig. 1), which was developed to provide greater detail about specific leak locations than the previously published method (2).

RESULTS: Directed cement flow kyphoplasty reduced the overall cement leakage rate. The leakage rate for SKS was 48.5% (leaks per levels treated), as compared to 73.7% for PVP and 52% reported in the literature for balloon kyphoplasty (3). CT leakage rates are often considerably higher than radiographic leakage rates, due to increased resolution and the additional axial view.

Treatment with SKS also effectively decreased cement leakage in the posterior direction (Fig. 2). The

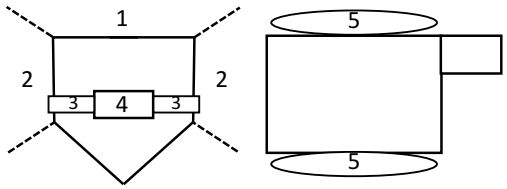

Fig. 1: Cement leak classification (axial vertebral body view left, sagittal view right): 1 - anterior cortical leaks, 2 - medial or lateral cortical leaks, 3 - leaks through the neuroforamen, 4 - spinal canal leaks, 5 - endplate leaks

number of Location 2 and Location 4 leaks were significantly reduced for SKS, as compared to PVP (two-tailed Wilcoxon test, p=0.005 and p=0.026, respectively). An insufficient number of Location 3 leaks were detected to enable analysis.

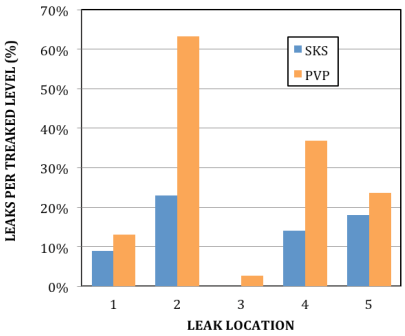

Fig. 2: Comparison of leak distribution by location.

CONCLUSIONS: Cement directed kyphoplasty represents a new advance in the treatment options for painful vertebral compression fractures, providing the capability for guided cement flow of cement into the anterior of the vertebral body. The potential for leakage into the spinal canal and the venous system is decreased by anteriorly directed cement flow, reducing the risk of serious leakage-related clinical complications. In addition, cement is allowed to fill spaces in the cancellous bone, interdigitating with the bone, stabilizing the fracture and providing long-term biomechanical reinforcement.

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Validation of a Novel Bone Tumor RF Ablation System – Physics and Animal Data

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☐ Biomaterials	☐ Biomechanics	☐ Clinical	☒ Innovation

INTRODUCTION: Bone metastases are likely to develop in more than 50% of cancer patients[1]. Metastatic bone tumors are most commonly found in the spine and can cause skeletal and neuropathic pain, adversely affecting patient quality of life. Current treatments for vertebral metastasis include radiation therapy, chemotherapy and surgical tumor debulking or resection. However, some tumors exhibit limited or no response to existing therapies due to resistant tumor morphology or location[2]. Thus, there remains an unmet need for minimally invasive spinal metastatic treatments and adjuncts that can ablate tumors and palliate pain.

Radiofrequency (RF) ablation is a minimally invasive technique whereby probes are inserted percutaneously into a targeted treatment site. High frequency oscillating electrical current is passed through the tip, which generates heat in the surrounding tissue and leads to cell death. RF ablation has been used to ablate soft tissue tumors such as liver, lung, and kidney neoplasms[3]. However, it is challenging to apply RF in the spine since bone is less thermally and electrically conductive than soft tissue. Furthermore, due to the large size and high vascularity of tumors, it is difficult to generate sufficient heat to effectively treat anatomically relevant volumes with currently marketed RF technologies[2].

This work investigates the physics and performance of a novel RF ablation system that is custom designed to treat bone metastasis. An internally cooled bipolar probe design permits creation of large lesions in heterogeneous bone tumor tissues in a consistent and controlled manner. Validation of this system for creating anatomically relevant tumor ablation lesions, as well as the pre-clinical safety of the treatment for spinal applications will be discussed.

METHODS: The efficacy of the bipolar RF ablation system was evaluated in a VX-2 metastatic carcinoma rabbit model. 6 lesions were created by direct bone injection of VX-2 tumor cells into the femoral canal. Lesions were treated with RF (65˚C cooled temperature, 15 minutes) 2 weeks following tumor injection. MRI analysis was performed immediately after treatment to characterize the size of treatment area, followed by histology analysis to determine tumor cell viability.

To evaluate the pre-clinical safety of the RF ablation system for vertebral treatment, RF lesioning was performed in a scale-up healthy porcine model with vertebral dimensions more relevant for potential human application (N=5; 65˚C cooled temperature, 15 minutes). The probe was inserted transpedicularly into the vertebral body with the aid of a 13G bone access needle under fluoroscopic guidance. A temperature monitoring probe was placed immediately outside the cortex to measure heat distribution to the surrounding area throughout the procedure. MRI scans of the resulting treatment area were analyzed at 0 days and 2 weeks following treatment. All animals were examined neurologically prior to and immediately after treatment, as well as periodically until the time of euthanasia.

RESULTS: All RF procedures in the rabbit femurs produced the desired controlled temperature response, demonstrating the ability of the RF system to generate tissue heating in bone tumors. MRI analysis of the treated femurs showed uniform ellipsoid lesions of 3cm x 2cm, while histology revealed corresponding tumor cell death. The RF system was also effective at treating porcine vertebrae, consistently eliciting the desired tissue heating response. The peripheral temperature remained at body temperature throughout all treatments, showing the protective effects of the vertebral cortex in preserving tissue beyond the treatment area. Post treatment MRI revealed clinically and anatomically relevant lesions spanning half the vertebrae (average 2.5cm x 1.3cm, projecting to the inner wall of the vertebral cortex). All animals demonstrated normal behavior during neurological assessment following treatment, indicating sensitive neural structures surrounding the treatment area remained intact.

CONCLUSIONS: This novel internally cooled bipolar probe design has proven to be effective at creating lesions in diseased and healthy bone that are anatomically relevant in size and shape. Furthermore, sensitive structures outside the treatment area were protected from undesirable heating effects by the vertebral cortex. As such, this RF system may represent a safe and effective treatment for vertebral tumor ablation and pain palliation.

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ACKNOWLEDGEMENTS: This work was supported by the Ontario Centres of Excellence.

Radioactive Bone Cement for the Treatment of Vertebral Metastases

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☐ Biomaterials	☐ Biomechanics	☐ Clinical	☐ Innovation

INTRODUCTION: Spinal metastases can cause pain, vertebral collapse, and serious neurologic complications. Conventional treatment often involves percutaneous vertebroplasty or kyphoplasty followed by radiation therapy such as external beam radiation therapy (EBRT) or stereotactic body radiotherapy (SBRT), which can require up to 10 separate treatment sessions. As a more convenient alternative, we propose that spinal metastases can be treated with radioactive bone cement, i.e., bone cement that contains a radionuclide, yielding a single procedure that would provide structural reinforcement to the bone while simultaneously irradiating the tumor from within (i.e. vertebral brachytherapy). In this study, we evaluated the clinical usefulness of the dose distributions from radioactive bone cement.

METHODS: The T12 vertebra from a 69 year old female donor was CT scanned, and a previously developed and validated CT scan-based Monte Carlo (MCNP) modeling method[1] was used to create an MCNP model of the vertebra. A 1.19 cm-diameter × 1.13 cm-height cylindrical volume of ArthroCare Parallax® PMMA bone cement (ArthroCare Corp., Sunnyvale, CA) containing a uniform distribution of phosphorus-32 (P-32) was simulated within the vertebral body.

From the MCNP model, a radial depth-dose curve was obtained and used to characterize the attenuation of dose with distance from the radioactive source. Based on the property that the dose distribution linearly scales with the initial activity, radial depth-dose curves were plotted for initial activities of 1, 2, 4, 8, and 16 mCi. For each initial activity, the resulting radial depth-dose curve was used to quantify: (a) the radial distance at which a therapeutic dose (TD) of 38 Gy was delivered (R_{TD}), where TD corresponded to a biologically effective dose[2] of 30 Gy delivered in 10 fractions of EBRT; (b) the maximum absorbed dose in the voxel directly adjacent to the cement (D_{Max}); (c) the radial distance at which the maximum allowable dose to the spinal cord (CD), 54 Gy, is delivered (R_{cord}), where CD corresponded to the biologically effective dose of 10 Gy delivered in a single fraction of SBRT[3]; and (d) the absorbed dose at the anterior surface of the spinal canal, corresponding to a radial distance of 7 mm from the cement (D_{7mm}).

RESULTS: The radial depth-dose curve for each initial activity is shown on a log scale in Figure 1, where the therapeutic dose of 38 Gy is also indicated. Dosimetric characteristics are summarized in Table 1.

CONCLUSIONS: Although R_{TD} can be extended by increasing the initial activity, D_{Max} doubles with each doubling of the initial activity, thus presenting an upper limit to the initial activity that can be safely implanted. Therefore, the practical limit on the level of implanted activity is likely 10-20 mCi, yielding a maximum R_{TD} for P-32 radioactive bone cement of about 5 mm. The clinical usefulness of this distance would depend on the accuracy with which the cement could be placed in the desired location within the vertebra. However, in the event of tumor progression or recurrence, retreatment with either radioactive bone cement or conventional radiotherapy could still be performed.

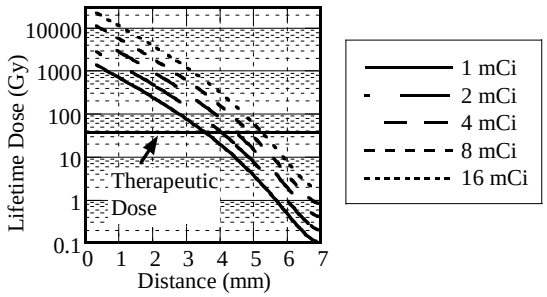

Fig. 1: Radial depth-dose curves for each initial activity.

Table 1: Dosimetric characteristics.

Initial Activity		R_{TD} (mm)	D_{Max} (Gy)	R_{cord} (mm)	D_{7mm} (Gy)
1 mCi	37 MBq	3.5	1445	3.2	0.10
2 mCi	74 MBq	4.0	2890	3.8	0.19
4 mCi	148 MBq	4.4	5780	4.2	0.39
8 mCi	296 MBq	4.8	11559	4.6	0.78
16 mCi	592 MBq	5.1	23119	5.0	1.56

Although the maximum dose in bone adjacent to the cement would likely lead to local bone resorption and necrosis, this effect would be mitigated by the presence of the cement itself, which would provide structural reinforcement to the affected region. Such high doses would also not be expected to considerably degrade the material properties of the cement itself, as only slight reductions result from doses as high as 100 kGy.[4] Additionally, the high dose near the cement may be useful for treating radiation-insensitive tumors such as melanoma, renal cell, and thyroid metastases.

Values for R_{cord} indicate that the radioactive cement should be kept at least 3-5 mm from radiosensitive tissues such as the spinal cord, similar to the 5 mm margin between tumor and spinal cord used in SBRT.[5] At 7 mm from the cement surface—the distance to the spinal canal in this vertebra—the absorbed dose (D_{7mm}) is much lower than the maximum allowable dose to the spinal cord. Thus, even in patients with prior spinal cord irradiation, the absorbed dose at this distance would be unlikely to cause spinal cord myelopathy.

With further development, radioactive bone cement may become a clinically-useful tool for treating spinal metastases.

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Calcium phosphate cements for local delivery of chemotherapeutics.

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■ Biomaterials	□ Biomechanics	□ Clinical	■ Innovation

INTRODUCTION. Several cancers can metastasize into bone tissue. If bone metastases are developed, palliative care can include surgical removal [1]. Subsequently, the remaining cavity needs to be filled and tumor regrowth needs to be avoided, necessitating additional chemotherapy [2]. An alternative strategy might be the direct injection at the metastasis site, of a bone filler supplemented with a chemotherapeutical agent. The obtained local delivery then avoids the necessity of systemic chemotherapy [3-5]. PMMA has been used for these purposes but there are several documented drawbacks with the use of this material such as cytotoxicity and poor delivery capacity [6, 7]. Calcium phosphate cements (CPCs) on the other hand are amply used as bone filling materials and might overcome these drawbacks. The aim of this study was develop local drug delivery model by using a CPC as a carrier for chemotherapeutic agents.

METHODS. CaP powders consisted of commercially available powders: alpha tricalcium phosphate (CAM BioCeramics BV, Netherlands), calcium phosphate dibasic (JT Baker Chemical Co., USA) and precipitated hydroxyapatite (Merck, Germany). Powders were ball milled (Pulverisette FRITSCH, Germany), and a 2% Na_2HPO_4 (Merck, Germany) solution was used as a liquid mixing phase in a liquid-to-powder ratio of 0.4 to create CPC pastes. CPC discs were created by injecting CPC pastes into molds. Scanning electron microscopy (SEM; JEOL 6310; Japan) was used in order to observe morphology of the powders. Transformation was studied by putting the CPC in contact with saline solution in a ratio of 10ml/g. Transformations were analyzed by X-Ray diffraction (XRD; PW3710 Philips, Netherlands) and Fourier-transform infrared spectroscopy (FTIR; Spectrum One Perkin Elmer, Netherlands). Paclitaxel (PX, Sigma-Aldrich) was used as the chemotherapeutic agent. PX was loaded on CPC discs by an absorption method. PX solutions -directly prepared or obtained after the release from the CPC - were used to test cell viability of osteosarcoma (U2OS) and metastatic breast cancer (MDA-MB-231) cells to different PX concentrations and the release effectiveness from CPCs. Cell viability was measured by an AlamarBlue assay. PX release was measured by High Performance Liquid Chromatography (HPLC). A loading model was performed to study the retention of proteins/drugs by the CPC. BSA was loaded onto the CPCs for this model. The release was measured by HPLC and the surface analyzed by XPS.

RESULTS AND DISCUSSION. Scanning electron microscopy showed changes in CPC morphology after immersion in Ringer's solution. X-Ray diffraction revealed the changes in the CPC phases due to immersion. The PX minimal lethal dose (LD_{50}) was found to be 90 µg/ml (Fig. 1). However, HPLC revealed that the real amount released of PX from the CPC after 24 hrs was 26.40 ± 2.50 µg/ml. Concluding that the retention of PX by the CPC was high. The loading model used for this CPC composition allowed to corroborate the retention behavior of this formulation and have an insight at the amounts retained. Cell viability confirmed the feasibility of using CPC as an effective delivery vector for these chemotherapeutic agents.

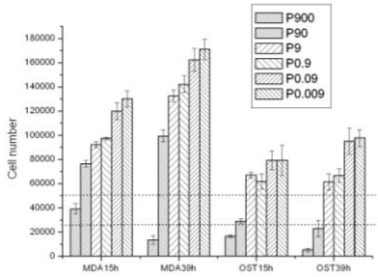

Figure 1. Cell viability with different PX solutions.

CONCLUSION. This study demonstrates that CPC is a feasible delivery vector for chemotherapeutic agents.

ACKNOWLEDGEMENTS: The authors gratefully acknowledge the support of the SmartMix TeRM Program of the Netherlands Ministry of Economic Affairs and the Netherlands Ministry of Education, Culture and Science.

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Session 7

CAVITY-ASSISTED VBA

Chairmen: Hansen YUAN, Sune LARSSON & Antonio KRUEGER

Kyphoplasty in Cancer Patients

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Kyphoplasty in Trauma Patients

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Kyphoplasty Using Calcium-Phosphate Cement Trauma Patients

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Abstract is included, page 54-55

Balloon Kyphoplasty in osteoporotic trauma

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Purpose
Kyphoplasty has become a standard procedure in the treatment of painful osteoporotic compression fractures. According to current guidelines, involvement of the posterior wall of the vertebral body is a relative contraindication.

Methods
From February 2002 until January 2008, 97 patients with at least one AO classification A 3.1 fracture were treated by kyphoplasty. There was a structured follow-up for the medium-term evaluation of the patients' outcome. The results were compared with a cohort of patients without involvemnt of the posterior edge of the vertebral body.

Results
Ninety-seven patients (68 of whom were females and 29 of whom were males) with involvement of the vertebra's posterior margin averaging 76.1 ± 12.36 (59–98) years were treated by kyphoplasty. The fractures of 75 patients were caused by falls from little height, 5 patients had suffered traffic accidents and in the case of 17 patients, no type of trauma was remembered. According to the AO classification, there were 109 A 3.1.1 and one A3.1.3 injuries. Prior to surgery, all patients were neurologically without pathological findings. Seventy-nine fractures were accompanied by a narrowing of the spinal canal [average of 15% (10–40)]. Overall, 134 vertebras were treated by Balloon kyphoplasty (81 x 1 segment, 22 x 2 segments, 3 x 3 segments). In 47.4% of the patients, cement leakage was observed after surgery. All patients with cement extravasation, however, were clinically unremarkable. Using the visual analog scale, patients stated that prior to surgery their pain averaged 8.1, whereas after surgery it significantly decreased and averaged 1.6 (p\0.001). In regard to pain reduction, 35% of the patients were free of pain. In 56.5% of the cases, the pain had decreased significantly. Overall, 91.5 of the patients profited from the kyphoplasty. At the time of the follow-up, however, 8.5% of the patients were still suffering from pain. At the time of the follow-up, the activity level of 69.8% of the patients was either the same or higher than compared to prior to the fracture. 30.2% of the patients were not able to achieve the same activity level as prior to the fracture. When asked about their subjective satisfaction with the treatment, 84.9% of the respondents said that they were very satisfied and 11.6% were moderately satisfied with the treatment. 3.5% of the respondents were dissatisfied with the treatment. Postoperatively it became necessary to release a subcutaneous hematoma in two cases. In 47.4 % of the patients, there was cement leaking outside the vertebras (23x intervertebral disk spaces, 7x basivertebral plexus, 38x paravertebral, 2x pedicle, 1x v. renalis (figure 2)). All cases of extravasation were clinically unremarkable. During their hospital stay, six patients were diagnosed with a urinary tract infection. Two patients died during their hospital stay. One female patient's death was caused by a mitral valve endocarditis, another female patient's death was caused by a cardiac insufficiency NYHA 4 and a severe obstructive pulmonary disease. The results of the patients suffering from a fracture with involvement of the posterior wall were compared to the ones with no involvement of the posterior wall. At the same time, between 01/2002

and 01/2008, 98 patients averaging 74.46 (50-92) years were treated. According to the AO there were 37 superior end plate impression fractures and 92 wedge compression fractures A 1.2.1. After conservative therapy, all patients continued suffering from persistently strong pain. The average ASA score was 3.03. In 42.86% of the patients there were cement extravasations. The difference between the cement extravasation in both groups was insignificant (p= 0,662). After surgery, the pain score on the VAS was reduced to 1.84 (±0,968) compared to 8.38 (±0,929) preoperatively.

Conclusion

In geriatric patients with osteoporotic traumatic vertebral fractures with partial inclusion of the posterior wall of the vertebral body, kyphoplasty is an effective procedure with few complications.

The use of calcium phosphate in percutaneous kyphoplasty: our experience in the treatment of spinal trauma patients

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Introduction and purpose: percutaneous kyphoplasty is an alternative technique in the treatment of spinal fractures.
Material and methods: we report our experience in 52 patients treated with calcium phosphate for the treatment of post-traumatic vertebral body fractures.
From January 2002 to December 2010, 387 patients (age ranging from 8 to 82 years) with A1-A2-A3 Magerl classification type post-traumatic vertebral thoraco-lumbar fractures were operated on by percutaneons Kyphoplasty. In 318 of these we used PMMA, in 17 "Activos" and in 52 calcium phosphate. Of these, 18 were treated with "Calcibon" and 34 with "Kyphos".
All patients underwent pre and post-treatment X-ray, CT scan and MRI evaluation.
Chronic pain, vertebral deformity and overall health state have been evaluated on outpatient basis using VAS score and Roland-Morris Disability Questionnaire.
Result: in our clinical cases, we performed the balloon kyphoplasty with calcium phosphate in 52 patients of 387 treated with balloon kyphoplasty for post-traumatic vertebral fractures. In the patients with calcium phosphate we obtained the immediate fractures stabilization with the satisfactory results. But, in the follow-up, we found the early resorption without an adequate replacement, with a significant discrepancy between radiological (very bad) and clinical (patients poorly symptomatic) findings. Ten patients showed the resorption without replacement and, ultimately within one month, 3 required open surgery with instrumentation and the other 7 a treatment with orthesis.
Conclusion: percutaneous kyphoplasty is a minimally invasive and promising technique for post-traumatic vertebral fractures even if long term follow up is required to fully evaluate the used materials. The authors report the results in the patients treated with calcium phosphate. Despite this material was used in the young, there was not evidence of adequate resistance to compression force. In conclusion, the calcium phospate must be used with extreme caution.

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Treatment of Non-Osteoporotic Burst-Type Vertebral Compression Fractures Using a New PEEK Implant In Combination with PMMA Cement

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☒ Biomaterials	☒ Biomechanics	☐ Clinical	☒ Innovation

INTRODUCTION: While much attention has been given towards treatment methodologies for osteoporotic vertebral compression fractures (VCF), minimally-invasive treatment options for non-osteoporotic fractures are more limited. Although vertebroplasty and kyphoplasty are used to treat acute traumatic fractures of the spine[1], many fracture morphologies are contraindicated for these technologies[2]. Fractures involving the posterior cortical wall, such as Magerl/AO Type A3 Burst-Type, may have elevated risk for extravasation into the spinal canal when injecting bone cement. A new alternative is the Kiva® VCF Treatment System, which utilizes a stacked coil PEEK implant (Fig. 1) to reduce the fracture and restore mechanical properties[3]. This device is used in combination with a small volume of bone cement, which is contained by the implant in order to prevent extravasation.
In this study, the restorative capability of the Kiva System was evaluated in a series of non-osteoporotic vertebrae with laboratory-created A3.1 burst fractures, and compared against a previous study[4] in which the device was used to treat osteoporotic A1.2.1 fractures. Biomechanical endpoints of compression stiffness and failure strength were compared to verify whether the Kiva System could be a viable alternative for treating *in vivo* burst fractures.

METHODS: 10 cadaveric vertebral bodies (VBs) harvested from 2 fresh-frozen human cadaveric spines were used for the study. BMD was measured to confirm the specimens were non-osteoporotic, with T-Scores above -1.0 SD.
Prior to treatment, all VBs were compressed to 35% height loss, as measured from the intact VB height, using a 3 degrees of freedom fixture mounted in an MTS material testing machine. A load path located central to the VB created a burst fracture. Radiographic evaluation showed posterior wall fracture involvement in all specimens. Per the Kiva IFU, each VB was cannulated unipedicularly, and a coiled nitinol guidewire deployed into the cancellous bone. The implant was then advanced over the guidewire to form a coiled construct. After removing the guidewire, approximately 2 mL of cement was injected into each VB through the implant. Each specimen was then tested at least 24 hours post-treatment to measure compressive failure strength and stiffness.

RESULTS: The compressive failure strength post-treatment exceeded the load required to induce fracture in all specimens, with a mean (SD) increase of 43% (31%). While this increase is consistent with the previous study, the treated non-osteoporotic VBs required more than twice the load to induce fracture (7.3 (1.1) kN v. 2.9 (0.4) kN, p<.001) over the osteoporotic VBs. Both studies used a similar cement volume (current study: 2.1 (0.3) mL v. 2.3 (0.2) mL, p= 0.21).
Compressive stiffness was significantly increased from the fractured state (Fig. 2) and is consistent with the results from the previous study.

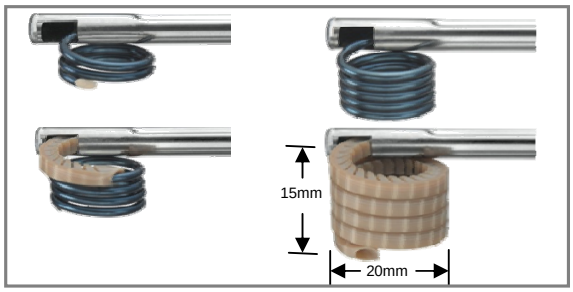

Fig. 1: Deployment sequence for the Kiva System

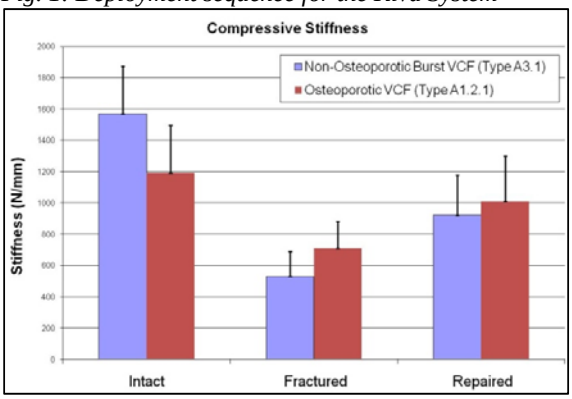

Fig. 2: Mean (+SD) compressive stiffness for all three conditions of each specimen

CONCLUSIONS: This study suggests the Kiva VCF Treatment System may be a good alternative to vertebroplasty and kyphoplasty for treatment of non-osteoporotic, trauma-induced, burst-type vertebral compression fractures. The PEEK implant, in conjunction with a small volume of bone cement, restores vertebral strength and stiffness comparable to that of previous research in osteoporotic fractures. The potential for enhanced cement containment may suggest a safer option for avoiding extra-osseous cement extravasation particularly in the posterior aspect of the VB. Further investigation with non load-bearing cements shall also be conducted.

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*US Regulatory Status: Subject of an FDA approved IDE Trial; EU: CE-Marked for VCF's due to osteoporosis or tumor.

NEW OSTEOCONDUCTIVE MATERIAL – CERAMENT - USED IN KYPHOPLASTY: RESULTS AT 1 YEAR

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☐ Biomaterials	☐ Biomechanics	☒ Clinical	☐ Innovation

INTRODUCTION:

The aim is study was to show safety and good clinical outcome for kyphoplasty treatment with a novel osteoconductive material with the ability to form new bone in osteoporotic and fractured vertebral bodies.

MATERIALS AND METHODS:

The study includes 20 patients with osteoporotic or traumatic vertebral body fractures, in sub-acute phase with pain and edema. The patients underwent kyphoplasty procedures with local anesthesia. Pre-operatory exams were the following: clinical visit using VAS and ODI score, X-ray, MRI and High Resolution CT. The kyphoplasty procedure was done using Kyphon BKP system and the cavity was filled with a novel osteoconductive and resorbable material (Cerament, Bone Support AB). X-ray, MRI and High Resolution CT as well as VAS and ODI scores were used to collect follow-up data. Follow-up examinations were done at 6 and 12 months post-op.

RESULTS:

No complications were recorded during the study Both the VAS and ODI scores were significantly reduced at both 6 and 12 months. ROI analyses of CTs on follow-up show signs of densification of the cancellous bone where the material had been injected. No further collapse and no new adjacent level fractures were seen during the study.

DISCUSSION:

This study shows that this new biological material, Cerament, can be safely used for treatment of sub acute and chronic vertebral body fractures using the kyphoplasty technique. The clinical outcome is excellent with significantly reduced VAS and ODI scores and no reported adjacent level fractures at 1 year. The material is osteoconductive and resorbable and will turn into bone in 1-1,5 years, which makes it especially interesting for younger patients. However, since 40% of the material is hydroxyapatite it may also be beneficial for osteoporotic patients since this hydroxyapatite will be incorporated in the new bony tissue and strengthen it.

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A Novel Device for Creating a Void During Vertebroplasty for Bone Metastases

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☐ Biomaterials	☐ Biomechanics	☐ Clinical	☐ Innovation

INTRODUCTION: Breast, prostate, lung, kidney and thyroid cancer, and even melanoma often metastasize to bone. The most common site of bone metastases is the spine, but tumors in other bones, especially the pelvis and femur, can also occur with some frequency. Procedures such as vertebroplasty or femoroplasty, or analogous procedures in other bones, sometimes called cementoplasty, can be performed to provide quick pain relief and to strengthen the bone. This procedure should then be followed by radiation therapy to inhibit further tumor growth, and we have developed a radioactive bone cement which will make it possible to alleviate pain, strengthen the bone and deliver radiation in one procedure[1]. Unfortunately, some cancers, particularly prostate cancer, produce lesions with blastic characteristics which can make access to the affected bone difficult and can make it impossible for cement to be injected. Thus, the goal of this work was to develop a device for minimally invasive surgery that can cut through and remove the dense bone created by blastic lesions so that a suitable cavity can be created for placement of bone cement.

METHODS: A novel device was developed to create a void inside a bone using minimally invasive surgery. This device was tested by performing vertebroplasty in the L2 vertebra of a 20-year-old human male donor who died from metastatic melanoma. After placing an 8-gage cannula into the vertebral body, the void-making device was inserted through the cannula and into the vertebral body. A void in the bone for placement of the cement was then created using the following procedure. After entering the vertebral body, the device was turned clockwise while pressing it against the bone to make the hole with the desired depth. The control wheel of the device was then rotated to open the blades (Fig. 1, top) and the device was rotated counter-clockwise to cut through the bone until a void of the desired length and width was created. The control wheel was then rotated to close the blades and the device was removed. Bone cement was then injected to complete the vertebroplasty procedure (Fig. 1, bottom). A similar procedure would be used if a tumor were present and were to be removed.

The device was also tested in a cadaveric proximal femur from a 74-year-old male donor with metastatic lung cancer. The device was used to create a void within the proximal femur in the proximity of blastic lesions identified radiographically.

RESULTS: This device has the following physical and operational characteristics[2]: it weighs 43 g, provides tactile feedback, is sterilizable, and does not interfere with existing procedures. In addition, this device is capable of creating a void 11.39 mm in diameter but it can pass through an 8-gage cannula with an inside diameter of just 3.71 mm. With this device, the physician can control both the shape and depth of the hole. This device is strong enough to remove blastic lesions from a bone, such as a vertebral body, sacrum, acetabulum or proximal femur, which we demonstrated on the proximal femur with blastic lesions from lung cancer. The void left by removal of the tumor can then be filled with bone cement (polymethylmethacrylate) (Fig. 1, bottom) to stabilize the bone, or filled with radioactive bone cement which would simultaneously alleviate pain, stabilize the bone and irradiate the residual tumor.

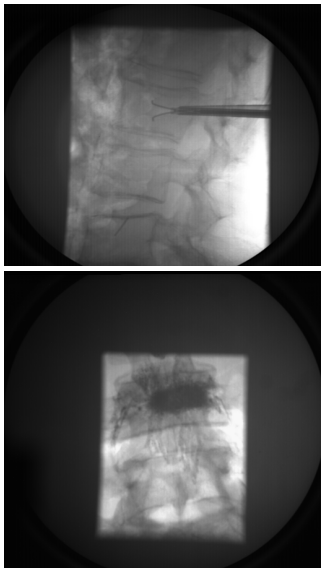

Figure 1. Lateral view of void-making device fully deployed (top), and anterior-posterior view of vertebra after cement injection (bottom).

CONCLUSIONS: This novel device can access a bone via a small cannula and can create a relatively large cavity. Unlike some other tools for creating a void for in a vertebral body, this tool does not just displace bone to create the void, and it does not just cut or break soft osteoporotic bone. This device can cut through dense bone and/or tumor material which can then be removed from the bone via suction. Thus, this new device has a significant advantage over other void-creation devices.

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COMPARISON OF RADIOFREQUENCY TARGETED VERTEBRAL AUGMENTATION (RF-TVA) TECHNIQUE VERSUS BALLOON KYPHOPLASTY IN AN *EX VIVO* VERTEBRAL COMPRESSION FRACTURE MODEL

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☐ Biomaterials	☐ Biomechanics	☐ Clinical	☐ Innovation

INTRODUCTION: Use of PMMA in balloon kyphoplasty (BKP) has been shown to be effective for pain relief VCF. However, balloon expansion in BKP crush trabecular bone to create cavities in an attempt to block PMMA extravasion.[1] This inadvertently can block PMMA interdigitation and been reported to result in a zone of necrotic bone surrounding the PMMA.[2] Subsequent resorption of necrotic bone may possibly cause PMMA loosening, PMMA mobility, adverse intravertebral stress and subsequent fracture across the remaining trabecular bone. Radiofrequency targeted vertebral augmentation (RF-TVA) procedure, has been developed to minimize trabecular destruction to permit targeted cavity creation and more controlled cement delivery. This *ex vivo* biomechanical study investigates and compares cavity creation, cement filling and height restoration during BKP and a targeted vertebral augmentation technique in a loaded and unloaded osteoporotic cadaveric vertebral compression fracture (VCF) model.

METHODS: Sixteen vertebral specimens (eight per treatment group) from six elderly human spine specimens were divided into loaded and unloaded groups within each treatment model. One half of the specimens were treated with bipedicular BKP and the other half with unipedicular RF-TVA. BKP was performed bipedicular, per manufacturer's recommendations. RF-TVA was performed unipedicular using the StabiliT Vertebral Augmentation System. RF-TVA utilized a navigational osteotome for unipedicular, site specific cavity creation and remotely controlled cement delivery via a controller that uses a hydraulic delivery system to deliver cement at 1.3cc/min and radiofrequency (RF) energy to modulate cement viscosity. Following VCF treatment, all specimens were imaged, measured for height restoration, and sectioned to evaluate PMMA distribution. Two specimens in each treatment group were imaged by CT to assess cavity creation and trabecular architecture *prior* to cement delivery.

RESULTS: Cadavers were 86.0 ±8.7 years of age. Bone mineral density of vertebra used averaged 0.64 ±0.15 g/cm^2. Mean PMMA volume delivered was 6.5 ±1.1 cc for the BKP group and 6.6 ±1.1 cc for the RF-TVA group with no statistical difference in volume delivered between the BKP and RF-TVA techniques under both loaded ($p = 0.133$) and unloaded conditions ($p = 0.474$). CT imaging, prior to cement delivery, revealed two large areas devoid of bone in the bipedicular BKP specimens and smaller more discrete cavities in the unipedicular RF-TVA specimens. Serial sectioning post cement delivery, revealed extensive PMMA interdigitation into the adjacent trabecular matrix peripheral to the discrete cavity in the RF-TVA specimens compared to little evidence of interdigitation beyond the large BKP created cavities. Significant difference was noted in mean anterior height restoration between the two vertebral augmentation methods. Loaded condition demonstrated a mean anterior height restoration of 57.7 ±23.1% for BKP and 73.9 ±15.3% for RF-TVA, $p=0.016$. In the unloaded condition, mean anterior height restoration was 77.6 ±17.0% for BKP and 91.0 ±14.8% for RF-TVA, $p = 0.015$.

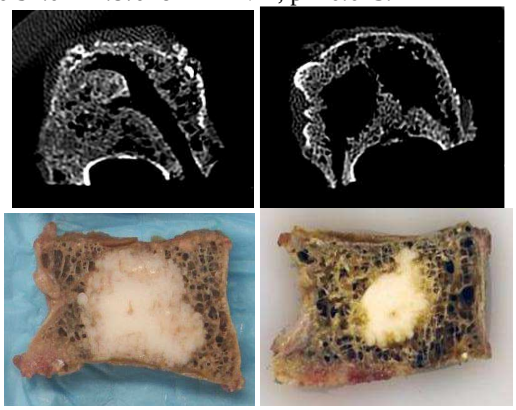

Fig. 1: CT images of RF-TVA (upper left) and BKP upper (right) cavities prior to cement delivery. Gross specimens demonstrating extensive interdigitation in RF-TVA specimen (left) compared to BKP (right).

CONCLUSIONS:
Both BKP and RF-TVA techniques achieved similar vertebral height restoration in this clinically relevant cadaveric model. However, there were significant differences in cavity location and morphology, the degree of trabecular displacement and degree of cement interdigitation peripheral to the cavity between kyphoplasty techniques. TVA resulted in a more discrete cavity and extensive PMMA interdigitation into the remaining trabecular structure peripheral to the initial cavity. The navigational cavity creation technique, and delivery of ultra high viscosity, RF warmed cement may permit targeted cement delivery enabling height restoration with less trabecular destruction. Creation of a bone-PMMA composite may result in a potentially more durable, mechanically favorable minimally invasive repair of VCFs.

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SIX MONTH RESULTS FROM A US IDE TRIAL EVALUATING THE OSSEOFIX IMPLANT FOR TREATMENT OF VERTEBRAL COMPRESSION FRACTURES

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Introduction: Vertebral compression fractures (VCF) are a burgeoning problem for the aging spine. The OsseoFix Spinal Fracture Reduction System is designed to improve symptomatic patients suffering from VCF between T6-L5 by providing internal fixation with a deployable titanium mesh OsseoFix implant and polymethylmethacrylate (PMMA) bone cement. This minimally invasive (one or two level) procedure takes about 30 minutes per vertebra. An in vitro study comparing kyphoplasty versus OsseoFix showed that the titanium mesh implant significantly reduced bone cement quantities and maintained vertebral height to a greater extent.[1] These preliminary data suggest the reduced quantity of bone cement and greater height maintenance makes OsseoFix a potential option for treatment of VCFs. We present the early combined clinical in vivo data from **only** three sites treating patients presenting with one or two VCFs that were treated with the OsseoFix implant and PMMA.

Left: OsseoFix titanium mesh implant
Right: Deployed OsseoFix titanium mesh implant

Experimental Methods: This analysis is a report on the initial experience/results from the prospective, multi-centered clinical study that follows patients for one year. Pain (VAS) and function scores (ODI) were collected starting pre-operatively with follow-up visits at four weeks, three months, six months and one year. Data were pooled from only three surgical sites involved in the ongoing study. From these three sites, the early experience/data for eleven patients are presented. Five of the eleven patients were evaluated for preliminary six month end point analysis.

Results: Eleven patients (8 females, 72.7% and 3 males, 27.3%) with an average age of 80.6±9.4 years were treated with OsseoFix for one level (10/11 or 90.9%) or two level (1/11 or 9.1%) VCF.

Table 1. VAS (0mm=no pain, 100mm=worse pain)

VAS (mm)	Baseline	4-weeks	3-months	6-months
N	11	11	7	5
Mean (SD)	76.8 (16.1)	23.9 (23.7)	15.5 (23.7)	15.5 (23.1)

At six months, improvement of VAS exceeded more than 60mm on average, demonstrating a dramatic and sustained relief in pain score.

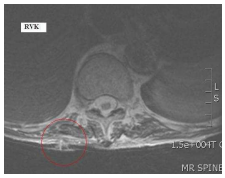
Table 2. ODI (0%= no disability, 100%=disabled)

ODI	Baseline	4-weeks	3-months	6-months
N	11	11	7	5
Mean (SD)	69.1 (16.6)	35.8 (19.2)	26.1 (20.8)	18.4 (11.2)

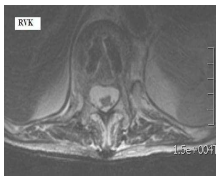
At six months, improvement of ODI exceeded more than 50% change on average, demonstrating a dramatic and sustained improvement in function.

A one-way ANOVA with a Tukey's post hoc test found a statistically significant improvement in pain (VAS $p<0.00001$) and function (ODI $p<0.0002$) at 4 weeks compared to pre-op which was maintained with no statistical difference between 4 week and six month time points. Although these results are promising--we are not implying a definitively conclusive difference rather simply presenting a limited statistical analysis for a very small incomplete cohort. There were no device complications that required intervention. One patient received an MRI study at 4 weeks to evaluate a subcutaneous abscess not involving the device. The MRI showed no appreciable artifact created by the device.

Below: MRI evaluation of Abscess



Axial T12 Abscess



Axial T12 Implants

This study is limited due to the early 6 month data summary but these initial data appear to support the clinical utility of the device.

Conclusions: Preliminary 6 month analysis shows OsseoFix augmentation for VCF between T6-L5 decreased pain and improved function in patients. The one or two level minimally invasive surgical procedure, taking approximately 30 minutes to complete, appears as a new option for the aging population that most often suffer from VCF. The surgical technique allows the surgeon to place and expand the device where desired as opposed to other pneumatic systems that do not allow for surgeon directed control. Further study and completion of the full enrollment is necessary prior to definitive confirmation of success.

Acknowledgments:
AlphaTec Spine http://www.alphatecspine.com

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Session 8

BIOMECHANICS IN VBA

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Computational Modelling for Pre-clinical Evaluation of Functional Spinal Interventions: Analysis of Prophylactic Vertebroplasty

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Efficacy of Vertebroplasty: Why Are We Neglecting Its Biomechanics?

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Computational modelling for Pre-clinical Evaluation of Functional Spinal Interventions: Analysis of Prophylactic Vertebroplasty

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☐ Biomaterials	☒ Biomechanics	☐ Clinical	☐ Innovation

INTRODUCTION: In recent years, investment in the development of new spinal interventions has increased and there has been a move towards minimally invasive and tissue-sparing treatments such as vertebroplasty. These new interventions pose a challenge in terms of pre-clinical biomechanical evaluation due to their interactions with the surrounding natural tissue. The limited availability and rapid degradation of in vitro specimens, as well as the variation between samples, can restrict both the number of experimental tests possible and the statistical power of the results. Computational techniques such as finite element (FE) analysis have several potential advantages over in vitro testing. However, the models require systematic development with robust validation. This study outlines the development of specimen-specific FE models for the assessment of vertebroplasty, using direct comparison with experimental specimens to provide one-to-one validation of the model outputs. In this case, the models were used to evaluate the biomechanical effects of prophylactic vertebroplasty.

METHODS: A series of specimen-specific FE models were generated from micro computed tomography (μCT) image data of specimens tested in the laboratory. The models were developed in four stages: (I): trabecular level μFE models of synthetic bone with and without cement augmentation; (II): continuum-level models of larger specimens of the same type; (III) models of whole vertebra, both before and after fracture, and pre/post cement augmentation; (IV) models of whole functional spinal units following prophylactic cement augmentation. At all stages, preliminary sensitivity analyses were undertaken to determine appropriate mesh size, material models and boundary condition approximations [1, 2], and different approaches were examined to derive the model properties from the μCT data. Direct comparisons were made between the model predictions and corresponding experimental results.
The full functional spinal unit model was then used to study the biomechanical effects of prophylactic vertebroplasty by undertaking a parametric analysis. Patient variables, such as bone and disc quality, and treatment variables, such as cement properties and volume were altered and their affects on the segment behaviour evaluated.

RESULTS: : In stages I and II, good agreement was found between the FE-predicted outcomes and the corresponding experimental findings (I: error <10% for predicted trabecular level deformation, II: average absolute error ~ 5% for predicted stiffness). Good agreement was also found for the vertebral specimens tested in stage III for both healthy porcine and osteoporotic human specimens (average absolute error ~ 10%).
From the parametric study undertaken in stage IV, the strain across the vertebra adjacent to that augmented was found to increase with disc degeneration, decreasing BMD, and increasing cement volume. There were also differences in mechanical behaviour between specimens which appears to be due to the initial vertebral shape.

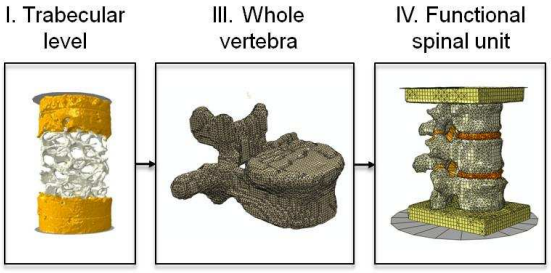

Fig. 1: Models generated from μCT images at different stages from (I) the trabecular level through to (III) whole vertebrae and (IV) the functional spinal unit.

CONCLUSIONS: The specimen-specific models developed in this study have been shown to be in good agreement with corresponding experimental results. This indicates that the FE method can be used to predict the mechanical behaviour of cement-augmentation providing that systematic development and validation is undertaken. In this case, the models were used to examine the mechanical effects of prophylactic vertebroplasty and the outcomes suggest that both the quality of the bone and adjacent disc tissue will affect the load transfer. There were also differences between models based on different specimens, indicating that the initial vertebral shape and level of kyphosis is important. These results go some way to illustrating why vertebroplasty may be affective in some patients but not in others. In particular, prophylactic vertebroplasty may reduce the risk of fracture in some cases, but further work is necessary to identify the patients for which this will be beneficial. The modelling techniques are now being extended to larger populations to evaluate the variance in outcomes across larger patient cohorts.

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Efficacy of Vertebroplasty: Why Are We Neglecting Its Biomechanics?

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INTRODUCTION: Vertebroplasty developed into a minimally invasive bone augmentation procedure that has been known and utilized for more than four decades. It converted from an open access procedure that required pre-operative CT images into a standard-care percutaneous procedure with limited fluoroscope usage. There also have been striking advances in the types and properties of the cements utilized in this procedure to mitigate complications such as pulmonary embolism and leakage. The main clinical indication for this procedure is pain relief, with a success rate of more than 90%, according to the literature. Through combinations of *in-vivo* and *in-vitro* research, it was concluded that the mechanism for pain relief is not due to the thermal effects of the bone cements or the cytotoxicity of the cement monomers but rather the mechanical stabilization of the fracture fragments. Although there are numerous publications on the biomechanics of vertebroplasty, evaluation of the biomechanical efficacy of this procedure has been neglected for decades, thereby hampering the full potential of its application.

METHODS: We conducted several computational and experimental studies on the biomechanics of vertebroplasty and performed a thorough review of the current literature. Even though pain alleviation is the only clinical outcome measure, mechanical stabilization of the fractured vertebra, functional restoration of the spinal segments and secondary injury risk reduction are additional objectives of this procedure.
In this study, the risk of secondary injury (adjacent fractures) was investigated in a series of single vertebral body models with the objective to characterize the load distribution within the anterior vertebrae before and after augmentation. Several disc degeneration levels, bone cement properties, and filling patterns were investigated. The results of this study were then used to design a bench experiment utilizing 12 cadaveric spinal segments. Six fresh-frozen spinal segments were treated with bi-lateral transpedicular vertebroplasty, while the remaining six spinal segments served as non-treatment control. The objective of this study was to determine adjacent fracture risk after preventive vertebroplasty. The samples were axially compressed beyond failure and their deformation pattern characterized. Special emphasis was placed on vertebral endplate deflection.

RESULTS: As expected, patient conditions such as degenerated intervertebral discs and low bone mass had a detrimental effect on the functional recovery through vertebroplasty. In addition, cement interdigitation required less fill to recover biomechanical properties of the vertebrae compared to localized placement (Fig. 1). Localized delivery of cement caused a more rapid loss of vertebral biomechanical properties compared to interdigitated distribution pattern in a repetitive loading experiment. In all specimens of the vertebroplasty group only the superior and inferior endplates of the untreated middle vertebral body were deflected, while the inferior endplate of the vertebral body above and superior endplate of the vertebral body below did not show any measureable deflection with increased load (Fig. 2).

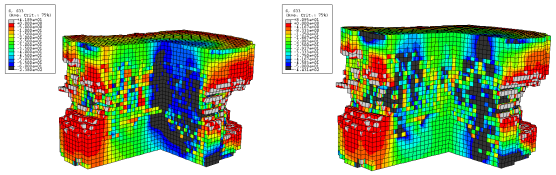

Fig. 1: Distribution of axial stress after vertebroplasty treatment utilizing PMMA (A) or CORTOSS (B).

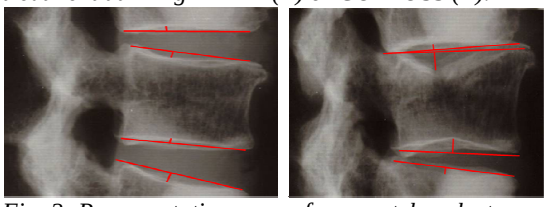

Fig. 2: Representative x-rays for a vertebroplasty group specimen taken at baseline (left) and 3000N (right).

CONCLUSIONS: There is a delicate balance between recovery of biomechanical properties after cement augmentation and internal stress distribution near the cement/bone interface. Our results indicated that interdigitated cement in preventive augmentation achieved the best biomechanical short and long-term outcome.
The results of our bench experiment support the hypothesis that vertebroplasty acts as a "stress-riser" thereby changing the load-transfer between adjacent vertebral bodies after vertebroplasty. This may reduces the effective cross sectional area for load bearing. New types of bone cements and modified bone cement distribution pattern may prevent adjacent bone failure.
Preventive vertebroplasty was more effective in reducing secondary fracture risk compared to fracture treatment. Furthermore, while acrylic augmentation is only able to recover vertebral stiffness to within 10 % of pre-fracture values, other types of bone cement and filling patterns can be far more effective.
Vertebroplasty altered the load-transfer along the anterior spinal column, thereby statistically significantly increasing fracture risk of the untreated adjacent vertebrae. Endplate deflection fracture was identified as cause of adjacent vertebra fractures after vertebroplasty.
Knowing the biomechanics of vertebral augmentation may open up opportunities for this procedure in long-term cancer treatment or regenerative medicine. Moreover, these new treatment options may allow young patients to benefit from this treatment as well.

Influences of pore and bone volume fraction on the mechanical properties of standard and low-modulus PMMA/bone biopsies extracted from augmented vertebral bodies

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INTRODUCTION: Injection of PMMA into vertebral bodies forms a porous PMMA/bone composite. The mechanical behavior of such a composite is important for the development of new cement materials such as low-modulus cements [1] with adapted stiffness as well as for finite element models of vertebroplasty. It was found previously [2] that the elastic modulus and yield stress of such PMMA/bone composites were significantly lower than that of pure cement and were not correlated with bone volume fraction (BV/TV). These results are surprising because trabecular bone tissue is 5-times stiffer than PMMA and, therefore, should reinforce the cement. It is not clear what determines the macro-mechanical behavior of PMMA/bone composites. Our aims were to study the effects of pore volume fraction (PV/TV), BV/TV and cement stiffness on the mechanical properties of such a composite by performing compression tests on standard as well as low-modulus PMMA/bone biopsies.

METHODS:
Nine human vertebral bodies (T9-L4, age 49-82) were augmented with standard cement or modified low-modulus cement [1,3] as in clinical practice. In parallel, ninety cylindrical samples of pure standard and low-modulus cement were produced. The vertebral bodies were scanned with a HR-pQCT system (82 µm voxel size, XtremeCT, Scanco Medical AG) before and after augmentation. These images were used to obtain the bone structure and to plan the biopsy extraction. Fourteen PMMA/bone biopsies were extracted from the cement region of the augmented specimens using a diamond coated core drill. The cylindrical biopsies were scanned with a micro-CT system (24 µm voxel size, µCT 40, Scanco Medical AG) to obtain the PV/TV. BV/TV was calculated from the HR-pQCT images before augmentation inside the registered biopsy volume. The PMMA/bone biopsies and the cement samples (8 mm diameter, 12 mm height) were tested in compression (2.5 mm/min) until failure (Fig. 1) on a servo-hydraulic testing machine (Mini-Bionix, MTS). Strains were measured with an extensometer (634.31F-24, MTS).

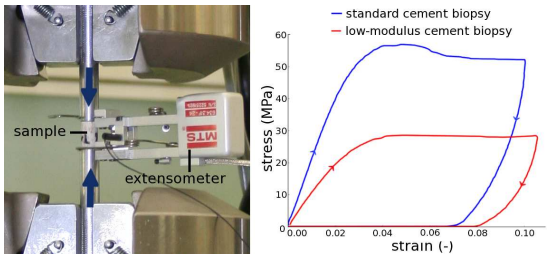

Fig. 1: Compression testing setup (left) and stress-strain response (right) for a standard (blue) and a low-modulus PMMA/bone biopsy (red).

RESULTS: A high correlation between corrected pore volume fraction PV/(TV-BV) and experimental elastic modulus (Fig. 2) was found for the standard (R^2=0.91) and low-modulus cement group (R^2=0.97). The elastic moduli of the pure cement samples (zero PV/TV) were very close to the respective regression line. A similar correlation was found between yield stress and PV/(TV-BV) (standard cement: R^2=0.92; low-modulus cement: R^2=0.83). Low correlation between BV/TV (range 5% to 13%) and elastic modulus was observed (R^2<0.05).

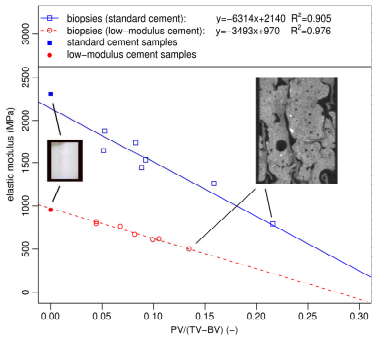

Fig. 2: Regression between PV/(TV-BV) and elastic modulus of the biopsies with correlation coefficients. Filled symbols represent elastic moduli of pure cement.

CONCLUSIONS: The mechanical properties of the standard cement biopsies were in line with previous results [2]. The material properties of the biopsies were determined by PV/(TV-BV) and elastic modulus of the cement. BV/TV had only a very small effect on the composite material properties in the investigated range of bone volume fractions. This means that trabecular bone inside the biopsy is mechanically "switched off" and that load is carried exclusively by porous PMMA cement which is more compliant than pure cement.

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HYPERKYPHOSIS INDUCED BY VERTEBRAL FRACTURE INCREASES COMPRESSIVE LOADS ON THE VERTEBRAE MORE THAN KYPHOSIS INDUCED BY DEGENERATIVE CHANGES

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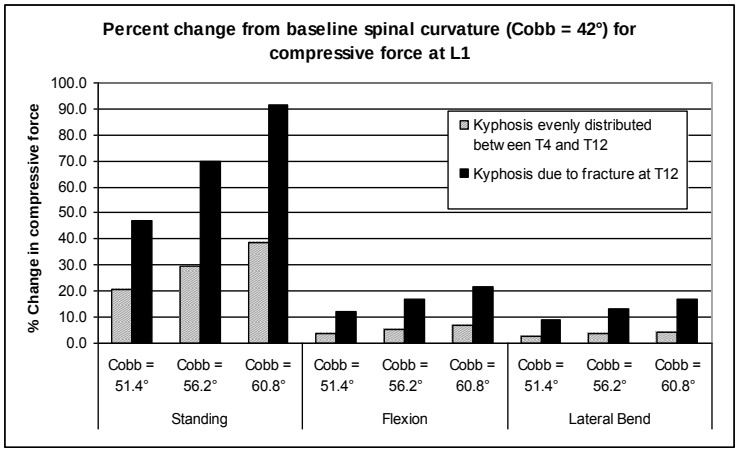
INTRODUCTION: Vertebral fractures (VFx) occur in one-third of women after age 50, leading to marked pain, disfigurement, and loss of function. Hyperkyphosis is believed to contribute to, as well as result from thoracic VFx. Hyperkyphosis of the thoracic spine comes from two main sources: 1) VFx, which tilts the spine forward due to a height reduction in the anterior cortex of the fractured level, and 2) age-related disc degeneration and loss of spinal muscle strength[1]. The increase in curvature due to age-related degenerative changes is likely more evenly distributed across the spine, as opposed to fractured-induced kyphosis which causes a localized increase in curvature about the fractured level (more like a kink). Therefore, for a given T4-T12 Cobb angle, it is unknown whether the mechanical loading of the spine differs when the kyphosis is caused by a VFx versus global degenerative changes. We hypothesized that a fracture-induced increase in kyphosis would increase compressive loading on the spine more than evenly distributed kyphosis.

EXPERIMENTAL METHODS: For a 66 yr old female subject (ht = 167 cm, wt = 69.4 kg), we used a quasi-static biomechanical model of the spine[2] to estimate compressive loading on the T6 through L5 vertebral bodies for three different spinal curvatures: 1) a baseline spine (T4-T12 Cobb angle of 42°); 2) a spine with a fracture at T12 (mild, moderate, and severe); and 3) a spine with the same amount of kyphosis as the fractured spine, but with the curvature changes evenly distributed among the T4-T12 intervertebral joints. We modeled a mild, moderate, and severe fracture at T12 by reducing the height of the anterior face of the vertebral body by 20%, 30%, and 40% respectively, and the new corresponding Cobb angles were 51.4°, 56.2°, and 60.8°. We examined the compressive force on the spine for three different body positions: upright standing with 10 kg weights in each hand, 30° of forward flexion with 10 kg weights in each hand, and a 20° lateral bend to the right with a 20 kg weight in the right hand.

RESULTS and CONCLUSIONS: For all three body positions, compressive force was highest for the spine with a VFx at T12, followed by the spine with evenly distributed kyphosis, with the baseline spine having the lowest compressive forces (Figure). Specifically, during standing compressive force at L1 increased 45 to 90% vs baseline given a Vfx at T12, whereas it increased 20-40% for an evenly distributed increase in kyphosis. Similar patterns were seen for the other loading conditions. In conclusion, VFx-induced hyperkyphosis leads to greater increases in compressive loading on adjacent vertebral bodies than hyperkyphosis due to degenerative changes. This observation may explain in part the marked increase in subsequent VFx risk once a single VFx has occurred.



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Towards Low-Modulus Bone Cements – The Effect of a Natural Oil in PMMA

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☒ Biomaterials	☐ Biomechanics	☐ Clinical	☐ Innovation

INTRODUCTION: Vertebroplasty is commonly used in order to stabilize spinal fractures and provide pain relief. Although the procedure has been reported to have a high success rate [1], there are concerns relating to the high occurrence of additional fractures next to augmented vertebrae [2]. These fractures have been hypothesized to be due to the relatively high stiffness of the bone cement used, poly (methyl methacrylate) (PMMA). Several studies have therefore been performed in order to produce injectable, low-modulus bone cements [3,4]. However, the decrease of the modulus through the introduction of pores via an aqueous phase [3,4] has led to an excessive amount of particle release *in vitro* [5]. This is probably due to the immiscibility of the aqueous phase with the monomer, which may prevent the polymerization of powder entrapped in the aqueous phase [5]. In this study, the addition of an oily phase to the PMMA was evaluated as a means of lowering the modulus of the cement with the aim of avoiding this effect. Castor oil was chosen as it is a polar oil, soluble in the MMA monomer, and is generally considered non-toxic [6,7].

METHODS: Commercially available bone cement for vertebroplasty, Osteopal® V (Heraeus Medical GmbH) was used in this study. Different amounts of castor oil (Sigma-Aldrich) were dissolved in the liquid monomer before adding the pre-polymerized powder and mixing the cement manually. The cements were assessed using ASTM F451 [8] for curing and mechanical (compressive) properties. The viscosity was evaluated using a stress-controlled rheometer equipped with a parallel-plate geometry with a time sweep mode at 5Hz and a displacement of 5×10^{-4} rad [9]. An *in vitro* toxicity study was also performed on MG-63 osteoblast-like cells, according to ISO 10993-5. A worst-case scenario was chosen, where cell culture medium was added to the curing cements directly after mixing and incubated for 24 hours. These extraction media were then used for monolayer cultures of MG-63 cells. After defined time points the cell viability was assessed using the alamarBlue® viability assay (Invitrogen).

Table 1. Curing and mechanical properties of cements containing different amounts (in wt%) of oil.

Group	Setting time (min)	Max Temp-erature (°C)	Stiffness (GPa)	Max Stress (MPa)
Control	18.2±0.9	41.3±2.1	1.53±0.06	88±3
2.5% oil	20.0±1.1	32.4±4.5	1.29±0.19	79±3
7.5% oil	15.3±1.3	30.3±1.8	1.04±0.15	46±4
12% oil	16.4±1.6	28.4±0.9	0.46±0.08	15±3

RESULTS: Curing and mechanical properties are summarized in Table 1. The maximum temperature decreased significantly with any addition of oil. Both the stiffness and the maximum stress were found to decrease with an increase in the amount of oil added. A statistically significant difference (ANOVA, $p<0.05$) was found between all groups for the mechanical properties. The oil is likely to act as a plasticizer within the cement.

The viscosity measurements (Figure 1) revealed a delay in the viscosity increase with time due to the addition of oil, giving a longer working time for the cements.

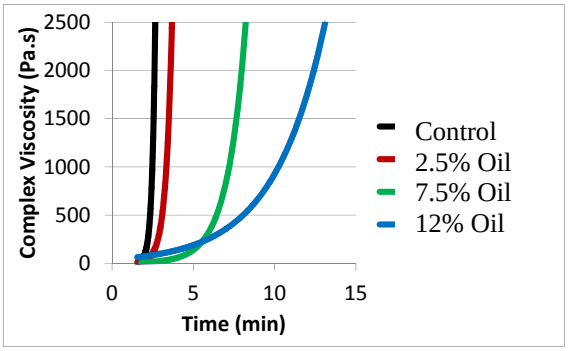

Figure 1. Viscosity over time (time zero corresponds to start of mixing of powder and liquid) for cements containing different amounts of oil.

Compared to the control, the cell viability tended to be lower with the higher amounts of oil in the cement. This may be due to an increase in monomer release and may limit the use of this type of cement *in vivo*. The decreased amount of monomer available for the reaction may also contribute to the lower temperatures and mechanical properties.

CONCLUSIONS: The addition of castor oil to PMMA bone cement gives rise to many apparent advantages such as a reduced polymerization temperature and stiffness. However, the oil leads to an increased cell toxicity of extracts, possibly rendering these cements unsuitable for use *in vivo.*

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Optimisation of calcium phosphate cements to augment traumatic spinal fractures using experimentally validated computational models.

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INTRODUCTION: This abstract outlines a combined computational and experimental approach used to assess the stiffness of burst fractured porcine vertebrae following vertebroplasty using calcium phosphate (CaP) or PMMA as an augmentation cement. The validated models were used to evaluate the desired optimum properties of the CaP cement by manipulation of the mechanical properties and injectability.

METHODS: Eighteen three-vertebra porcine specimens were fractured using a drop weight method. The middle vertebra was extracted from each segment and set between plane-parallel PMMA cement mounts to enable testing. The specimens were imaged in a microCT system (Scanco µCT80, Switzerland) and then tested under axial compression at a loading rate of 1mm/min. The load-displacement data exhibited a region of elasticity in all specimens, which was used to obtain experimental stiffness for each vertebra. Three cement types were tested in this study: two CaP formulations (type A, with compressive modulus of 1.01 GPa and type B with compressive modulus of 0.585 GPa) and a lab grade PMMA cement (type C, with a modulus of 1.035 GPa). Cement types A and B were developed and tested at the Queens University Belfast, UK as part of a parallel project [1]. Each cement type was injected into 6 different fractured specimens using a bipedicular vertebroplasty procedure. Following injection of the CaP cements, the specimens were immersed in a ringer's solution for 5 days at 37°C to allow the cement to fully harden. Once the cements had set, the specimens were imaged again using the microCT system. Following the scanning the specimens were tested under axial compression at a loading rate of 1mm/min until complete failure occurred.

The image data collected for all 18 specimens both pre- and post-augmentation was converted into FE models using proprietary software (ScanIP/FE, Simpleware, UK). For the pre-augmentation specimens, six of the models were used to develop a method of converting bone density greyscale into element specific mechanical properties using the experimental data to tune the results. The fracture gap was characterised as a material with low modulus 10^{-9} GPa. The rest of the specimens were used to validate this method by predicting the stiffness of the remaining specimens and comparing the results to the mechanical testing.

The post augmented models were created using the conversion method developed for the pre-augmented specimens to obtain material properties for the bone. The cement was assigned values of elastic modulus appropriate to the type, stated earlier. The FE predicted and experimental stiffness' were then compared.

The material properties of the cement were then manipulated for each model and the volume of cement injected was quantified, to asses which factor most affected the stiffness of the models.

RESULTS: From the experimental tests, the respective increases in stiffness and strength after augmentation compared to the post-fracture, pre-augmentation values were 3% and 0% for type A, 12% and 38% for Type B and 32% and 37% for Type C.

The absolute percentage error of the FE predictions specimen stiffness was 19.2% when compared to the experimental data, shown graphically in Figure 1. The absolute percentage error of post augmented FE stiffness predictions was calculated as 24%, 16% and 8% for the cement types A, B and C respectively.

Cement infiltration was calculated based on the percentage fill of the fracture void; the mean fills were 27 %, 36 %, 54 % for cement types A, B and C respectively. From the results of the cement modulus manipulation, the models were shown to be more sensitive to the percentage fill than to the cement type (Figure 2)

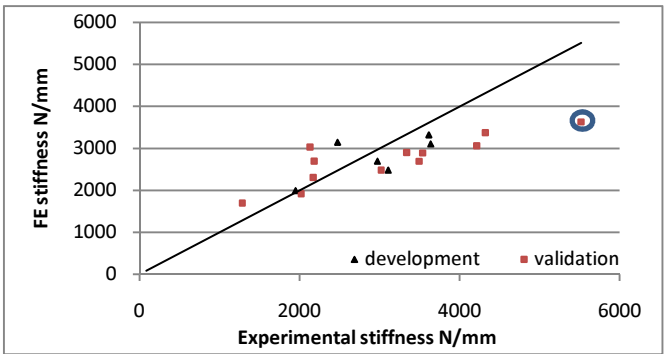

Figure 1: Pre-augmented FE predictions of stiffness

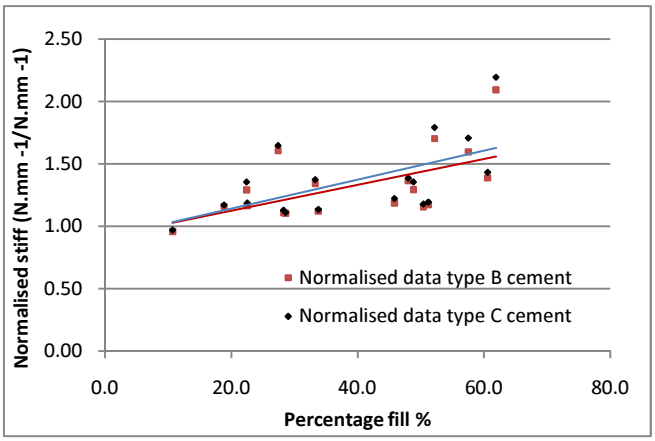

Figure 2: Computational analysis of stiffness variation at different percentage void fills using all specimens and two different cement properties (types B and C)

CONCLUSION: The PMMA cement infiltrated the fracture better than both the CaP cements and resulted in the most improved specimen stiffness. Further FE evaluation demonstrated that the percentage fill of the cement into the fracture is the most significant factor determining the restored stability of vertebrae. The effectiveness of calcium phosphate cement seems to be determined by its injectability. Despite CaP type A having the highest compressive modulus, there was virtually no mean increase in the experimentally recorded stiffness and strength. For the cement with the lowest value of compressive modulus, CaP type B, both stiffness and strength were considerably improved by the augmentation. This is almost certainly due to the better percentage fill of the fracture void using this cement. Therefore, further development of CaP cements should focus on increasing injectability even if this reduces the elastic modulus.

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Bipedicular versus unipedicular approaches in vertebroplasty: effect of cement volume

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☐ Biomaterials	☒ Biomechanics	☐ Clinical	☐ Innovation

INTRODUCTION: An important consideration in vertebroplasty (VP) is whether to augment the vertebrae via one or both pedicles. However there is little evidence relating uni- or bipedicular approaches to biomechanical factors[1] and no evidence when controlling for the volume of cement injected. The aim of this study is to ascertain the overall biomechanical effects of cement quantity as a percentage of VB volume using a unipedicular versus bipedicular approach.

METHODS: 35 human vertebrae (T7-L5) were randomised with stratification into three groups. Vertebrae were loaded eccentrically to create a wedge fracture with the end-point being 25 % of the pre-fracture anterior VB height. The yield load and stiffness were recorded. Group 1 underwent unipedicular VP and group 2 bipedicular VP. Both group 1 and 2 received an estimated 20% cement volume fill, based on the gross vertebral body dimensions. Group 3 underwent bipedicular VP with an estimated 30% fill. Specimens then underwent microCT imaging to calculate exact fill volume and cement bolus to vertebral endplate distance (within any vertebra this can be both endplates in contact, one endplate in contact or no cement-endplate contact). All specimens were then loaded to failure using the same method used to create the initial fracture.

RESULTS: There was no difference between the three groups with regards to BMD, vertebral body volume, initial stiffness or initial yield load. There was no difference between groups 1 & 2 with regard to cement fill with a mean percentage cement fill of 22 ± 5% for group 1, 22 ± 3% for group 2 and 31 ± 5% for group 3. The mean change in relative yield load in group 1 was 1.60 ± 070, in group 2, 1.12 ± 0.39 and in group 3, 3.00 ± 1.87. There was no significant difference in post augmentation yield load between group 1 and 2 (p=0.63) but there was a significant difference in post augmentation yield load between group 1 and group 3 (p=0.026) and between group 2 and group 3 (p=0.003) (Figure 1). Further analysis examining the exact nature of cement–endplate contact revealed that both change in relative yield load (p=0.0005) and change in relative stiffness (p=0.0091) are dependent on whether or not the endplate was in contact with the cement. It should be noted that the cement fill volumes between the 20% fill groups (groups 1 and 2) and the 30% fill group were significantly different (p=0.0001) and may act as a confounding factor.

CONCLUSIONS: This is the first study to directly compare unipedicular with bipedicular VP and control for the volume of cement injected. Previous studies comparing VP approaches have not controlled for cement fill[1] which is an important determinant of post augmentation strength.[2] It shows that there is no difference in yield load between these two approaches for the same percentage cement fill. The study also demonstrated an association between load restoration and interaction with the endplate in keeping with previous studies[3], irrespective of VP approach, though cement volume may be a confounding factor in this relationship. If all other considerations are equal then a unipedicular approach, which has a comparatively shorter operating time and obviates the need for a second needle, is recommended due to the equivalence in strength between Groups 1 and 2.

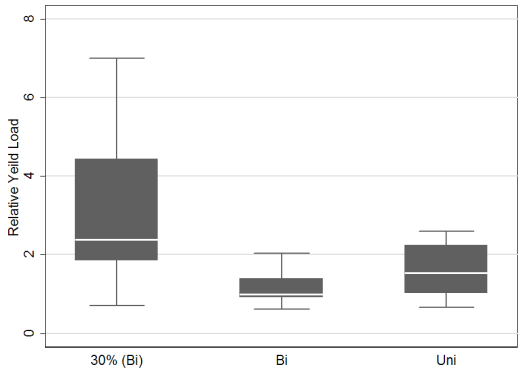

Fig. 1: Relative yield load versus approach for augmented vertebrae.

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ACKNOWLEDGEMENTS: Synthes UK, suppliers of PVP kit & PMMA cement (Vertecem, Synthes Inc.) & Leeds Teaching Hospital Charitable foundation (funding). In addition, the study was partially funded through WELMEC (Wellcome Trust and EPSRC) and additionally supported by the NIHR (National Institute for Health Research) and the LMBRU (Leeds Musculoskeletal Biomedical Research Unit).

Session 8

BIOMECHANICS IN VBA

Chairmen: Mary BOUXSEIN & Ruth WILCOX

Effect of Cement Viscosity on Mechanical Behaviour: an Osteoporotic Bone Model

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Abstract is included, page 72.

Effect of Cement Viscosity on Mechanical Behaviour: An Osteoporotic Bone Model

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☒ Biomaterials	☒ Biomechanics	☐ Clinical	☐ Innovation

INTRODUCTION:

Vertebroplasty is a minimal invasive surgical procedure developed to treat vertebral compressive fractures. The efficacious percutaneous delivery of the cement through a cannulated needle is an essential determinant in restoration of strength and stiffness in osteoporotic vertebral bodies. Extra-osseous cement leakage has been reported to be a major complication of this procedure. Ideally, cement uniformly infiltrates the trabecular bone skeleton and remains within the structure. Cement viscosity is believed to influence the injectability, leakage and cement wash-out. Altering the liquid to powder ratio modifies the viscosity of bone cement; however, the cement viscosity-response association between cement fill and augmentation of strength and stiffness is unknown. The aim of this study was to determine the relationship between cement viscosity and the potential augmentation of strength and stiffness in an osteoporotic vertebral body using an in-vitro prophylactic vertebroplasty model.

METHODS:

Calcium phosphate cement (CPC) was produced by mixing alpha-tricalcium phosphate, calcium phosphate, calcium carbonate and hydroxyapatite with an aqueous solution of 5 wt% disodium hydrogen phosphate [1]. Three different liquid:powder ratios (LPR) were used 0.35 mL/g (HV), 0.45 mL/g (MV) and 0.5 mL/g (LV). The powder and liquid components were mixed for 1 min to produce a cement paste for a particular LPR, and time of 4 min was designated for manual delivery into an osteoporotic bone model (#1522-5055, Sawbone® Europe) using a 11G cannulated needle (A202; Medtronic Inc.) [2]. Accurate and repeatable delivery of the cement (1 mL) into the centre of the bone was ensured using specifically designed apparatus. The CPC-vertebrae composite was then placed in an oven (37 ± 1^{o}C) for 20 min and then immersed in Ringer's solution (37 ± 1^{o}C) for 3 days. Different techniques were used to understand the relationship between cement viscosity and the augmentation of strength and stiffness. Potential for leakage and wash-out was determined using gravimetric analysis. Extent of cement fill was determined using computer tomography (CT). The CPC-vertebrae composite were tested in a materials testing machine (Lloyds Instruments UK) under axial compression at a rate of 1 mm/min and the strength and stiffness for each specimen was calculated. For each property determined, the results were evaluated for statistical significance against the osteoporotic bone (control) using a one-way analysis of variance ($p<0.05$). Post-hoc tests were conducted using the Dunnett method. Linear correlation analysis was also performed with Pearson's coefficient (R) and the coefficient of determination (R^2) (SAS Institute, USA).

RESULTS:

All CPC systems demonstrated 100% injectability into the vertebrae. Cement leakage was more pronounced ($p=0.512$) for the lower viscosity cement. Similarly cement wash-out increased ($p=0.476$) after 3 days in Ringer's solution was shown as cement viscosity reduced. Qualitative assessment of cement fill within the vertebral body using CT imaging supported the wash-out results. The compressive strength ($p<0.05$-0.01) and compressive stiffness ($p<0.01$) of vertebrae significantly increased on cement introduction, the extent of this increase was greater at the higher viscosity level (Fig. 1).

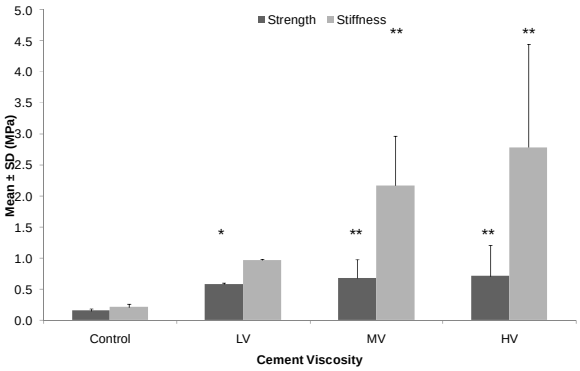

Fig. 1: Strength & stiffness of control & CPC-bone composites.

CONCLUSIONS:

Good agreement was observed when comparing the results from the *in-vitro* prophylactic vertebroplasty model used in this study and other cadaveric and animal based *in-vitro* models [3-4]. Linear correlation analysis showed a definite association between the mechanical properties and percentage cement fill, the level of which was strongly dependent on the cement viscosity. Greater stabilisation of the osteoporotic bone using the higher viscosity cement was due to a greater proportion of CPC being maintained within the vertebral body post-setting. However significant forces were required for delivery of high viscosity cement, which may approach or exceed the normal human physical limit of injection forces.

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COMPARISON OF FRACTURE PREDICTION IN OSTEOPOROTIC SAMPLES

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☐ Biomaterials	☒ Biomechanics	☐ Clinical	☐ Innovation

INTRODUCTION: The lack of suitable models for the prediction of the vertebral body (VB) failure load for a variety of pathologies hampers the development of indications for surgical and pharmaceutical interventions and the assessment of novel treatments. Similar models would be of benefit in the laboratory environment in which predictions of failure load could aid experimental design. Finite element modelling shows great promise but the expertise required to effectively deploy this technology in the clinical environment precludes its use routinely at the present time. Its deployment within the laboratory environment is also time consuming. An alternative approach may be that outlined by Whealan et al [1] in which structural analyses that take account of both vertebral geometry and the BMD distribution are utilised to predict the loads at which vertebrae will fail. The following study compares this methodology to that used by Brinckmann et al [2] for calculating vertebral body fracture load.

METHODS: Sixty-nine vertebrae were harvested from elderly donors. Ethical approval was gained from the appropriate Ethical Committee. All specimens underwent microCT scans (microCT80, Scanco Medical AG, Bassersdorf, Switerzland) with 0.148 mm voxel size. The resulting data was used to determine both the vertebral geometry and BMD distribution within each single vertebrae. The first method, which was based on structural analyses [1, 2], used proprietary software (Matlab, MathsWorks, USA), in which microCT images were segmented and each voxel converted to an elastic modulus with which to create a series of modulus maps of the axial slices. Failure load was taken as yield load of the weakest slice with the yield at failure set to 1%. The second method predicted vertebral fracture load from a previously derived equation using BMD and the average cross sectional area [3]. For each vertebrae compression fractures were generated in the laboratory under specific loading conditions similar to those utilised by Furtado et al [4]. Fracture load was measured at the first zero slope yield on the force-displacement curve. Association between the predicted and actual yield load were determined using Pearson's correlation statistic whilst agreement was assessed through an Bland and Altman analysis.

RESULTS: With regard to the structural analyses, the mean difference, the limits of agreement and the correlation coefficient for the whole data set were -0.149 kN, (-1.462 to 1.165kN) and 0.8875. The results for the analyses proposed by Brinckmann et al [2] were significantly poorer in terms of both agreement and association (mean diff = -0.828; limits of agreement; -3.386 to 1.730 and a correlation coefficient of 0.35). Figure 1 displays the data from which an number of observations can be made. Firstly, despite the high correlation for the structural analyses, the model tends to overestimate the failure load for small loads but this is reversed for higher ones. The analyses by Brinckmann et al [2] tends to underestimate the loads for all loads except those with the osteophytes present.

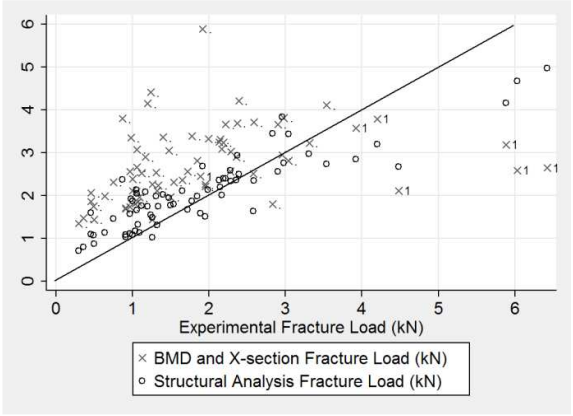

Figure 1: Plot of the predicted versus the experimentally determined failure load. The marks identified with '1' are those which refer to vertebrae with osteophytes.

In an attempt to discern the reasons for the discrepancy in the two models the presence of osteophytes in 7 vertebrae was investigated. Excluding these vertebrae from the analyses had a minimal effect on the results for the structural analysis, whilst those for the second analyses were much improved reducing the limits of agreement to (-2.762 to 0.517) and increasing *r* to 0.53.

DISCUSSION: Structural analyses similar to that previously used by Whealan et al [1] provide fracture predictions with a greater association with the experimental results than those derived from those of Brinckmann et al [2]. The presence of osteophytes is an issue with the latter analysis but can be taken into to account with the former and is worth further exploration as to the exact effect of these pathologies. However, even for the structural analyses the errors between the expt. and the predicted value showed structure and further work is required before the method can be used effectively, although this depends on the precise application.

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Thermomechanical modeling approach for the representation of coupled curing processes in acrylic bone cements used in vertebroplasty

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☐ Biomaterials	☐ Biomechanics	☐ Clinical	☐ Innovation

INTRODUCTION: Acrylic bone cements are widely used in vertebroplasty. After mixing a polymer powder and a liquid monomer the material gets injected into the vertebrae. Therein it cures during an exothermal chemical reaction called polymerization from a fluid to a viscoelastic solid. Due to this process heat gets dissipated and leads to an increase in temperature. This in turn affects both the mechanical behavior and the polymerization. Furthermore, a change in volume occurs due to chemical shrinkage and heat expansion.
In order to describe these strongly coupled processes, a constitutive material model has been developed. The application of the modeling approach to a specific acrylic bone cement will be provided. Moreover, simulation results will be compared with experimental observations.

METHODS: The material model is based on an approach proposed by [1] and includes several aspects of the curing process that result from different physical fields, which are mechanics, thermodynamics and chemistry. The chemical process is represented by a variable called degree of cure $q(t)$. It is derived from an evolution equation (1) given by a function of temperature and the curing process itself.

$$\dot{q} = f(q,\theta) \qquad q(t) = \int \dot{q} dt \qquad 0 \le q(t) \le 1 \qquad (1)$$

Furthemore, this variable is used to capture all curing dependent effects within the material model.
The kinematics are defined by using the deformation gradient $\underline{\underline{F}}$. Besides, a decomposition of $\underline{\underline{F}}$ into a thermochemical part and a mechanical part is carried out (cf. Fig. 1 (a)). The first part describes the heat expansion and the chemical shrinkage, which both are assumed to be isotropic. The remaining mechanical part is used to model nearly incompressible material behavior with viscoelastic responses due to isochoric deformations. The viscoelastic behavior is modeled by a parallel connection of several Maxwell elements, which include curing and temperature depending material parameters (cf. Fig. 1 (b)).

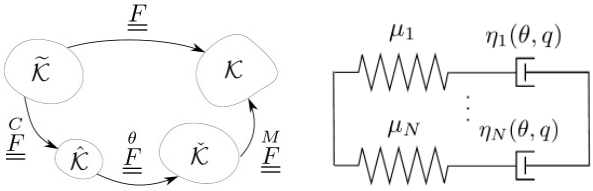

Fig. 1: (a) Decomposition of the deformation gradient, (b) Maxwell elements in parallel

In order to achieve a thermodynamically consistent material model, a free energy function has been formulated. Moreover, the laws of thermodynamics have been evaluated. This leads to equations for the evaluation of the stresses and an equation of heat conduction.
The thermomechanical coupled system of equations has been implemented into a scientific finite element code for the simulation of 2D problems. This code was developed at the Chemnitz University of Technology and offers enhanced solution methods for thermomechanical coupled problems. Since the implementation is based on the user-subroutine HYPELA2, it can also be used within MSC.MARC for more complex 3D simulations.

RESULTS: The proposed approach has been applied to model a specific acrylic bone cement. The curing kinetics, the heat expansion and the chemical shrinkage have been measured and the material parameters of chosen material functions have been identified [2]. Furthermore, experimental setups and related simulation models have been developed for the identification of the mechanical properties. One of these models is shown in Fig. 2 (a). It contains a hollow cylinder filled with initially liquid bone cement. A stamp gets dipped in the material and moved by a sinusoidal displacement in vertical direction. The resulting reaction force at the stamp is plotted in Fig. 2 (b).

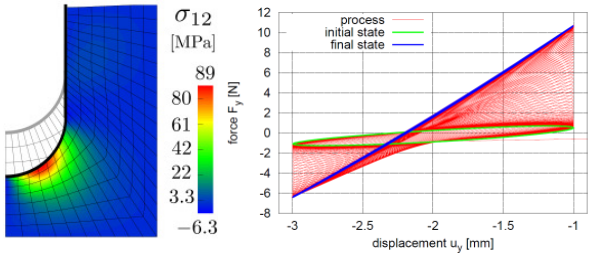

Fig. 2: (a) Finite element model, (b) Reaction force vs. displacement on stamp

CONCLUSIONS: It can be shown that the proposed material model is able to represent the thermomechanical-chemical coupled curing process in acrylic bone cements. The next steps will be the identification of material parameters of the mechanical sub-model by using inverse methods and nonlinear optimization algorithms. Furthermore, realistic processes in vertebroplasty will be investigated by using thermomechanical coupled finite element simulations.

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Minimising subsidence in lumbar total disc replacement through effective cement placement

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☐ Biomaterials	☒ Biomechanics	☐ Clinical	☐ Innovation

INTRODUCTION: Total disc replacement (TDR) is becoming an increasingly popular alternative to interbody spinal fusion as a treatment for degenerative disc disease (DDD) in younger patients.[1] The procedure places an artificial bearing within the intervertebral disc space, an area of load-bearing importance, and requires sufficient strength in the supporting bone to maintain optimum performance. Conversely, poor bone quality is often a contraindication for surgery with subsidence of the device a primary concern.[2] In an ageing population, a large demographic of patients are currently denied TDR due to poor bone quality through osteoporosis. However, TDR has shown to be successful in patients over the age of 60 when combined with vertebral body (VB) PMMA cement reinforcement, a modification of percutaneous vertebroplasty (PVP).[3] Experimentally, the hybrid treatment of interbody devices combined with cement augmentation has shown to significantly increase the failure strength of the device-endplate interface.[4,5] However, no detail has been published regarding the optimum cement volume required and whether cement placement significantly effects the distribution of subsidence. The aim of this study was to explore the effect of these factors in augmented vertebrae, when loaded with a TDR-shaped indenter.

METHODS: Thirty-two vertebrae (L2-L5) were taken from eight fresh-frozen human cadaveric spines. Four groups were characterised by the method and volume of cement augmentation; 1) Control with no cement fill, 2) Bipedicular approach with 10% cement fill, 3) Bipedicular with 20% fill, and 4) Anterior approach with 20% fill. All injections were performed under fluoroscopic guidance with the cement fill volume calculated from VB volume. Bipedicular groups utilised a standard PVP technique aiming to fill the anterior two-thirds of the VB. The anterior approach group inserted two needles bilaterally through the anterior cortex and retro-filled from the posterior, distributing cement evenly ether side of the midline. The specimens were indented on the superior endplate at 1 mm/min until 25% strain. Indenters were manufactured using a generic TDR profile in three sizes to achieve a 40% endplate coverage. Mechanical properties were defined via a previously reported method.[4] Change in indenter angle was measured in the sagittal and coronal planes using a height gauge. Finally, a repeated measures ANOVA was used to analyse the data.

RESULTS: Within subjects analysis showed that cement augmentation significantly changed failure stress ($p=.002$). The 20% bipedicular fill group achieved the highest mean average failure strength of 6.6 ± 2.2 MPa, a 106% increase over the control group strength, 3.2 ± 1.6 MPa. Failure stress for the anterior 20% fill group was 5.5 ± 2.3 MPa, a 72% increase over control. However, the 10% fill group showed no increase in strength. Compressive modulus displayed the same trend and proved to be significantly effected ($p=.010$). Indenter angle in the sagittal plane was significantly increased towards the posterior in the 20% bipedicular group ($p<.001$). The 10% bipedicular group also produced increased posterior subsidence but less substantial. Both the control and 20% anterior groups showed reverse trends and produced marginal tilting towards the anterior. Indenter angle magnitude in the coronal plane was consistently low across all four groups with no significant differences.

CONCLUSIONS: Cement augmentation significantly increased vertebral strength and modulus when loaded with a TDR-shaped indenter but only when using a 20% volume fill. It is hypothesized that a larger volume of cement is able to distribute loads to a larger volume of surrounding trabecular bone, thereby, increasing failure strength.[5] The volume fill of 20% used in this study is larger than suggested guidelines for standard PVP.[6] However, these are based on tests that load the entire VB, recruiting the support of the vertebral shell. The traditional PVP bipedicular approach showed a subsidence bias towards the posterior, with the 20% group being significantly different from the control and anterior approach groups. When analyzing post-loading fluoroscopy images, the indenter is unsupported posteriorly but in full contact with the cement pillar anteriorly, prompting the indenter to pivot. However, for the anteriorly filled group, the cement is distributed evenly in the sagittal plane offering full support to the indenter, resulting in negligible tilting. Therefore, a 20% cement volume combined, evenly distributed throughout the sagittal depth of the VB, should be utilised to prevent subsidence.

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Session 9

NON SPINAL APPLICATION

Chairmen: Peter MUNK & Sean TUTTON

Sacroplasty

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Augmentation in the Pelvis

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Radiofrequency (RF) Kyphoplasty in the treatment of osteolytic vertebral fractures

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☐ Biomaterials	☐ Biomechanics	X Clinical	☐ Innovation

INTRODUCTION: Radiofrequency Kyphoplasty (RFK) provides a new minimally invasive procedure to treat vertebral compression fractures (VCF).
The purpose of this study was to investigate the functional outcomes, safety and radiographic outcomes after the treatment of painful osteolytic vertebral fractures treated with a novel minimally invasive procedure, RFK.

METHODS: 88 patients (50 females and 38 males) with 158 osteolytic vertebral fractures were treated with RFK using the StabiliT Vertebral Augmentation System (Dfine Inc, San Jose, CA). The StabiliT System provides a navigational osteotome to create a site and size specific cavity prior to delivering an ultrahigh viscosity cement with an extended working time (done by applying radiofrequency energy to the cement immediately prior to entering the patient). Six months follow up in 63 patients (38 females and 25 males) with 116 treated vertebrae are reported. Pre- and postoperative, 3 and 6 months clinical parameters (Visual Analogue Scale, Oswestry Disability Index score), and radiological parameters (vertebral height and kyphotic angle) were measured.

RESULTS: The median pain scores (VAS) ($p<0.001$) and the Oswestry Disability Score ($p<0.001$) improved significantly from pre- to post-treatment and maintained at 3 and 6 months follow up. Postoperative, 3 and 6 months follow-up RFK restored and stabilized the vertebral height and avoided further kyphotic deformity. No symptomatic cement leaks or serious adverse events were seen in the RFK group during 3-months of follow up. In 7 out of 158 vertebrae (4.4%) a cement leakage into the disc or lateral wall could be determined by radiograph postoperatively.

CONCLUSIONS: Radiofrequency Kyphoplasty is a very safe and effective minimally invasive procedure for the treatment of osteolytic vertebral fractures. Radiofrequency Kyphoplasty shows excellent clinical and radiological results in the 3 and 6 months follow up. Site specific cavity creation and delivery of ultra-high viscosity cement in RF Kyphoplasty with extended working time resulted in the added benefits of height restoration and lower cement leakages intra-operatively.

Continuing Conservative Care versus Cross-Over to Radiofrequency Kyphoplasty: A comparative Effectiveness Study on the Treatment of Vertebral Body Fractures

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Abstract

Background: There is controversy about how to treat vertebral fractures. Conservative care is the default approach, despite lack of evidence. Radiofrequency kyphoplasty uses ultrahigh viscosity cement to restore spinal posture and stabilize the fracture. The aims of this study were to compare radiofrequency kyphoplasty to conservative care and assess the usual algorithm of starting all patients on conservative care for 6 weeks before offering surgery.

Methods: Elderly patients with painful osteoporotic vertebral compression fractures were all treated with 6 weeks of conservative care (analgesics, bracing, and physiotherapy). They were then offered the choice of continuing conservative care or crossing over to radiofrequency kyphoplasty, at 6 and 12 weeks. Clinical success was defined as: 1) VAS pain improvement ≥ 2, 2) final VAS pain ≤ 5, 3) no functional worsening on ODI.

Results: After the initial 6 weeks of conservative care, only 1 of 65 patients met the criteria for clinical success, and median VAS improvement was 0. After 12 weeks of conservative care, only 5 of 38 patients met the criteria for clinical success, and median VAS improvement was 1. At the 6 week follow-up after radiofrequency kyphoplasty, 31 of 33 surgery patients met the criteria for clinical success, and median VAS improvement was 5.

Conclusion: For the vast majority of patients, conservative care did not provide meaningful clinical improvement. By contrast, nearly all patients who underwent radiofrequency kyphoplasty had rapid substantial improvement. Surgery was clearly much more effective than conservative care and should be offered to patients much sooner.

Comparison of clinical and radiological data in the treatment of patients with osteoporotic vertebral compression fractures with radiofrequency kyphoplasty or balloon kyphoplasty

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☐ Biomaterials	☐ Biomechanics	X Clinical	☐ Innovation

INTRODUCTION: Since the 1990s, balloon kyphoplasty has been proven as an effective method of treating patients with painful vertebral fractures. However, uncontrollable cement leakage with corresponding risks due to the low viscosity of the PMMA cement is often the focus of discussions on this procedure. The Radiofrequency Kyphoplasty is an innovative procedure available since 2009, for which an ultra-high viscosity cement is used. It also offers the advantage of over 30 minutes constant processing time. For the statistical comparison of the two methods of augmentation clinical and radiological data of 2 larger patient groups were evaluated.

METHODS: As part of the surgical treatment of patients with conservative therapy-resistant osteoporotic vertebral fractures a prospective study of radio frequency kyphoplasty was performed between 2009 and September 2010. The treatment was minimally invasive using the stability ® Vertebral Augmentation System by DFine for which the stability ® multiplex controller, the articulating Vector ® Midline osteotome, and the radiofrequency-sensitive stability ER2 ® bone cement were applied.
Measurement parameters for efficacy and safety were from the clinical aspect the course of pain intensity using a visual analogue scale (VAS: 0 to 100 mm) and the Oswestry Disability Score (0-100%). For the radiological outcome the increase in the middle and anterior parts of the operated vertebra and also the reduction of kyphosis after surgery and after 6 months were evaluated. Furthermore, the extent of cement extrusion was compared.
There were chosen 2 groups of patients with the same indication, age and the same average VAS prior to treatment. For the balloon kyphoplasty the Kyphon ® technology was used. For the BKP-group the same parameters like in the first group were evaluated. To compare the data statistically parametric and nonparametric tests were applied.

RESULTS: For the radio-frequency kyphoplasty group (RFK) 114 patients (ø 70 years) were recruited. For the balloon kyphoplasty group (BKP) 122 appropriate patients (ø 66 years) were selected. In 48% of the RFK-patients and in 44% of the BKP-patients more than one vertebral body were treated (thoracic or lumbar). Prior to treatment in both groups 84 mm on the VAS were calculated. The decrease in VAS values was (RFK vs. BKP) immediately after surgery, 58.8 mm vs.54.7 mm
($p = 0.02$), and. 73.0 vs. 58.9 mm after 6 months ($p < 0.001$). In both groups improvements in the Oswestry scores were registered after 6 months (median: RFK: BKP = 44:48 percentage points), without a statistically significant difference. In both groups, the middle part of the vertebral bodies was increased by an average of 3.1 mm. RF yielded a decrease in the average kyphosis angle of 4.4, the BKP resulted in about 3.9 degrees. Concerning cement leakage a key difference in favor of the radio frequency kyphoplasty was detected (6.1% vs. 27.8%; $p < 0.0001$).

CONCLUSIONS: The RFK has proven to be a clinically very effective procedure that does somewhat better than BKP in long-lasting pain relief. No differences could be detected regarding improvement of functioning and the mean restoration of mid- and anterior vertebral height.
As the security aspect is concerned the RFK offers the advantage of a statistically significant lower proportion of cement extrusion.

Title: Significance of Fill Patterns Observed with Two Different Bone Augmentation Materials Used in Percutaneous Vertebroplasty

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Introduction: Polymethylmethacrylate bone cement (PMMA) is the most widely used material in vertebral augmentation procedures. The search for new bone augmentation materials that are biomechanically similar to native bone, and thus would be capable of re-establishing normal physiologic load-bearing conditions in the spinal column, has been going on for years.

The limitations of PMMA based materials include their working time, which is limited to approximately 5-10 minutes after preparation; their continuously increasing viscosity which renders injection more difficult; their hydrophobic nature which prevents the material from easily flowing into the vertebrae; the significant amount of unreacted monomer that can cause adverse cardiovascular effects; and their high exothermic reaction content which results in fibrous encapsulation of the injected material. Today, many different and modified preparations are available in an attempt to mitigate some of these limitations; however, the basic characteristics are the same for all PMMAs.

Following PMMA, Cortoss™ is the first non-resorbable synthetic bone augmentation material cleared by FDA. It is a self setting composite that forms after two pastes containing one third di-functional methacrylates and two thirds radiopaque and bioactive fillers are mixed. The material is prepared as and when needed, if necessary at multiple times. It can be injected for about 4 minutes before it sets. During this time it maintains a constant viscosity and because its' hydrophilic nature it readily flows into the vertebrae. The energy imparted by the polymerization process is low and does not lead to the formation of fibrous encapsulation, and there are no volatile unreacted monomers.

Both materials were compared in a prospective randomized study in 256 patients with painful osteoporotic VCFs.

Experimental Methods: Injection volume data and post-PVP CT scans were used to compare the material distribution patterns obtained in 356 vertebral levels treated with these two different bone augmentation materials. Patterns were classified as trabecular, bolus, cleft, or combinations thereof. Fill patterns were then correlated to pain results at last follow-up on a 100-point VAS scale. Pain success was divided into 3 categories: negligible (worse to 20

point improvement, moderate (20 to 40 point improvement), and good (> 40 point improvement)

Results: Over the 24 months of the study, overall pain and functional results were comparable between the two materials, with a slight edge in favor of Cortoss. On average, 3.5cc of PMMA and 2.3cc Cortoss were used per treated level. PMMA thus required ~ 50% more volume than Cortoss to obtain similar clinical benefits. Of the 256 patients, 198 had a single level fractured, and 87 of thos displayed either a pure trabecular (63) or pure bolus (24) fill. The remaining patients had either more than one level treated, clefts, a mixed fill pattern or a combination thereof. Of the 53 Cortoss patients, 46 or 86.8% had a trabecular fill, compared to 17, or 50%, of the 34 PMMA patients. The pain results correlated to the fill pattern as follows:

Pain success	**Trabecular fill**	**Bolus fill**
Negligible	9/63 (14.3%)	6/24 (25%)
Moderate	7/63 (11.1%)	3/24 (12.5%)
Good	47/63 (74.6%)	15/24 (62.5%

Discussion: Although the number of patients that show pure distribution patterns is relatively small at 44%, the results suggest that a trabecular fill pattern leads to a more favorable result regarding pain than a bolus pattern. One reason could be that the more dispersed nature of the trabecular fill pattern is more effective in reaching all the locations of the microfractures in the vertebrae. Because of the differences in material characteristics Cortoss more often achieves a trabecular fill pattern than PMMA.

Which is the best for osteoporotic vertebral compression fractures: balloon kyphoplasty or conservative therapy?

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INTRODUCTION: Over past decade, vertebral augmentation procedures for vertebral compression fractures have become commonplace (1, 2). In 2009, a randomized controlled trial at 21 sites in eight countries assessed the efficacy and safety of the balloon kyphoplasty (3, 4). Osteoporotic vertebral compression fractures are a true challenge (5). Our aim is to evaluate and to compare the results of balloon kyphoplasty and conservative therapy in this specific indication at short outcome (≤ 6 months), in terms of quality of life, function, pain and radiological follow-up.

PATIENTS AND METHODS: Between July 2007 and June 2010, 24 consecutive osteoporotic patients with an A.1 compressive fracture according Magerl's classification (6) from T12 to L4 were recruited at Laon Medical Centre. There were six men and 18 women with mean age of 73.9 years (50 to 87). Exclusion criteria were chronic fracture, pedicle fracture, previous surgery, neurological deficit, spinal cord compression, canal narrowing, infection, carcinoma and inability to complete a questionnaire. Patients were allocated to kyploplasty (n=12) or nonsurgical care (n=12). The mean age of the fracture established between the date of the trauma and the kyphoplasty was 15.2 days (3 to 45). All patients had general anesthesia. Kyphoplasty was done with a percutaneous, bilateral, transpedicular approach. The mean injected volume per vertebral body of the polymethylmethacrylate cement was 6.4 ml (2 to 10.5). All patients received bed rest for only one day and were authorized to walk with back brace for one month without physiotherapy. Nonsurgical care was standardized and consisted in bed rest in dorsal and principally ventral decubitus for a month with physiotherapy and mobilization as soon as possible in a swimming pool. After this delay, the walking with back brace for two months was authorized. The back brace removing was realized with one-month physiotherapy.

For each patient, the pre-and post-operative clinical and radiological characteristics were obtained, including the SF-36 PCS score, Visual Analog Scale for back pain and the 1-point EuroQol questionnaire to determine quality of life. Outcomes included scores at 1, 2, 3 and 6 months.

RESULTS: The primary endpoint at 1 month showed that the improvement in PCS of the SF-36 was significant in both groups, but the difference between groups showed that the improvement in the kyphoplasty group was greater with a difference of 5 points between the groups at 1 month and a difference of 2 points at six months. The same improvement was found for quality of life, low back pain relief and back function at six months. The rehabilitation was faster and the antalgic consumption was fewer in the kyphoplasty group. The mean kyphotic angulations improved from 15° to 5° at the time of the latest follow-up in cases of kyphoplasty excepted two subsequent fractures at one and three months in two men 69 and 75 years old. The CT scans did not show extra-vertebral cement expulsion. There was an important low back pain without neurological deficit. Continuous acetaminophen treatment was necessary. In cases of nonsurgical treatment, the post-traumatic deformity increased from 15° to 25° in 45% of the patients. Isolated chronic low back pain was noted in 50% of these patients. All these patients needed acetaminophen treatment. Among them, two patients had incomplete invalid radiculalgia.

CONCLUSIONS: Kyphoplasty led to greater improvement in mean SF-36 physical component summary scores than did nonsurgical care. The quality of live was improved. The reduction of back pain was obtained earlier. The deformity of the vertebra was almost corrected. All these results were stable at 3 and 6 months with only 16% of subsequent fractures before three month follow-up. When there is no contraindication, balloon kyphoplasty is an effective and safe procedure for patients with osteoporotic compression vertebral fracture.

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Safe and successful treatment of vertebral compression fractures with the OsseoFix™ Spinal Fracture Reduction System: first 2 years of application

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Introduction: Vertebral compression fractures (VCF) have a highly negative influence on a patient's quality of life through pain and reduced mobility. The current standard care for VCF is vertebroplasty or kyphoplasty. However, there is still room for improvement as these techniques are known for their drawbacks.

Aim of the study: To present our 2-years experience as well as to evaluate the long-term efficacy and safety of the OsseoFix Spinal Fracture Reduction System to treat vertebral compression fractures.

Patients and methods: 78 patients with VCF due to primary or secondary osteoporosis, malignancy or trauma were treated with the OsseoFix Spinal Reduction System at 182 different vertebral levels. Outcomes included pre-operative and follow-up Oswestry Disability Index (ODI) and Visual Analogue Scale (VAS) questionnaires and radiographic analysis of pre-, post and follow-up X-rays.

Results: Follow-up period was 4 – 24 months. ODI and VAS scores showed a marked and significant decrease up to 80% upon treatment ($P < 0.05$ for all patient groups. For osteoporosis and cancer patients, treatment resulted in immediate kyphosis correction and restoration of vertebral height that sustained for all patients up to 12 months after surgery ($P < 0.005$), as well as for those exceeded 2 years follow-up. Osteoporosis and cancer patients also showed a significant increase in vertebral height measurements upon treatment ($P < 0.05$). No infection, or pulmonary embolism were reported. Moreover, no incidences of implant displacement, cement extravasation into the spinal canal, vessels or intevertebral disc space were reported.

Conclusions: Based on our results, the OsseoFix Spinal Fracture Reduction System can be used to safely treat VCF patients, resulting in a rapid and significant increase in quality of life and sagittal alignment of the spine that sustains up to 12 months. Although these initial data are very promising, we will proceed to perform a prospective, multi-center study in which more patients will be included to strengthen our findings.

Session 10

INTRADISCAL INJECTIONS

Chairmen: Stephan BECKER & Thomas STEFFEN

Non-Spinal Fusion Techniques: Status

S. Becker

IMSART, Vienna, Austria

Nucleoplasty – Indications, Surgical Challenges and Risks

T. Steffen

Orthopaedic Research Laboratory, Division of Orthopaedic Surgery, McGill University, Montreal, QC, Canada

An injectable self-setting hydrogel doped with an exopolysaccharide from marine origin as a synthetic extracellular matrix for cartilage tissue engineering

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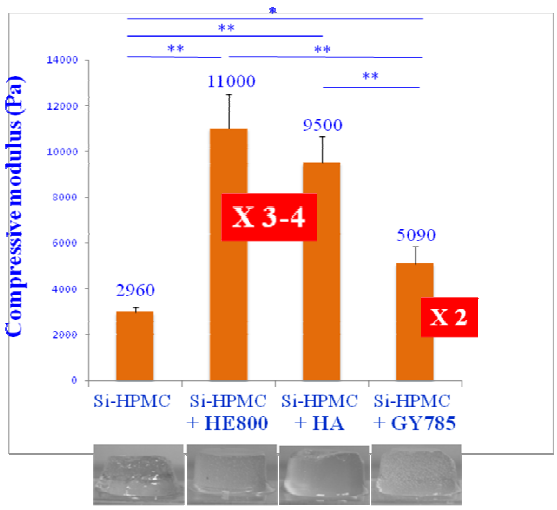
☒ Biomaterials	☐ Biomechanics	☐ Clinical	☐ Innovation

INTRODUCTION: Polysaccharides-based hydrogels such as chitosan, alginate or glycosaminoglycans (GAG) derivatives have been widely used as 3D scaffolds for cartilage tissue engineering. However none of them showed both mechanical and biological adequate properties. To develop a biomechanically and biologically competent hydrogel for bone and cartilage tissue engineering, a cellulose-based hydrogel (Si-HPMC) was reinforced with marine exopolysaccharides (EPS) GY785 and/or HE 800 compared with hyaluronic acid HA. These two marine exopolysaccharides (EPSs), HE800 EPS and GY785 EPS are a hyaluronic-like polysaccharide and a branched sulfated GAG-like polymer, respectively. Both EPSs were secreted under laboratory conditions from marine bacteria originating from deep-sea hydrothermal vents. Their large scale production is therefore convenient, low cost, reproducible, and free of non-conventional transmissible agents. HE800 is a non-sulfated linear polysaccharide with a high molecular mass (7.4x105g/mol on average). Its repeating unit is a tetrasaccharide composed of two glucuronic acid units, one N-acetyl-glucosamine and one N-acetyl-galactosamine. GY785 is a branched nonasaccharide of high molecular mass (1.4x106g/mol on average) containing 3.2% of sulfate.

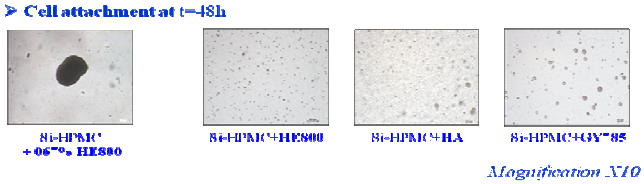
METHODS: By adding HE800 and GY785 EPSs into the Si-HPMC hydrogel, the aim of our work was two-fold: (i) to assess the mechanical properties of the Si-HPMC hydrogel supplemented with HE800 and GY785 EPSs, and (ii) to evaluate the ability of the Si-HPMC hydrogels supplemented with HE800 or GY785 EPSs to support the viability, attachment and/or proliferation of osteoblasts and chondrocytes cultured in two and three dimensions. Hyaluronic acid (HA) was chosen as a positive control for the addition of HE800 or GY785 within Si-HPMC hydrogel. We evaluated the effects of the addition of a GAG-like polysaccharide (HE800, GY785 or HA) on the physical, chemical and bioactive properties of the Si-HPMC hydrogel using osteoblasts (MC3T3-E1) and chondrocytes (C28/I2). The two GAG-like marine exopolysaccharides, HE800 and GY785 were associated with an Si-HPMC hydrogel to assess both the mechanical and biological properties of the new hydrogels built. For rheological studies we used a Mars rheometer (Haake, Germany) in oscillatory mode to measure the gel point and the conservative shear modulus and for the mechanical test, we used a texture analyser TA HD plus (Stable Micro Systems Lts, England). SEM was performed on all the mixtures. Cells were used in 2 ways. First, we analysed the attachment of cells on the surface of hydrogels and second we encapsulated cells inside the construct and we controlled the viability and the cell behaviour under fluorescence microscopy.

RESULTS:

HE800 and GY785 polysaccharides significantly improved the rheological and mechanical properties of the Si-HPMC hydrogel:



EPSs induced the attachment of MC3T3-E1 and C28/I2 cells when these were cultured in 2D on the top of the hydrogels. HE800 had the highest compressive modulus (11kPa) and allowed the best cell dispersion, especially with MC3T3-E1 when cultured on top of the hydrogels. GY785 seemed more adapted for use as a injectable 3D scaffold for cell cultures.



CONCLUSIONS:

The two GAG-like marine exopolysaccharides, HE800 and GY785 were associated with an Si-HPMC hydrogel to assess both the mechanical and biological properties of the new hydrogels built.

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ACKNOWLEDGEMENTS: ANR Tecsan and « Région Pays de La Loire » (Bioregos).

The infected bone graft
In-vitro evaluation of staphylococcal biofilm formation on *fresh (fr), fresh-frozen (ff)* or *processed human (ph) a*nd *processed bovine (pb)* spongiosa

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x Biomaterials	☐ Biomechanics	☐ Clinical	☐ Innovation

INTRODUCTION: The use of bone grafts to fill bone defects during surgery is increasing. Bone defects can be filled by *fresh* or *fresh-frozen* cancellous bone grafts or *processed spongiosa grafts*.
Aim of this study was to compare under standardized in-*vitro* conditions (i) the initial adhesion and (ii) biofilm formation of a standard laboratory strain of *S. aureus* (ATCC 29213) on *fresh (fr)* and *fresh-frozen (ff)* human bone grafts harvested from femoral heads and commercially available bone grafts consisting of *processed human (ph)* and *processed bovine (pb)* cancellous bone grafts.

METHODS: *fr* and *ff* bone grafts were harvested out of femoral heads during total hip replacement, *ph* and *pb* bone grafts were obtained as ready-to-use product from the manufacturer (cylinders, 6.5x10mm). Biofilm formation was performed in TSB for either 3h or 24h with *S. aureus* (ATCC 29213), static conditions, 37°C, ambient air. Bone grafts were afterwards washed and sonicated (BactoSonic, Bandelin) [1]. Sonication fluid was plated, bacterial counts enumerated and expressed as $\log_{10}$ cfu/sample (mean ± SD). Sonicated samples were further analysed in a microcalorimeter (TAM III, TA Instrument) and heat-flow was monitored over a 24h [2]. Experiments were performed in replicates of 5. One-way ANOVA analysis was used for statistical analysis.

RESULTS: After 3h incubation, bacterial counts were highest on the *ff* bone grafts (5.5 ± 0.3) compared to *fr* (5.1 ± 0.3, p<0.05), *ph* (4.0 ± 0.3, p<0.001) and *pb* (4.5 ± 0.2, p<0.001) bone grafts. After 24h incubation bacterial counts were lowest on the *fr* bone grafts (6.7 ± 0.2, p<0.001) but we found no difference between the 3 other groups (*ff* 7.8 ± 0.2, *ph* 7.6 ± 0.2, *pb* 8.0 ± 0.4; p>0.05). The slightest increase in bacterial density ($\Delta\log_{10}$ cfu/sample) was detected on *fr* bone grafts (1.6± 0.1, p<0.001, Fig 1 The plating of ph and pb showed normal sized cfu' while we found cfu´s with a small and a normal diameter on the plates of the fr and ff bone grafts. Microcalorimetry showed a decreased time to detection (TTD), implicating an increased bacterial density for *ph* and *pb* at 24h compared to 3h incubation, but no changes for *fr* and *ff*. (Fig 2a-d). Furthermore microcalorimetry showed two different shapes of Heat-Flow curves: *ph* and *pb* bone grafts showed one single peak exceeding 100µW for early biofilm as well as for the mature biofilm. The *fr* bone grafts showed two peaks for both investigated time points. One peak was found for the *ff* bone grafts after 3 h incubation while two peaks were observed after 24 h incubation. Further analysis showed that peak 1 represents normal sized cfu´s while peak 2 represent small sized cfu´s.

Fig. 1: *Increase in biofilm density between 3h and 24h incubation*

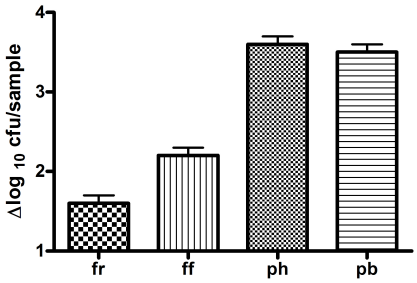
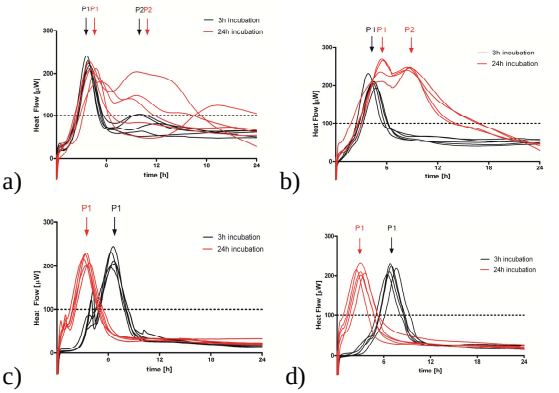


Fig. 2 a-d: Heat-flow signals for fr, ff, ph, pb bone grafts.



CONCLUSIONS: Our data showed that despite an initially increased adhesion a quantitatively reduced increase in bacterial density on *fr* and *ff* bone grafts within 24h compared to *ph* and *pb*. The use of *fr* and *ff* bone grafts therefore seems to be favourable to *ph* and *pb* bone grafts regarding the risk of a peri-operative infection. Further investigations on the relevance of small cfu and biofilm formation is needed to develop better strategies in prevention of biofilm formation on bone grafts.

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ACKNOWLEDGEMENTS: Grants from RMS Foundation (E09_0001), the Swiss Orthopaedic Society (SSO) and Swiss National Foundation (#3200B0-112547/1

Role of Injectable Bone Graft Substitute in Functional Outcome of Distal Radius Fractures

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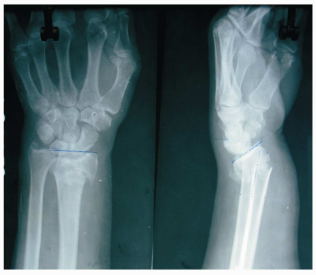
☒ Biomaterials	☐ Biomechanics	☐ Clinical	☐ Innovation

INTRODUCTION: In the comminuted fractures of distal radius with cortical comminution and metaphyseal defects, metaphyseal collapse may occur even after accurate reduction and immobilization in cast or after removal of cast or external fixator device. To avoid such collapse, injection of an injectable bone graft substitute along with cast or fixator can be used to fill the trabecular defect of fractures of the distal radius for a better functional outcome.

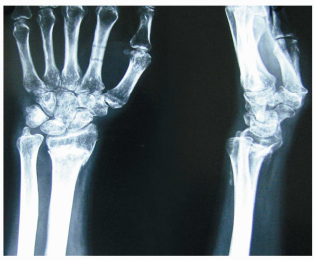
METHODS: The authors undertook a prospective review (with a level IV evidence) of 30 patients with distal radial fractures (with metaphyseal comminution) treated with external fixation and bone graft substitute (ostim) injection at site of metaphyseal comminution over a period of 2 year (2008-10).
The bone graft substitute (ostim), a nanocrystalline hydroxyapatite is available as preformed paste which is easy to apply and is also available in prefilled syringes.
We analysed data regarding metaphyseal collapse via radiological parameters (Radial length, radial angle, and dorsal tilt) and functional outcome (assessed by Modified Gartland and Werley scoring system) at the end of 6 months.

RESULTS: Final results regarding radiological/anatomical outcome of the patients in study group were evaluated using scoring given by Stewart et al. (1984). The parameters used were dorsal tilt, radial shortening, and loss of radial angle. 3(10%) patients showed excellent results at the end of 6 months and 27(90%) of patients showed good results at the end of 6 months.
Out of 30 patients 13 showed excellent, 15 good and 2 patients showed fair functional outcome (as per Modified Gartland and Werley Scoring System)
CONCLUSIONS: Injectable bone graft substitute prevents late collapse in comminuted distal radial fractures as seen by measurement of radial length/ radial angulation at 6 months follow up.

CASE 1 (RADIOLOGICAL RESULTS)



Pre operative (AP/Lat)



Post operative (AP/Lat) at 6 months compared with normal hand

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The functional outcome is good in patients treated with injection of injectable bone graft substitute.
Our data suggest that injectable bone graft substitute in the treatment of distal radius fractures is effective.

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Session 11

BIOLOGICS AND FUNCTIONALIZATION

Chairmen: Jim TRIFFITT & Kerong DAI

A Study of Titanium Fiber Balls Combined with Nano-Sr-HA in the Bone Defect Repair and Vertebral Augmentation

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Abstract is included, page 93.

Mesenchymal Stem Cells

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Botnar Research Centre, Institute of Musculoskeletal Sciences, Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, University of Oxford, Oxford, UK

Abstract is included, page 94.

A study of titanium fiber balls combined with nano-Sr-HA in the bone defect repair and vertebral augmentation

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*Corresponding author and presenter

√Biomaterials	☐ Biomechanics	☐ Clinical	☐ Innovation

INTRODUCTION: Since the application of injectable bone cement or other materials in bone repair or reconstruction having the feature of minimal invasion, it has been attracted more and more attention. Currently, the most widely used is the injection of bone cement into vertebral body for augmentation, but several problems still have to be considered: 1) bone cement may be forced into the pulmonary circulation through vertebral venous sinus; 2) it may leak into the spinal canal or intervertebral foramen, and induce spinal cord or nerve root injuries; 3) it is a non-biological therapy, and the cement will loose or fracture if stays in vertebra for a long time; 4) it is non-biodegradable, and could not be integrated with bone tissues; 5) it may induce high temperature damage when the cement is polymerized. This study will explore the repair effect for bone defect using titanium fiber balls (TFBs) coated with nano-Sr-HA and probe into its application possibility in vertebral augmentation.

METHODS: TFBs used in this study was made by Titanium fiber and was 2mm in diameter. Its porous diameter is 100-200μm with 84% of porosity. Bone drill defects were created in the bilateral femoral condyles in 24 SD rats. TFBs with nano-Sr-HA (NSH) coating were inserted into the right femora bone defects and served as experimental side. TFBs without NSH were implanted in the other side for comparison. 6 rats were sacrificed respectively at 1, 2, 4, and 8 weeks after surgery. The specimens were observed by X-ray and histological examination.

RESULTS: With the extension of postoperative time, the X-ray film showed that the interspaces between TFBs with NSH, as well as the interfaces between balls and bones were gradually blurred. After 8 weeks, the interfaces between TFBs with NSH and host bones were vanished. It was revealed that the new bone formation between TFBs with NSH and host bone, as well as the bone growth into TFBs were found (Fig.1). Statistical evaluation indicated that the amount of bone formation inside of TFBs with NSH in the experiment group at the 4th and 8th weeks postoperatively was significantly more than that in the control one (Fig.2).

DISCUSSION: The porous structure of TFBs increases the surface area, and benefits the ingrowth of blood vessels and bone, so as to provide a long term support of the vertebrae. The small balls can fill various shapes of bone defects. Owing to its small volume (it can easily reduce its diameter to 1mm±), it provides a possibility for injection and fulfills the requirement of minimally invasive technique. And it is easy to sterilize. Furthermore, nano-Sr-HA can promote cell adhesion, proliferation and osteoconduction while its osteogenic potential is improved by nano-Sr-HA.

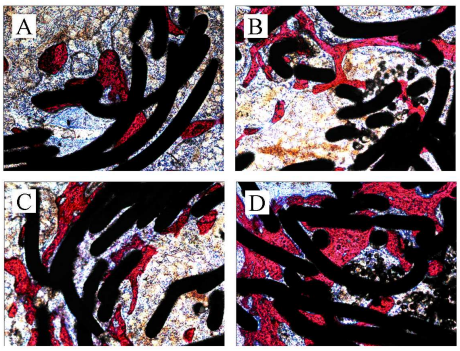

Fig.1: New bone formation of TFBs with (B, D) or without nano-fermorite (A, C) at 4 (A, B) or 8 (C, D) weeks after implantation (Van Gieson's picric–fuchsine stain; original magnification×100)

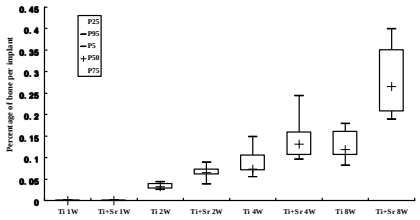

Fig.2: Percentage of new bone formation after implantation.

CONCLUSIONS: There is a possibility for the application of titanium fiber balls with nano- Sr-HA coating in bone defect repair and vertebral augmentation.

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ACKNOWLEDGEMENTS: This study was supported by the Program for Shanghai Key Laboratory of Orthopaedic Implant (08DZ2230330).

Mesenchymal Stem cells

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The potential uses of stem cells for cell therapy have aroused great interest and controversy over the past few years, but the stem cell concept was introduced almost one-hundred years ago. Stem cells are unique in that they exhibit asymmetric cell division such that they both self-renew and also give rise to cell types different to themselves. They exist in embryonic development but also occur in adult tissues. The latter are thought to be present in almost every adult tissue, even in those tissues that do not exhibit pronounced turnover.

Current research emphasizes the possibilities for using both embryonic and adult stem cells in an assortment of clinical transplantation strategies for tissue engineering and regenerative medicine to treat human disease and improve health and the quality of life. In addition, basic work on stem cells is providing new fundamental knowledge about the nature of these cells and their participation in normal and pathological cell function and development. Furthermore, reprogramming differentiated somatic cells into a stem cell-like state to form induced pluripotent stem cells is a significant development and an intensive area of current investigation.

In bone marrow are found two major and distinct stem cell types: the haematopoietic stem cells, producing blood cells, and marrow stromal fibroblasts, or 'mesenchymal stem cells'. The latter have the capacity to differentiate into all characteristic connective tissue types, including bone, cartilage, fat, fibrous tissue, muscle and haemopoietic stroma. These mesenchymal stem cells are considered to be part of a heterogeneous set of multipotent stromal stem cells that can be isolated and cultured *in vitro* from many tissues. Bone marrow cells of the haematopoietic lineage have proved valuable for treatment of certain anaemias and cancers and such successful therapies suggest possibilities for use of other tissue stem cells to provide similar benefits in diseases affecting other tissues. The observed plasticity of differentiation of mesenchymal stem cells indicates potential use of these cells to augment, replace and repair these diseased and damaged tissues. Hence these cells are being actively studied for use in cell-replacement therapies, in particular for injuries involving bone, tendon, or cartilage and possibly for providing benefit to treatment of certain skeletal disease conditions. Additionally, these mesenchymal stem cells are now shown to have immunomodulatory actions with pronounced anti-inflammatory and antiproliferative effects. Tissue-deposited stem cells after transplantation or local or systemic injection are shown to be influenced by microenvironmental cues and furthermore may provide factors that promote tissue-cell survival at the damaged tissue site. The mesenchymal stem cells are easily transduced with exogenous genes and are being tested for gene therapy of a number of conditions. Thus observations from studies on these multipotent cells are central to the fields of Regenerative Medicine and Tissue and Genetic Engineering and particularly to the pathology of musculoskeletal diseases.

Injectable Alginate Polymers for Bone Tissue Regeneration: Physico-Chemical Properties and *In vitro* Mesenchymal Stem Cell Response

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☒ Biomaterials	☐ Biomechanics	☐ Clinical	☐ Innovation

INTRODUCTION: Ideally, scaffolds for regenerative medicine should organize cells into a 3D architecture, offering structural support and preserving cells viability and function. Our focus concerns the development of injectable multifunctional biomaterial for minimally invasive bone regeneration applications. We have designed alginate-based hydrogel networks, modified with biochemical cues, which are expected to provide an adequate microenvironment for cells cultured under 3D conditions. Alginates are extracted from brown seaweeds and can form gels in the presence of divalent cations, such as Ca^{2+}, under mild conditions. Alginate was modified with cell adhesion (RGD) peptides, and with a designed cell protease-sensitive peptide (GGYGPVGLIGGK) that establishes links between the polymer chains. We have shown that 3D cultures of mesenchymal stem cells (MSC) immobilized within the proposed scaffold promoted a more dynamic cell-matrix and cell-cell interactions. MSC were able to form cellular networks within functionalized alginate hydrogels, by creating their own pores and pathways via cell–secreted proteases [1]. Here, we investigated the hydrogel morphology, swelling, mechanical properties and the ability of the proposed model to adjust into complex forms and crosslink *in situ*. 3D cultures of MSC within modified alginate scaffolds under osteogenic conditions were established and cell viability and differentiation were evaluated.

METHODS: Alginate was irradiated and oxidized to increase cell viability and further modifications through carbodiimide chemistry were adopted to functionalize alginate with RGD and PVGLIG. The amount of immobilized peptides was estimated by UV spectroscopy and the BCA assay. *In situ* crosslinking was promoted by combining alginate solutions with $CaCO_3$/GDL and gel-precursor solutions were casted into different moulds. Cryo-SEM was used to access morphology of alginate hydrogels composed by different concentrations of the polymer (0.5-2.5wt.%). Dynamic Mechanical Analyser (DMA), in compression mode, was used to measure mechanical properties of 2wt% alginates hydrogels modified with RGD combined with different amounts of alginates modified with PVGLIG (0, 10, 50 or 200mg per gram of alginate), in either crosslinking or tethered positions, to verify the influence of the peptide linkage density on hydrogel properties. 3D cultures of MSC under osteogenic condition were established and cell differentiation was assessed by alkaline phosphatase staining. MSC viability was monitored by calcein acetoxymethyl/ ethidium homodimer-1 fluorescence (live/dead) assay.

RESULTS: Peptides were effectively grafted to alginate, as confirmed by the BCA assay and by the presence of characteristic peaks at 230/275nm on the UV spectra. Alginate hydrogels can be formed into different shapes depending on the mould employed, demonstrating the capacity of the system to adjust into complex shapes. By varying the alginate concentration, the characteristics of the hydrogels can be manipulated, to form a loose network with large pores (0.5wt%) or a dense mesh (2.5wt%) according to the application required. DMA tests showed that the storage modulus increased with the amount of crosslinking PVGLIG and decreased with the amount of tethered peptide, showing how PVGLIG may regulate hydrogel elasticity. Loss modulus was not significantly affected. The extent of swelling was equivalent across different PVGLIG densities, although higher than in a control not subjected to the carbodiimide procedure. Preliminary studies on osteogenic differentiation of 3D cultures showed that MSC immobilized within alginate modified with both peptides were able to differentiate along the osteoblastic lineage demonstrating that the proposed system supports osteogenesis. Cells immobilized within the hydrogels maintained a high viability along the 30 days of culture, as verified by live/dead assay, suggesting that the highly hydrated matrices enable an adequate exchange of nutrients and cellular metabolites.

CONCLUSIONS: The developed multifunctional cell-interactive alginate hydrogels possess a range of relevant properties that can be easily tailored, namely gelation time, geometry, porosity and stiffness. These hydrogels also provide an adequate 3D microenvironment for MSC osteogenic differentiation. Based on these advantages, we believe that the developed hydrogels may find applicability as injectable cell vehicles for bone regenerative medicine.

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ACKNOWLEDGEMENTS: Portuguese Foundation for Science and Technology (FCT) for PhD grant SFRH/BD/30057/2006; Work carried out under contract PTDC/SAU-BEB/101235/2008 (FCT) and FCOMP-01-0124-FEDER-010915 (FCT)

FATE OF HUMAN MESENCHYMAL STEM SELLS IN IMMUNODEFICIENT MICE: DIFFERENTIATION OR TRANSDIFFERENTIATION?

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INTRODUCTION: The aim of this study was to track the fate of enhanced green fluorescent protein (eGFP)-labelled human mesenchymal stem cells (hMSCs) in immunodeficient mice, and to investigate whether any expression of eGFP and human osteogenic marker mRNA after xenotransplantation were due to the survival and function of hMSCs or to transfection and expression of hMSC DNA and messages in mouse cells.

EXPERIMENTAL METHODS: hMSCs were genetically labelled with eGFP. The eGFP-labelled, antibiotic (G418)-selected hMSCs were expanded *in vitro*. Cells were divided into 3 groups, 1) eGFP: Normal eGFP-hMSCs; b) IR: eGFP-hMSCs γ-irradiated to block cell proliferation; and 3) CF: Fragmented eGFP-hMSCs produced by freezing the cells at -80°C followed by ultrasonicating to break the cells into fragments. Cultured cells from each group were implanted into the left anterior tibialis muscle of CB17 Scid/beige immunodeficient mice (6 mice per group). Sham-operated mice were used as the control group. Mice were sacrificed at 7 and 14 days after implantation. Survival and differentiation was assessed by fluorescent microscopy and histomorphometry of the area implanted with eGFP cells, PCR to detect the human alu-sequence, and RT-PCR for eGFP, human RUNX2, alkaline phosphatase, osteocalcin, collagen type I, and osteopontin mRNA expression.

RESULTS: Implanted eGFP-labelled cells showed bright green fluorescence when observed by fluorescent microscopy. The fluorescent areas were segmented by threshold and the areas were calculated using image analysis software. This confirmed the absence of eGFP cells in the sham samples. In the CF group, there was a small area of eGFP tissue at 7 days after implantation but no eGFP tissue was detectable at 14 days. In the IR group, large areas of eGFP tissue were observed at 7 days after implantation but were sharply decreased at 14 days. In the eGFP group, the areas of eGFP tissue remained stable over 14 days. Expression of human osteogenic differentiation markers was found in both the eGFP and IR groups. Interestingly, eGFP mRNA was also detected in the CF group, although expression levels were low.

In summary, eGFP-labelled hMSCs survived in CB17 SCID/beige immunodeficient mice for up to 14 days, and expressed osteogenic differentiation markers, eGFP and the human alu sequence. γ-irradiated eGFP-hMSCs survived for 7 days and also demonstrated osteogenic differentiation; however after this there was a sharp decrease in cell number. Sites implanted with hMSC cell fragments did not show any human osteogenic differentiation markers, but traces of eGFP tissue, and mRNA expression of eGFP was detectable at day 7. We conclude that intramuscular xenoimplantation of hMSCs into immunodeficient mice results in osteogenic differention; however, the transdifferentiation, if any, appears to be at a very low level.

Bone Graft Substitute -Antibiotic Impregnated in Chronic Osteomyelitis

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Abstract:

Chronic Osteomyelitis (COM) is a debilitating , complex problem in terms of its management and long term outcome. Options of treatment include Incision & Drainage, Debridement with systemic antibiotics, local or distal flap, external or internal stabilization with impregnated antibiotics bone cement and in extreme cases amputation. Essence of the problem is the bone loss & infection which is the source of recurrent local and systemic morbidity. Dead space management is difficult problem to deal with, previous options are not uniformly effective, difficult , need additional and repeated surgeries. We conducted pilot study looking into feasibility of the bioabsorbable materials like calcium sulfate based bone graft substitute ē impregnated antibiotic in 12 patients, 8 males (60%) and 4 females (40%), Age 2-45 year (avg. 29 years). Seven patients had COM tibia, two of ulna, two of distal femur and one Calcanium, Osteolysis, cortical thinning, sequestrum and, involcurm confirmed on X-ray and MRI. All the patients went through debridement of necrotic tissue with removal of all dead bones until bleeding bone edges are achieved. Cavities filled ē bone substitute impregnated with antibiotics. We have good clinical & radiological outcome& found this method safe and effective solution in COM with dead space, are easy to handle, cost effective and do not need repeated surgical intervention.

BoneWelding® Technology: Enhanced Biomechanical Stability for Pedicle Screws

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☐ Biomaterials	☐ Biomechanics	☐ Clinical	X Innovation

INTRODUCTION: The BoneWelding process employs ultrasonic energy to liquefy a thermoplastic interface between orthopaedic implants and host bone. The liquefied thermoplastic polymer penetrates the pores of the surrounding bone and, following a rapid solidification due to immediate cooling, forms a strong and uniform bond between implant and bone. This results in enhanced stability [1, 2] and reduces surgical time [3]. It also demonstrates the potential of avoiding migration of the implant even in osteopenic bone [4]. The BoneWelding process is compatible with many thermoplastics, including current resorbable orthopedic polymers like polylactides. The safety of the process has been demonstrated in-vivo in a number of sheep studies for various indications and implant configurations, including pelvis, spine, mandibula [3], femur and tibia studies [5]. The BoneWelding technology is used clinically in cranio-maxillofacial surgery (SonicWeld RX® System, KLS Martin) since 2005 [6, 7]
In the presented biomechanical study the effect of the BoneWelding process on the stability of a cannulated titanium pedicle screw has been investigated by testing the pull-out performance in human vertebrae as well as in Sawbones of various densities.

METHODS: Applying the BoneWelding process, a polymer rod (polylactide (PLDLLA 70/30, LR706, Boehringer Ingelheim, Germany) inside the cannulation of a fenestrated pedicle screw (thread diameter 6.5 mm, Thread length 45mm) was liquefied using ultrasonic energy (20 kHz) and extruded through distal fenestrations into the vertebral body after implanting the screw using a standard technique. Identical pedicle screws were used as reference. Pullout tests were done in Sawbones (10pcf and 7.5pcf, modelling medium and low bone densities) and in human cadaver vertebrae placing the reference screw contra-laterally. The mechanical indentation resistance was measured with a 2mm steel rod to relate the results to the strength of the cancellous bone.

RESULTS: Direct visualization revealed homogenous infiltration of the polymer into the bone or Sawbones. The ultrasonic insertion process required about 12 seconds of ultrasound application to extrude a polymer volume between 80 and 330 mm^3 that was related to the local bone density. The polymer infiltration was limited since the melt starts to solidify as soon as the ultrasonic process has been stopped. The diameter of the polymer infiltration torus did not exceed 16 mm (fig 1, left). The initial failure force for the BoneWelding reinforced pedicle screw was 50-430% (fig 1, right) higher than for the contra-lateral reference screw. The final pull-out strength significantly ($p< 0.05$) exceeded the reference by 107 or 77% in 7.5pcf or 10pcf Sawbones and by 39% in the human vertebrae. Final failure always occurred at the polymer-bone interface.

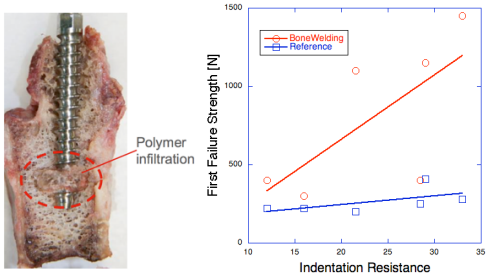

Fig. 1: (left) Polymer torus inside vertebral body. (right) Comparison of biomechanical stability between the BoneWelding (red) and reference (blue) screws.

CONCLUSIONS: The ultrasonic liquefaction process enabled to complete the bone infiltration process in less than 20 seconds. The thermoplastic character of the reinforcing polymer prevented uncontrolled flow and provided full stability immediately after insertion. The improved mechanical performance of implants bonded with the BoneWelding process can be attributed to the favourable mechanical micro-environment created by the excellent interdigitation of bone, polymer and implant. These results demonstrate the potential of the BoneWelding technology to improve primary stability - especially in poor bone - not only for pedicle screws but for a variety of spine implants.

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Session 12

INJECTABLE BIOMATERIALS

Chairmen: Marc BOHNER, Christele COMBES & Pierre WEISS

Cements in Orthopaedic Surgery

S. Deb

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Abstract is included, page 101.

Influence of Particle/Agglomerate Slze of B–TCP on its Reactivity as Component for Brushite Forming Bone Cements

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Abstract is included, page 102.

CEMENTS IN ORTHOPAEDIC SURGERY

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x☐ Biomaterials	☐ Biomechanics	☐ Clinical	☐ Innovation

INTRODUCTION: Disease conditions, such as osteoarthritis, osteoporosis, or rheumatoid arthritis cause degeneration of the joint. Total joint replacement has been widely adopted to treat these debilitating illnesses, as it is often the only course of treatment to alleviate pain and improve the quality of life. The number of joint replacements worldwide is rising and is expected to continue to do so, given the increase in population of the elderly and associated disease and trauma. The success and widespread use of joint replacements in the management of arthritic conditions and trauma has made a significant impact in modern healthcare. Acrylic bone cements[1] have been traditionally used in placing hip and knee joints, which fills the space between the implant and the joint and cements of very similar composition are being used in vertebroplasty and kyphoplasty. Surgeons replace a dysfunctional joint using metal alloys and polymeric materials, with a functional, long-lasting prosthesis.

Infection is often a complication following joint replacement surgery and the use of antibiotic impregnated acrylic cements is emerging to be a potentially effective clinical procedure that may assist in reducing the incidence of deep infection. The main advantage of local antibiotic delivery is the ability to achieve high levels of antibiotic at the target site without increasing systemic toxicity. An emerging trend in clinical medicine is the use of combination devices and the bone cement is being exploited as a potential drug carrier. This paper will highlight the effect of inclusion of antibiotics[2] and additives on the properties of bone cements that may decrease the incidence of infection promote bone healing or decrease bone resorption and its efficacy as a drug delivery vehicle. Furthermore newer approaches for the improvement of acrylic bone cements will be discussed[3]. Furthermore, methods of enhancing injectability and conferring bioactivity in the acrylic bone cements will be discussed for applicability as an injectable cement.

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Influence of particle/agglomerate size of β–TCP on its reactivity as component for brushite forming bone cements

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☒ Biomaterials	☐ Biomechanics	☐ Clinical	☒ Innovation

INTRODUCTION: The research and development of calcium phosphate cements (CPC) with improved mechanical properties, suitable for bone graft applications in the most demanding surgical procedures such as vertebroplasty and kyphoplasty, have attracted much attention in the last years. However, the injectability of calcium phosphate cements is still far from being satisfactory. The flow properties of CPC pastes depend on a number of factors such as particle size (PS) and particle size distribution (PSD), nature of the phases presented (amorphous or crystalline), solid-to-liquid or powder-to-liquid (P/L) ratio, presence of additives, etc. [1]. All these factors affect the reaction kinetics of cements. It is known that decreasing PS accelerates the setting reactions and shortens both initial and final setting times, but the effects on mechanical properties are unclear [2]. The influence of the agglomeration/aggregation state on the reaction kinetics and injectability is still far from being well understood [1-5]. Therefore, there is a need to shed more light on these issues by using well controlled experimental conditions. The aim of this work is to study the influence of particle size distribution and the state of agglomeration of β-tricalcium phosphate powder (β-$Ca_3(PO_4)_2$, β-TCP) on setting time, reaction rate and injectability of brushite ($CaHPO_2.2H_2O$, DCPD) forming CPC.

METHODS: The β-TCP precursor powder was prepared by an aqueous precipitation method from $Ca(NO_3).4H_2O$ and $(NH_4)HPO_4$ salts. The precipitated powder was separated by filtration, dried and calcined at 800ºC to obtain crystalline β-TCP phase. Different PS/states of agglomeration were obtained by ball milling. Spherical granules of β-TCP were also prepared from a well dispersed suspension sprayed in liquid nitrogen followed by freeze-drying and sintering up to near full density, sieved and separated by sizes. β-TCP powders and granules were characterized by particle size distribution (PSD), surface area (BET model), scanning electron microscopy (SEM) and X-ray diffraction (XRD). β-TCP spherical granules with different PS and PSD were used to prepare cements and to study the influence of the powders' characteristics on reaction kinetics. X-ray diffraction analysis (XRD) was selected to assess the crystallinity of the powders and the extent of phase transformations occurring during the setting of cements after different reaction times.

RESULTS: The β-TCP powder allowed preparing high concentrated suspensions with shear thinning behaviour suitable for freeze granulation. Full dense β-TCP spherical granules (Fig. 1) could be obtained by sintering at a temperature below that of β-TCP to α-TCP phase transformation. The uniform geometry and the use of granules with different sizes enabled to establish a good correlation between the particulate sizes of reacting components and the kinetics of transformation of β-TCP into brushite.

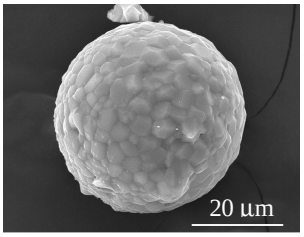

Fig. 1: Full dense β-TCP spherical granule

The spherical geometry also enabled to better distinguish between the effects of particle/agglometate sizes on injectability of cements.

CONCLUSIONS: The most important achievements in this work were as follows: (i) obtaining well dispersed β-TCP suspensions that allowed preparing spherical full dense granules, which simulate uniform particles with different size ranges; (ii) the possibility of better modelling the influence of particle size and size distribution on the reaction kinetics and injectability of CPC.

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Application of Marine Derived Collagen to a Calcium Phosphate Cement System for Spinal Fracture Fixation

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☒ Biomaterials	☐ Biomechanics	☐ Clinical	☐ Innovation

INTRODUCTION:

Previous work considered a calcium phosphate cement (CPC) with the incorporation of bovine collagen for the application of vertebroplasty [1]. These composite cements demonstrated an improvement in the associated brittle nature of CPCs, but did not achieve all clinical requirements for vertebroplasty therefore an alternative must be sourced. There are also additional risks associated with the use of bovine materials like that of bovine spongiform encephalopathy (BFE) [2]. One such alternative is the use of collagen derived from a marine source. Marine collagen has a number of advantages like the ability to reproduce asexually, hence providing a means for harvesting on a commercial scale. This form of collagen is easily suspended within a liquid phase, providing an alternative means to effectively incorporating collagen within CPCs. With this in mind, this study describes the addition of marine collagen fibres and its effects on the properties in relation to the clinical requirements stated for vertebroplasty.

METHODS:

An optimum cement composition has been developed and tested using a Design of Experiments (DoE) approach [3]. This system contained 100% alpha tricalcium phosphate and di-sodium hydrogen phosphate solution (Na_2HPO_4) using a liquid to powder ratio of 0.35mL/g. Marine collagen fibres (MFs) were added to the liquid phase at 1, 3 and 5wt% to produce a suspension, with a control for comparison. Compressive properties were tested in accordance with ISO 5833:2002, that being compressive strength (CS) and Young's modulus (YM). Injectability (I) was measured by extruded the cement through a syringe at a constant extrusion rate of 10mm/min with a maximum load of 100N. Initial (t_i) and final (t_f) setting times were analysed using the Gillmore needle apparatus complying with ASTM C266-89. Scanning electron microscopy (SEM) was carried out on the surface of all fractures samples were a JEOL 6500 FEG SEM system was used.

RESULTS:

Table 1 shows the material properties of all cement formations studied. Increasing the MF loading produced a decrease in CS ($p<0.01$), however there was no significant difference when comparing the control and 1wt%MFs. The control, 1 and 3wt% were all within the range stated for vertebroplasty i.e. $\geq$ 30 MPa [4]. The YM results showed a similar trend to the CS results, were an increase in MF loading produced a decrease in YM ($p<0.01$), with no significance between the control and 1wt% MFs. The highest recorded value (55.96%) for I was observed by 1wt% MF, and an increase in MF loading decreased the level of I achieved ($p<0.01$). With 5wt% MF, the cement was extremely difficult to mix and hence injection was not possible. During extrusion, the MF occluded the cannulated needle causing the decrease in I. In order to accomplish successful fracture fixation, a cement must achieve as close to 100% I as possible. Hence improvements are still required for the presented composites. The incorporation of MFs reduced both t_i and t_f ($p<0.01$) to within the clinical requirements. The recommended setting times for vertebroplasty are between 3 and 8min for t_i and $\leq$ 15min for the t_f.

Table 1: *Material Properties of Cements*

Property	*Control*	*1wt% MF*	*3wt% MF*	*5wt% MF*
CS (MPa)	31.64 ± 3.87	37.80 ± 6.44	36.13 ± 8.87	24.42 ± 6.57
YM (GPa)	1.11 ± 0.14	1.28 ± 0.21	1.25 ± 0.22	0.83 ± 0.25
I (%)	52.60 ± 7.30	55.93 ± 11.49	23.79 ± 3.79	1.07 ± 1.59
t_i (min)	14.0 ± 0.9	8.7 ± 0.5	4.6 ± 0.5	2.3 ± 0.5
t_f (min)	23.0 ± 0.9	12.0 ± 0.9	9.3 ± 0.5	7.3 ± 0.5

CONCLUSIONS:

This study explored the use of marine collagen CPC composites for the application of vertebroplasty. The results indicate that the greatest improvements were achieved by 1wt% MF collagen-CPC, with CS and setting times within the clinical range for vertebroplasty. Future studies are needed to improve the injection capabilities of this collagen-CPC cement. These results highlight a promising new composite which has the potential to improve the fixation of traumatic vertebral fractures.

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Injectability of Portland cement for orthopaedic application

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☒ Biomaterials	☐ Biomechanics	☐ Clinical	☐ Innovation

INTRODUCTION: Portland cements (PCs) are durable[1], possess high compressive strengths[2] and set in aqueous environments (such as those found *in vivo*)[3] and recently have also demonstrated biocompatibility when used as an endodontic sealing material[4]. PCs therefore possess many beneficial properties for potential use in orthopaedic load bearing applications such as vertebroplasty, which involves injecting a stabilising bone cement into a collapsed vertebra[5]. However, before PC could be used as an orthopaedic cement, appropriate injectability through a syringe needs to be established and setting times decreased. Most recognised liquefiers used in civil engineering cannot be used due to a lack of biocompatibility.

METHODS: Modified cements were prepared by adding calcium chloride, calcium nitrate, calcium acetate, sodium hexametaphosphate and sodium aluminate at 5 or 10wt% into the powder phase of grey Portland cement. Distilled water was added to the cement at a powder-to-liquid (PLR) of 4.0g ml^{-1} and samples were hand mixed for 1 minute. The injectability of the cement pastes was calculated as wt% of 5g of cement slurry extruded through a 5ml syringe with a 2mm opening using a universal testing machine (Instron 5544, Bucks, UK) with a cross-head speed of 30mm min^{-1} and a maximum force of 100N. The initial setting times of the cements were measured using the standard Gilmore needles test. X-ray diffraction patterns of the set cements were recorded on a D8 Advance diffractometer (Bruker, Germany). Data sets were collected from 2θ = 5-40° with a step size of 0.02 and the count time was normalised to 1s/step. The phase compositions of the cements were determined according to the "Inorganic crystal structure database", calcium hydroxide (PDF Ref. 04-010-3117), calcium silicate (PDF Ref. 04-011-1393) and ettringite (PDF 00-041-1451). The results for statistical significance were analysed using 1-way ANOVA.

RESULTS: A 5wt% addition of calcium chloride, calcium nitrate, sodium hexametaphosphate, calcium acetate and sodium aluminate significantly ($p<0.001$) increased cement injectability compared with the PC standard (fig 1.) There was also a further significant increase in injectability when admixture content was increased to 10wt%. All of the additives accelerated the initial setting time of the cement to below 55 minutes, a significant reduction compared with the PC standard (120minutes). All of the modified cements demonstrated reduced setting times at 10wt% compared with 5wt%. The majority of accelerants at 10wt% set in under 20 minutes including calcium chloride, sodium hexametaphosphate and calcium acetate. After 24h of setting both calcium hydroxide and ettringite were both present in cements containing calcium nitrate and calcium chloride.

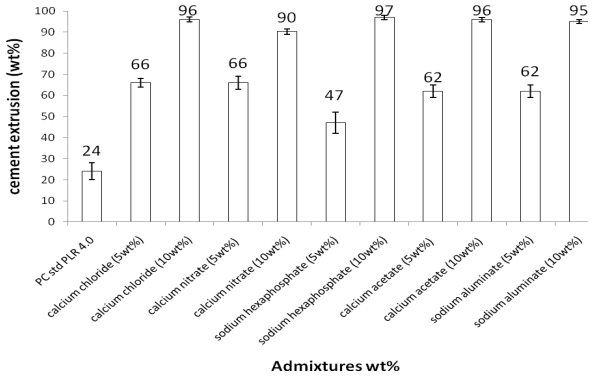

Fig. 1: Increase in cement injectability when a range of admixtures were added to standard Portland cement.

DISCUSSION: It has previously been inferred using zeta-potential measurements that the liquefying abilities of certain additives were due to the binding of these highly charged anions onto the surface of PC[6]. Binding results in both an electrostatic and due to the large size of some of the anions, a steric repulsion between the cement particles[7]. The reduced setting times of the cements containing the additives calcium chloride and calcium nitrate may be linked with the accelerated formation of PC hydration products. Calcium hydroxide is a by-product of calcium silicate hydration and ettringite is formed by the reaction of tricalcium aluminate with calcium sulphate dihydrate[8]. The XRD patterns for cements containing either chloride or nitrate additives indicated that the quantity of both hydration products was higher than in the PC standard after 24-h setting.

CONCLUSIONS: By using additives Portland cements can be made injectable through a narrow aperture and brought to set in a time period appropriate for orthopaedic procedures such as vertebroplasty.

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Injectability of antibiotic-loaded brushite bone cement

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☒ Biomaterials	☐ Biomechanics	☐ Clinical	☐ Innovation

INTRODUCTION: Calcium phosphate cements (CPCs) have been extensively studied as orthopaedic biomaterials and bone substitute materials for several decades [1]. More recently, CPCs have been investigated for use as drug delivery devices [1].
The injectabilities of CPCs, particularly brushite-forming bone cements have been reported as poor [2], and as a result, liquefiers have been added to these cements to increase injectability [2, 3]. Brushite-forming CPCs have the advantage of resorbing *in vivo* [1]. The aims of the study were to evaluate the injectability of antibiotic-loaded brushite bone cements, without the addition of known superplastercizers, and the effect of the drug load on mechanical strength and setting properties of these cements.

METHODS: Equimolar amounts of phase pure sintered β-tricalcium phosphate (β-TCP) and monocalcium phosphate monohydrate (MCPM) [4] were mixed with 1wt% tetracycline hydrochloride (TCH), chlorhexidine diacetate (CHX), ciprofloxacin (CIP) or gentamicin sulphate (GS). Cement powders were hand-mixed with 800mM aqueous citric acid (a setting retardant) solution at a powder to liquid ratio (PLR) of 2.5 and 4.0g/ml.
Antibiotic-loaded cement paste was extruded from a syringe (n=5) using a mechanical testing machine (crosshead speed: 1mm/min, a maximum force of 100N) to calculate injectability. Initial setting times of cement pastes were measured with a Gilmore Needles test. Cement pastes were moulded into cylindrical samples (6mm diameter x 12mm height). After initially setting (>1h) at 37ºC, samples were stored in distilled water at 37ºC for a further 23h. Wet compressive strengths (CS) of samples (n>10) were obtained using a mechanical testing machine (crosshead speed: 1mm/min). Strut densities of dry cement fragments were obtained using helium pycnometry and in conjunction with apparent dry densities, relative porosities were calculated (RP). Mean values for significance testing ($p<0.05$) were compared using a one-way ANOVA with Tukey Post-hoc test.

RESULTS: Brushite bone cements became more injectable with the addition of 1wt% antibiotics. GS additions increased the injectability of brushite cement the most (table 1).
Initial setting times of brushite cements (with a PLR of 2.5g/ml) remained similar with 1wt% TCH, CHX and CIP additions. However, GS addition increased the initial setting time to 24±3min. Brushite containing 1wt% CIP (PLR 2.5g/ml) had a significantly higher CS and lower RP than the control and all other antibiotic-loaded cements (table 1). Brushite cements containing 1wt% CHX and CIP, with a PLR of 4.0g/ml, accelerated the setting slightly, whereas GS additions had a retarding effect and increased initial setting times (table 1). CS increased considerably for CIP and GS additions, whilst RP was unchanged.

Table 1: The injectabilities, initial setting times, compressive (Comp.) strengths and relative (Rel.) porosities of antibiotic-loaded brushite cement.

Antibiotic loaded	Initial setting time (min)	Comp. Strength (MPa)	Rel. Porosity (%)	wt% of cement paste extruded
PLR 2.5g/ml				
Control	18 ± 3	11.7 ± 2.4	32 ± 1	94 ± 4
TCH	20 ± 3	8.0 ± 1.2	37 ± 1	97 ± 2
CHX	21 ± 3	11.7 ± 2.5	36 ± 1	97 ± 2
CIP	18 ± 3	21.9 ± 3.9	27 ± 1	99 ± 1
GS	24 ± 3	13.4 ± 2.2	36 ± 1	99 ± 1
PLR 4.0g/ml				
Control	15 ± 3	30.9 ± 6.1	19 ± 1	82 ± 5
TCH	15 ± 3	28.0 ± 3.9	22 ± 1	89 ± 5
CHX	12 ± 3	34.3 ± 6.4	21 ± 1	87 ± 6
CIP	12 ± 3	43.3 ± 4.5	20 ± 1	92 ± 2
GS	18 ± 3	42.2 ± 7.0	21 ± 1	95 ± 3

CONCLUSIONS: Antibiotic-loaded injectable brushite cements are potentially advantageous for implantation as drug-delivery carriers via minimal invasive surgery, and for treatment and prevention of bone infections, such as osteomyelitis.
Antibiotics additions improved the injectability of brushite bone cements. Therefore, there was no need for the incorporation of additional superplastercisers to antibiotic-loaded brushite cements. Mechanical strength and setting properties did not deteriorate as a result of the antibiotic load. For ciprofloxacin additions the mechanical properties of the cement were even significantly improved.

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POSTER PRESENTATIONS

Injectable Calcium Phosphate Based Biomaterial Platform for the Delivery of Antibiotics in the Treatment of Infected Traumatic Fractures

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☒ Biomaterials	☐ Biomechanics	☐ Clinical	☐ Innovation

INTRODUCTION:
Injectable bone graft substitutes (BGS) are used increasingly in the treatment of traumatic skeletal injuries. In many traumatic applications local infection is a serious clinical issue, leading to interest in therapies combining BGS with antibiotics to prevent and/or treat local infection. However, little is known about how these additives affect the physical or chemical properties and performance of these grafts. Calcium phosphate cement based products are of particular interest because they are provided as two component systems, a powder and hydrant, facilitating addition of the additive by replacement of the hydrant.

One such platform of commercial BGSs, based on a calcium phosphate technology shown to perform equivalently to autograft in tibial plateau and calcaneous clinical studies, compromises multiple formulations targeted at specific clinical indication; Beta-bsm - a high strength injectable form, CarriGen - a fast resorbing macroporous form, and EquivaBone - an osteoinductive form. Three different types of antibiotics were evaluated with the goal of determining the highest concentration of additive at which graft performance is maintained.

MATERIALS & METHODS:
Each product was mixed with either saline (control), Tobramycin (5 to 40 mg/mL), Clindamycin (18 to 150 mg/mL) or Vancomycin (50 mg/mL). Mixing was achieved by replacing the indicated product hydrant with the specified solution at a fixed hydration volume. Samples were incubated at 37 C and tested for compressive strength, setting rate, Injectability and chemical composition. For EquivaBone an additional set of samples were implanted in an intramuscular athymic rat model to test for osteoinductivity

RESULTS & DISCUSSION:
A summary of testing results is given in Tables 1 through 3. Each formulation exhibited a similar dose dependent sensitive to addition of different antibiotics. Vancomycin had no negative impact on the performance of the graft material up to a concentration of 50 mg/mL. Tobramycin had no negative impact at a concentration of 5 mg/ml but delayed the setting reaction at higher concentrations. Clindamycin had the greatest negative impact, retarding setting time and inhibiting osteoinductivity at 18 mg/ml.

CONCLUSIONS:
Adding antibiotics is a promising method for enhancing the performance of synthetic bone grafting materials. BGS formulations combined with antibiotics at specific concentrations maintain their chemical, physical and performance characteristics.

Table 1: Results Summary for Beta-bsm Mixed with Antibiotics

Additive	Concen-tration (mg/ml)	Setting Time (minutes)	Compressive Strength (MPa)	Chemical Composition	Injectable
Saline	100%	5	25-35	NCHA	Yes
Tobramycin	40	> 20	25-35	NCHA	Yes
	20	> 20	25-35	NCHA	Yes
	10	> 20	25-35	NCHA	Yes
	5	10	25-35	NCHA	Yes
Vancomycin	50	10	25-35	NCHA	Yes
Clindamycin	150	> 20	-	-	-
	37.5	> 20	25-35	NCHA	Yes
	18	20	25-35	NCHA	Yes

Table 2: Results Summary for Carrigen Mixed with Antibiotics

Additive	Concen-tration (mg/ml)	Setting Time (minutes)	Compressive Strength (MPa)	Chemical Composition	Injectable
Saline	100%	5	10-15	NCHA	Yes
Tobramycin	40	> 20	10-15	NCHA	Yes
	20	> 20	10-15	NCHA	Yes
	10	> 20	10-15	NCHA	Yes
	5	10	10-15	NCHA	Yes
Vancomycin	50	10	10-15	NCHA	Yes
Clindamycin	150	> 20	-	-	-
	37.5	> 20	10-15	NCHA	Yes
	18	15	10-15	NCHA	Yes

Table 3: Results Summary for EquivaBone Mixed with Antibiotics

Additive	Concen-tration (mg/ml)	Setting Time (minutes)	Compressive Strength (MPa)	Chemical Composition	Osteo-inductive	Injectable
Saline	100%	10	2	NCHA	Yes	Yes
Tobramycin	40	> 20	-	-	-	-
	20	> 20	-	-	-	-
	10	> 20	-	-	-	-
	5	10	2	NCHA	Yes	Yes
Vancomycin	50	< 10	2	NCHA	Yes	Yes
Clindamycin	150	> 20	-	-	-	-
	37.5	> 20	0	-	-	-
	18	20	2	NCHA	No	Yes

Autologous nasal chondrocytes and a cellulose-based self-setting hydrogel for the repair of articular cartilage in horses.

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☐ Biomaterials	☐ Biomechanics	☐ Clinical	☒ Innovation

INTRODUCTION: Spontaneous healing of articular cartilage is limited. To promote the repair of this tissue, amplification and transfer of autologous chondrocytes using a three dimensional matrix appears promising. In this attempt, we have developed a self-setting hydrogel consisting of a silanized cellulose derivative (Si-HPMC). In previous works, we have demonstrated that our Si-HPMC hydrogel containing human nasal chondrocytes allowed the production of cartilage-like matrix subcutaneously[1]. The proof of our concept has been also demonstrated through the design of a rabbit model of autologous nasal chondrocytes transfer with Si-HPMC in articular cartilage defects [2]. The aim of the present study is to extend the proof of our concept to a large animal model: the horse.

METHODS: Horse nasal chondrocytes (HoNC) were isolated from small pieces of nasal septum. Isolated HoNC were associated with Si-HPMC at a density of $2.5.10^5$ cells/ml and injected (250µl) in subcutaneous pocket of nude mice for 5 weeks. Implants were histologically characterized for the presence of sulfated GAG (alcian blue staining) and type II collagen (immunostaining).
To evaluate the ability of HoNC associated to Si-HPMC for repairing of articular cartilage defect, isolated autologous HoNC were expanded in vitro for 4 weeks, associated with Si-HPMC at a density of $2.5\ 10^6$ cells/ml and injected arthroscopically in a critical sized defect in horses. 2 months later, the defect were investigated arthroscopically and cartilage formation was evaluated histologically as previously described.

RESULTS: Histochemical analysis of subcutaneous implants of HoNC/Si-HPMC evidences the formation of chondrogenic nodules positively stained by alcian blue, indicating the presence of sulfated GAG, and positively immunostained for the presence of type II collagen (figure 1).

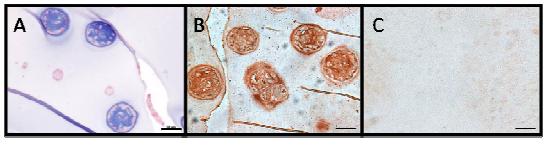

Figure 1: Histochemical analysis of tissue engineered cartilage. HoNC/ Si-HPMC (A-B). A: sulfated GAG production (Alcian Blue). B: type II collagen immunostaining . C: Si-HPMC alone. Bar: 50µm.

When injected arthroscopically in articular cartilage defect the association of autologous HoNC with Si-HPMC leads to the formation of a repair tissue exhibiting the smooth surface of articular cartilage (figure 2). Moreover, histological analyses indicate the presence of a cartilage like matrix.

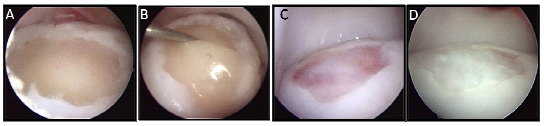

Figure 2: Arthroscopic observation of A: empty defect at day 0. B: defect filled with HoNC/Si-HPMC at day 0. C: defect filled with HoNC/Si-HPMC 1 month-post surgery. D: 2 month-post surgery.

CONCLUSIONS: Discussion and Conclusions
The transplantation of Si-HPMC hydrogel with autologous nasal chondrocytes led to the successful repair of an articular cartilage defect in horse. This study therefore indicates that Si-HPMC is a promising scaffold for regenerative medicine of articular cartilage

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Poor improvement in the evaluation and treatment of hypovitaminosis D in fracture patients despite intervention

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☐ Biomaterials	☐ Biomechanics	☒ Clinical	☐ Innovation

INTRODUCTION: The prevalence of hypovitaminosis D in orthopaedic trauma patients is alarmingly high[1]. Vitamin D has an interrelationship with calcium homeostasis and bone metabolism, helping to maintain strong, healthy bones and muscles. Decreased vitamin D levels contribute to osteoporosis and subsequent vertebral body and skeletal fractures. Vitamin D insufficiency has shown to be prevalent in fracture patients admitted at a level 1 trauma center, but mandatory protocol for measurement of vitamin D levels does not exist.

Hypovitaminosis D is prevalent in both high- and low-energy fracture patients and needs to be evaluated and treated in an orthopaedic setting[2]. The purpose of the present study was to determine whether educational interventions to raise physician awareness have led to an improvement in evaluation and treatment of hypovitaminosis D in orthopaedic patients at a level 1 trauma center.

METHODS: A retrospective analysis was conducted after institutional review board approval on all patients admitted to the orthopaedic trauma service at an academic level 1 trauma center from June 2010 through November 2010. Educational interventions to raise physician awareness were performed and protocols for evaluation and treatment of hypovitaminosis D were instituted before data was collected over the six month period. Patient data was obtained from medical records and included the number of patients who had vitamin D levels measured and the number of patients who were treated for insufficient vitamin D levels.

RESULTS: The percentage of patients from June 2010 through November 2010 who received blood draws of vitamin D levels while admitted to the level 1 trauma center was only 9.1%. Of the 450 patients admitted to the level 1 trauma center over the six month period, 55.8% were males and 44.2% were females. The percentage of patients who received blood draws while admitted in each month from June to November was 3.37%, 3.03%, 5.63%, 14.83%, 9.76%, and 12.86%, respectively. Including the patients who had vitamin D levels measured in an outpatient facility after being discharged from the hospital, the percent of values measured increased to 16.4%. The percent of levels measured each month then increased to 11.2, 13.1, 15.5, 16.0, 18.3, and 15.7%, respectively.

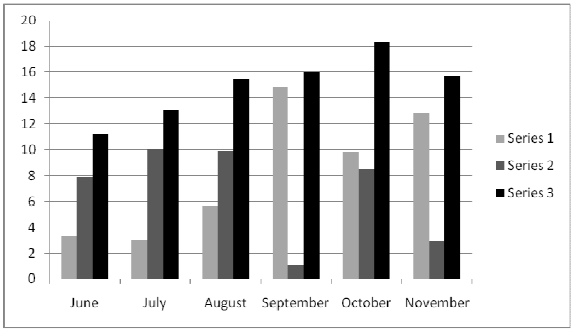

Fig. 1: Percentages of patients who had vitamin D levels taken over time. Series 1 shows the percent of patients who had vitamin D levels taken while admitted to the level 1 trauma center each month. Series 2 shows the percent of patients who had vitamin D levels measured outpatient. Series 3 shows the total percentage of patients who had vitamin D levels taken each month.

CONCLUSIONS: There was a progressive increase over time in the evaluation and treatment of hypovitaminosis D after educational interventions and protocol implementation. Nevertheless, the percent of patients who are evaluated and treated in an orthopaedic setting remains low. Educational interventions alone are insufficient to improve the evaluation and treatment of hypovitaminosis D in orthopaedic patients. Physicians need to be aware of the prevalence of hypovitaminosis D in orthopaedic patients and strict protocol for evaluation and treatment of the disorder needs to be implemented.

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Hypovitaminosis D in orthopaedic trauma patients admitted at a level 1 trauma center

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☐ Biomaterials	☐ Biomechanics	☒ Clinical	☐ Innovation

INTRODUCTION: Hypovitaminosis D is an insufficiency in the levels of vitamin D in the body. Vitamin D has an interrelationship with calcium homeostasis and bone metabolism, helping to maintain strong, healthy bones and muscles. Decreased vitamin D levels contribute to osteoporosis and subsequent vertebral body and skeletal fractures. It has been estimated that 47% of women and 22% of men will suffer from an osteoporotic fracture after 50 years of age, which could be due to hypovitaminosis D[1]. The influence of vitamin D insufficiency on muscle strength and bone health may be increasing the risk of fracture among the general population[2].

Hypovitaminosis D is alarmingly high in the general population; however, prevalence of this disorder has never been evaluated in orthopaedic fracture patients admitted at a level 1 trauma center. Admission to the level 1 trauma center presents a unique opportunity for evaluation and treatment of this disorder. The purpose of the present study was to measure the prevalence of hypovitaminosis D among orthopaedic surgery patients admitted at an academic level 1 trauma center.

METHODS: A retrospective analysis was conducted after institutional review board approval on all patients admitted to the orthopaedic service at an academic level 1 trauma center from June 2010 through November 2010. Data obtained from patient medical records included serum 25-hydroxyvitamin D levels, age, and gender. Normal (≥32 ng/mL), insufficient (<32 ng/mL), and deficient (<20 ng/mL) 25-hydroxyvitamin D levels were determined. Vitamin D levels were reported for males and females as well as for the age groups 18 to 50 years of age, 51 to 70 years of age, and greater than 70 years of age.

RESULTS: Of the 450 patients admitted to the level 1 trauma center from June 2010 through November 2010, 74 patients were evaluated for vitamin D levels and 78.4% were found to be vitamin D insufficient. Of the patients who were found to have insufficient vitamin D levels, 55.2% were vitamin D deficient. The 450 patients were 55.8% males and 44.2% females.
Of the vitamin D insufficient males, 42.3% were deficient with a mean vitamin D level of 22.0ng/mL. Of the insufficient females, 60.0% were deficient with a mean vitamin D level of 18.0ng/mL. The highest rate of inadequate vitamin D levels was found in the youngest population (18 to 50 years of age) compared with the older populations (51 to 70 years of age and more than 70 years of age). The youngest population had a mean vitamin D level of 16.7ng/mL, 100% were vitamin D insufficient, and 71.4% were vitamin D deficient.

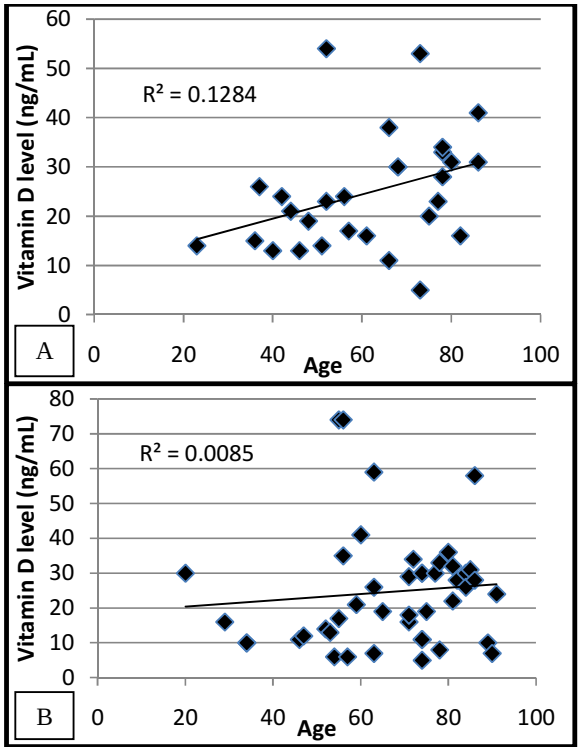

Fig. 1: (A) Vitamin D levels and ages of male patients who had values taken. (B) Vitamin D levels and ages of female patients who had values taken.

The prevalence of vitamin D deficiency is highest in females and in the youngest population (18 to 50 years of age).

CONCLUSIONS: The prevalence of hypovitaminosis D among orthopaedic trauma patients at a level 1 trauma center is alarmingly high. Adult fracture patients are at high risk for vitamin D insufficiency, with higher rates of deficiency among women and younger populations. Hospitalization provides a unique opportunity for evaluation and treatment of this disorder, and levels of 25-hydroxyvitamin D should be measured in all patients admitted to a level 1 trauma center. It is warranted that institutions have protocols for evaluation and treatment of hypovitaminosis D.

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MECHANICAL, BIOMECHANICAL AND HISTOLOGICAL EVALUATION OF AN INJECTABLE CALCIUM PHOSPHATE BASED BIOMATERIAL

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INTRODUCTION:

The present work describes the evaluation of an injectable calcium phosphate based biomaterial with setting agent (CPBSA) both in vitro and in vivo. The CPBSA material uses a mix-on-demand delivery system that allows for controlled start and stop delivery. Material properties of CPBSA were determined in vitro under uniaxial compression and tension. CPBSA demonstrated in situ setting, osteoconduction, resorption, and bone healing in a bilateral tibial metaphyseal defect model in New Zealand White rabbits.

EXPERIMENTAL METHODS:

in vitro

Mechanical test articles of CPBSA were prepared according to ASTM F451-99(1) and ASTM D638-03(2). Fully set samples were tested to failure in tension and compression with a uniaxial MTS machine. The endpoints included yield load, peak load, strain, UCS/UTS, E, and break location.

in vivo

Bilateral defects (5-mm x 15-mm) spanning the metaphyseal and diaphyseal region were created 3 mm below the joint line in the anteromedial cortex of the proximal tibiae of (22) 6 month-old female New Zealand White rabbit, according to the following references (3,4,5). On one side, the defect was filled with CPBSA; the contralateral defect was filled with Norian SRS (Synthes), an injectable calcium phosphate bone void filler. Bilateral defects in four animals (n=8) were left empty as control. Animals were sacrificed at t = 0, 12, and 24 weeks, and endpoints included Faxitron x-rays, biomechanical evaluation, histomorphometry, histology of the implant site and distal organs, and haematology. Tibiae were x-rayed and graded semi-quantitatively for healing and implant resorption, and were biomechanically tested in torsion to failure using a biaxial MTS machine. The peak torque and stiffness were evaluated using a 3-way analysis of variance. Two specimens per time point were decalcified for H&E histology as well as the protein expression (MMP1 and, IL-1, IL-6 , Cathepsin K). Six tibiae per group per time point were processed for PMMA histology and stained with methylene blue and basic fuschin to determine the amount of new bone, remaining material, void and soft tissue in each defect. Histomorphometry data was analysed using a two way general linear model of analysis of variance followed by a Games Howell post hoc test.

RESULTS:

Mechanical Testing of CPBSA demonstrated tensile properties of UTS = 43.75MPa E=439.75MPa, and compressive properties of UCS = 64.75MPa E=445.50MPa.
Haemtology and Biochemistry revealed no abnormal findings in any animal compared to historical controls.
Faxitron did not demonstrate any adverse reactions to either material in terms of any osteolysis or bone resorption. Radiographs revealed both treatment groups present in the defects at 26 weeks, and the cortex of the empty defects had not healed by 26 weeks. Radiographic grading data demonstrated a statistically equivalent resorption over time for both groups at 12 and 26 weeks. Cortical bridging grading data did not differ with time or treatment group.
Biomechanical Testing demonstrated a progression in healing between 12 and 26 weeks for all groups. No differences were detected. The mean torque values did not reach the values of an intact tibia (Walsh et al., 2003).
Paraffin and PMMA histology showed new bone formation on all material surfaces at 12 and 26 weeks. No adverse reactions were found with either implant at 12 or 26 weeks. Normal bone remodeling and marrow space development were observed. Bone ingrowth was noted in the CPBSA material while this was not observed with the Norian SRS material. Empty defects were not healed at 12 or 26 weeks, although a progression in maturity of the cortex was noted. The medullary canal appeared normal. Paraffin histology of the heart, kidney, liver, lung and spleen revealed no adverse findings were in any animal.
Histomorphometric data analysis revealed an increase over time in the percent bone for both implants as the anteromedial cortex healed. More bone was observed with the CPBSA material than the Norian SRS material by post hoc analysis at 12 weeks (P=0.041). Mean implant material differences we not observed between treatment groups at 12 or 26 weeks in post hoc analysis.
Immunohistochemistry demonstrated expression of Cathepsin K in all groups at 12 and 26 weeks. Cathepsin K expression appeared linked with the presence of bone on the surface of the materials and reflected the increased amount of new bone formation associated with the CPBSA material at 12 and 26 weeks. No differences were noted in IL-1ß or MMP-1 staining intensity/distribution, and no TNFα or Mouse IgG expression was noted at 12 or 26 weeks in the empty or treatment groups.

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PRELIMINARY STRUCTURAL ANALYSIS OF SPINE METASTASES

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Biomaterials	Biomechanics	Clinical	Innovation

INTRODUCTION: Spinal metastases are an increasingly challenging pathology presented to the clinician as patient survivorship improves. A number of these metastases are osteolytic in nature and subsequent fracture is associated with significant morbidity. Previous research has indicated a strong link between structure as the bone disease progresses and the fracture [1, 2, 3]. Improved methods of fracture risk and prediction are urgently required to aid clinical planning and the assessment of treatment outcomes. Such methods would also be deployed in laboratories providing a better means of experimental design.

Aim of this study was to investigate mechanical impact of metastatic lesions using structural analyses and the effect of extra-vertebral neoplastic formations.

METHODS: Twelve vertebrae from a spine containing metastatic lesions from primary bladder cancer were were acquired from the GIFT Tissue Bank (Leeds, UK) following ethics committee approval. Each vertebrae underwent a micro-CT (CT80, Scanco Medical AG, Bassersdorf, Switzerland) assessment to obtain information on the vertebral morphology including lesion characteristics and the BMD distribution. The prediction load was obtained using an adapted structural properties technique [3]. In summary, the grayscale pixel value was converted to an elastic modulus using a previously derived relationship for the bone tissue [1]. This conversion was used to create a modulus map of each slice of the specimen obtained from microCT scan following which beam theory was used to determine the weakest slice and hence the minimal fracture force of each specimen.

This predicted value was compared to the actual fracture load acquired in a previous experimental study [2] Briefly, a compressive force was applied eccentrically to create a combination of bending and axial loading. Load-displacement curves were recorded and the initial point of zero-slope yield was considered as the fracture load.

RESULTS: From the initial analysis the mean difference, the limits of agreement and the correlation coefficient for the structural analyses were poor with values of 1.1 kN, (-1.2 kN to 3.4 kN) and 0.26. Further analysis was undertaken to exclude the extra-vertebral lesions from the modulus maps which resulted in an improvement in the results (Figure 1) with statistical output of 0.50 kN, (-0.53 kN to 1.53 kN) and 0.73.

DISCUSSION: This preliminary study highlighted two important findings. Firstly, structural analysis may be a promising method for fracture prediction of the metastatically affected vertebrae in keeping with previous studies [3]. Secondly, the analysis is complicated by the presence of extra vertebral bone formation in which the contribution to the fracture load may be minimal unlike the formation of osteophytes in osteoporosis reported in previous results which appear to act with significant resistance to compressive load. This is in keeping with previous finding in which it has been demonstrated that the extra-vertebral lesions arising from the metastatic bone formation are akin to relatively immature woven bone which provides relatively little structural support. Further research is required to confirm this finding specifically and in the relationship between vertebral morphology and failure load in metastatic vertebrae more generally.

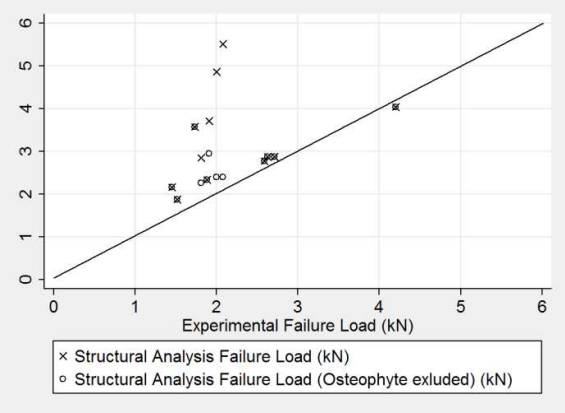

Figure 1: Plot of the predicted fracture loads with and without extra-vertebral osseous lesions versus the experimentally determined failure load.

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Hydraulic internal distractor, operated by remote control, for the correction of deformities of the spine, and the elongation of long bones in the human.

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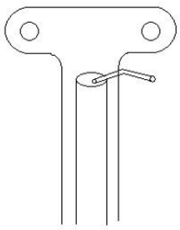
☐ Biomaterials	☐ Biomechanics	☐ Clinical	x☐ Innovation

INTRODUCTION: Diseases of the musculoskeletal system have always existed, the degenerative (osteoarthritis, rheumatoid arthritis, etc) and the congenital (congenital hip dislocation, limb length discrepancy, etc) as found in the fossil of our ancestors. Mankind has always been interested in these diseases and in attempting to prevent and cure as well as provide rehabilitation lowering as much as the possible its consequences. Such task, however, wasn´t easy due to the many obstacles met then and now. There were also positive results in many occasions to the point of finding total cure, but still this task remains unfinished. Nowadays, the concern and commitment of the orthopedic surgeons is to take the most advantage of the technology progress for the benefit of our practice and patients.Just to mention a few of these benefits, I can mention the joint prostheses which substantially enhanced and improved the quality of life of patients, something unthinkable in past times when patients would become confined to a bed or, in better cases, to a wheelchair. However, there is much to be done and my idea is to contribute with a remote controlled hydraulic-electronic device, to be used in the correction of anomalies of the vertebral column such as scoliosis, kyfosis and others, as well as elongation of lengthy bones. It´s important to mention that, historically, the osseous elongation dates from the 50´s, when the first one was accomplished. Before that, the procedure in cases of lower limb length discrepancy was to cut a fragment of the longer bone. However, since the 50´s, the elongation became one of many options. Other techniques were designed and new studies carried out. The most important contributions came from Anderson 1952, Cauchoix 1963, Kawuamura 1968, Wagner 1971 (progressive distraction and fitting with neutralization plate of the obtained elongation), Ilizarov 1972, describing the osteogenic distraction, emphasizing the importance of a stable system and a stretching speed of 1mm per day, with !which good blood contribution with no harm to nerve structures are guaranteed. In relation to the abnormalities of the column such as scoliosis, since Hippocrates, there has been attempt to correct these curves with distraction and mold fittings, followed by the Milwuokee brace, the Harrington bar distraction, the Luque instrumentation with sublaminar wiring and all other procedures such as shortening surgery, sublaminar traction, and instrumentation with hooks and/or transpedicular screws as well as the use of external distracters, have all had the same objective, many times incurring in great correction of the condition. However, the condition was many times limited by other factors such as curvature stiffness or risk of neurological damage during the correction, or the discomfort in bringing the external distracter for many weeks. With all inherent risks, the present project aims to create a device which will work as an internal distraction consisting of a remote controlled dynamic-hydraulic-electronic instrumentation, to be used in the correction of the previously mentioned abnormalities, and others for which it could be applied.

METHODS: The device is made of 2 parts, of titanium (ti6al4v grade 5), or AISI 316 L stainless steel, sliding parts, part A, and part B. This device is based on the mechanics principle which states that fluids are not compressible. For that reason a passage is created allowing the flow of liquid from a chamber of lower pressure to another of higher pressure through a one way valve, with which the distraction of one of the parts (A) is obtained in relation to the other part (B). Part A is a hollow cylinder with a diameter of 7mm and a 2.5mm wall, a one way valve, 2 openings at the extreme for transpedicular anchorage with a diameter of 4mm, and a 2mm pipe connected to an injector system (Fig. 1). Part B is a cylinder with a diameter of 6.9mm, 2 openings with diameter of 4mm for transpedicular anchorage (fig. 2). the type of seals that will be used to avoid leakage of liquid from the assembly of the parts would be the A AND B orring existing on the measures required to meet the target, inner diameter 6.9mm and 7mm external diameter, there is also the alternative pneumatic seals.

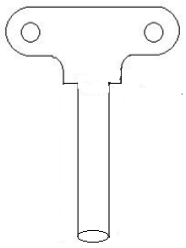
The injector system is a box of 2 x 7 x 9cm with 1 cylinder inside with a diameter of 1.8cm x 7 cm

long containing the liquid to be injected, and a cylinder of 0.5 cm in diameter by 2 cm long, which will be the injection cylinder, the cylinder injector is attached to the cylinder through a tube container a one-way valve, and like a syringe will have a piston, that embolus attached to 1 engines of 7.7 kg/cm of torque. Inside the metal box, there are also 4 batteries which allow the engines and electric connections to work, and the electronic sensor to receive the signals from the remote control. From the box, a 2mm pipe comes out and connects to the device on part A. The injector system receives the signal and sends enough quantity of liquid aiming to obtain a distraction of 1mm. (Fig. 3). The remote control is programmed to automatically send another signal in 24 hours, the length of the device will be assembled and 50% part A and part B 50%, and will be variable as required, increasing from 2 in 2cm, starting at 16cm and can reach 30cm or more long, the device will work as injecting the liquid part A part B is moved achieving distraction, reaching a peak, will be needed to achieve a cap in the parts assembled, the final distraction happen 60 or 70% the length of Part B, according to the results of routine mechanical tests shall be submitted to the device once manufactured, such as the cycle of compression, distraction, flexion, and the coefficient of elasticity



Part A:

Fig 1. A hollow cylinder of 7mm in diameter and a wall of 2.5mm, giving an external diameter of 12mm, ranurao with a square to join the groove with them or b square of part to prevent rotations between the two parties with valve via one, and 2 to 4 mm hole for anchor in the extreme, and through a hose is connected to a system injector.



PART B:

Fig 2, A solid cylinder 6.9mm in diameter with a groove, or square joining a slot with its square or in part to prevent a rotation between both sides and two mounting holes 4mm to anchor in the extreme.

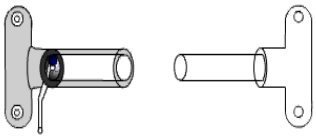
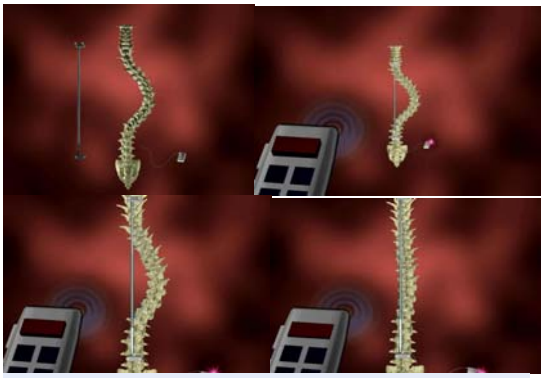


Fig 3 The device works by injecting the liquid, it is slipping Part B Part A



Sequence photographs of a scoliosis correction,

RESULTS: The clinical results of this work cannot be evaluated until the device is produced and tests are carried out, firstly mechanical tests and then experimentation in animals in order to prove its efficiency, which is already proved from the mechanics point of view, since the jacks used for lifting vehicles, or heavy objects, are supported by the same principle. In terms of application for the column correction and/or osseous elongation in humans, it would certainly be a great orthopedic tool nowadays, and its application would increase according to needs and results obtained. We are committed to our practice and our patients, and for that reason we shall offer and make all technology resources available for the treatment of

different diseases. I believe that all new devices and/or ideas oriented to the treatment of any diseases should be submitted to tests in order to prove their efficiency, and should be improved constantly with the objective to better treating the diseases.

CONCLUSIONS: Evidently findings may do, when making biomechanical testing, and after its use in human, clinical findings, however, experience has demonstrated the effectiveness of hydraulics in a mechanical application, such as hydraulic jacks, which have proved the great effectiveness to move and lift heavy weights, so we can apply the mechanics principle which states that fluids are not compressible, for the correction of spinal deformities and for the elongation of long bones in humans.

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Development of posterior vertebral wall defect model to analyze cement leaking during Kyphoplasty procedures

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☐ Biomaterials	☐ Biomechanics	☐ Clinical	☐ Innovation

INTRODUCTION: Kyphoplasty and Vertebroplasty are important tools for stabilizing spine fractures due to osteoporosis or cancer. However, cement leakage during these procedures, especially in the cases of posterior vertebral wall defects, is a major source of morbidity and degraded outcome. The aim of this study was to create a standardized and reproducible model, that allows us to analyze posterior wall cement leakage, during Kyphoplasty procedures.

METHODS: Artificial vertebral analogs (Saw Bones™) made of *polyurethane* have been used for this study. In 15 L3 vertebrae we drilled 10 mm wide holes with a depth of 10mm into the posterior wall using a 10mm drill bit. 15 more intact L3 vertebrae where used as controls. The standard existing Kyphoplasty ™ System was used in all cases. A custom made targeting jig system was used in order to achieve the exact same targeting of the trocars into the tested analogs. Under fluoroscopic control, balloon kyphoplasty was done in all analogs. After balloon deflation, Cement was allowed to cure until 1 cm could be extruded out of the bpne filler device without cement droop. Cement injection was stopped when the whole created cavity was filled or (in the sawbones with the posterior wall defect) when posterior cement leakage was observed, either fluoroscopically or under direct vision. The amount of injected cement was measured and registered using 3D volumetric CT scan.

RESULTS: Posterior cement leakage occurred in all but one of the posterior wall defect analogs, where the standard kyphoplasty instrumentation was used. 3D CT volumetric measurement showed that posterior leakage appeared after the injection of 4 ±0.4 ml of high viscosity cement. On contrary, we were able to inject 9.8 ± 1.1 ml of high viscosity cement, to the intact vertebral analogs (P<0.0001).

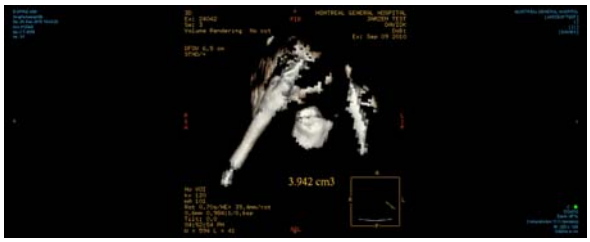

Fig. 1: 3D volumetric CT scan has been employed to assess the volume of cement injected in each vertebra.

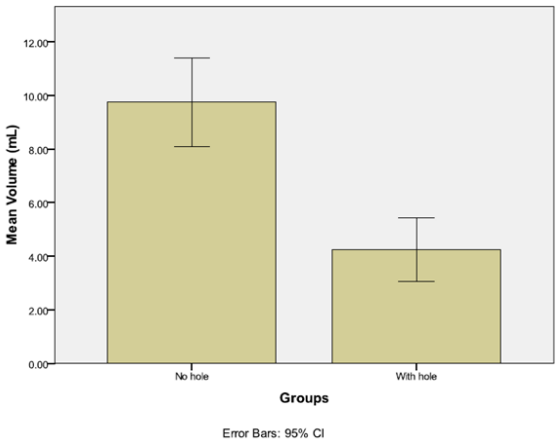

Figure 1: The amount of cement injected at the two study groups.

CONCLUSIONS: We have successfully created a posterior vertebral wall defect model for the testing of the posterior leakage during kyphoplasty procedures. This model is highly standardized and easily reproducible. Such models are useful in further studying the cement leakage during kyphoplasty procedures and can also assist the development of new instrumentation/implants that will safely allows for kyphoplasty procedures in patients with posterior vertebral wall defects, due to cancer or fractures.

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METHYL METHACRYLATE CROSSLINKED WITH POLYISOBUTLYENE: A MORE DUCTILE BONE CEMENT

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INTRODUCTION: Our previous research indicated that 3-arm star telechelic polyisobutylene (PIB) could be copolymerized with methyl methacrylate (MMA) to form a PIB-MMA copolymer which is more ductile than PMMA. The purpose of this study is to investigate potential usage in orthopaedic surgery.

Experimental Methods: Samples of PIB-MMA with molecular weight of 6,000 and 10,000 grams per gram mole, and with 10, 20 and 30% concentration (wt %) of initiator will be tested. After injection of these compositions of PIB-MMA into trabecular bone and synthetic foam with similar porosity as bone, compressive tests will be carried out.

Results: PIB-MMA with molecular weight of 6,000 grams per gram mole and 20% concentration has tensile modulus (E) of 970 MPa, yield strength (σ_y)of 23.6 MPa and elongation at failure (ε)of 20.1%. Modulus, yield strength and ductility of this compound is comparable to trabecular bone (E=200-1000MPa, σ_y=8-50MPa, ε=2-4%). PIB-MMA has desirable properties for as a ductile bone cement in many orthopaedic applications.

References: US Patent 5,242,983

Different Bone-Cement Interfaces after augmentation of vertebral compression fractures – a cadaver study

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Introduction

The treatment of painful vertebral compression fractures via transpedicular cement augmentation is well accepted. There is still uncertainty about long- and midterm effects of the PMMA in the trabecular bone of the vertebral bodies. Preservation of the trabecular structures as well as interdigitation of the cement with the surrounding bone have become very interesting. Different companies provide a wide range of products to achieve secure and efficient results. We decided to perform a histologic examination of different products.

Materials and Methods

One fresh frozen human cadaver spine was used. The bone density measurement showed a T-score of -5,31 representing substantial osteoporosis. The spine was dissected into single vertebral bodies, the surrounding soft tissue, the laminae and spinal processes were removed. Altogether 13 undamaged vertebral bodies were prepared (from the 3rd thoracic to the 3rd lumbar vertebral body). The endplates were embedded in Technovit. Using a standardized protocol wedge compression fractures were created (Instron 5566). The axial load was continuously increased until the hight of the anterior edge of the vertebral body was reduced to 50%. The load was maintained for 15 minutes. After creation of the wedge fractures the vertebral bodies were assigned into four similar groups concerning size and needed force to produce the fracture. The four groups were randomized to different cementing techniques. The treatment options were Balloon-Kyphoplasty (Kyphon, Medtronic), StabiliT^{TM} RF-Kyphoplastie (DFine), Shield-Kyphoplasty (Soteira) and Vertebral Body Stenting (VBS, Synthes®). All procedures were performed by the same surgeon using a image intensifier. To attain a relevant result clinical judgement was used to proceed or stop the cement injection. After the procedure all vertebral bodies were fixed in 10% formalin cut in 2mm slices using a diamond band saw (EXACT). Dehydration and Degassification was performed in a precooled desiccator. The probes were embedded in Technovit 7200 using blue light polymerization. The polymerised tissue blocks were removed from the embedding mould and trimmed to the needed size with a diamond band saw (EXACT). The blocked surface of the embedded tissue probe were grinded with the EXACT micro grinding machine. After the probes were grinded to an appropriate thickness staining was performed. A protocol for histologic analysis was desgned. From the center of the cement a actinomorphic grid was placed on the specimens (24 radiuses, 15°). The relation between length of radius and preserved cancelous bone was evaluated. Additionally the distance between the cement and trabecular bone (bone/cement interface) was ascertained (Leitz Aristomet) and calculated using the Image-Pro-Plus Software ausgewertet.

Results

In all vertebral bodies vertebral wedge fractures could be established. The average force needed was 2164,25 N (±514,35). All surgical procedures could be performed without technical problems. All the equipment worked without technical difficulties. In

the procedures that use a balloon to create a void in the vertebral body the distance between bone and cement was 494,45 (VBS) bzw. 519,57 (Kyphon) µm on average. The trabecular bone was condensed around the cement. The procedures without a balloon resulted in distances of 352,46 (DFine) and 442,76 (Soteira) µm on average.
The relation of the radiuses from the center of the cement to visible trabecular bone along the radius was 16,44% Balloon-Kyphoplasty (Kyphon, Medtronic), 65,63% StabiliT™ RF-Kyphoplastie (DFine), 48,19% Shield-Kyphoplasty (Soteira) and 21,04% Vertebral Body Stenting (VBS, Synthes®).

Summary
To our knowledge there is no comparative study that deals with cement interdigitation. The cutting and grinding technique that was used to prepare the probes was also not used before to evaluate cement interdigitation. All procedures were performed without technical complications. The protocols for the production of comparable wedge fractures, cutting and grinding process and microscopic evaluation seem to be reasonable. The interdigitation between trabecular bone and cement seems to be better in procedures that do not use ballons to create a void. On the other hand there is no condensed trabecular bone that could work as a shield to protect from cement leakage.

Bone Scan Analysis and Correlation to Radiographs of Silicated Calcium Phosphate Bone Graft Substitute in Patients with Posterolateral Fusion

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☒ Biomaterials	☐ Biomechanics	☒ Clinical	☐ Innovation

INTRODUCTION: Efforts to avoid iliac crest harvesting have led to the development of suitable bone graft substitutes. Silicated Calcium Phosphate Bone Graft Substitute (Actifuse®, Apatech, Inc., Foxboro, MA) is a contemporary biologically active ceramic where selective substitution of the silicate ion is incorporated into a three-dimensional calcium phosphate matrix, which closely resembles the structure of bone.

Patients within a larger retrospective observational cohort status post posterolateral fusion (PLF) using SiCaP graft underwent a post-operative bone scan for co-morbid conditions to (1) evaluate the surgical site (2) confirm graft viability and the presence of metabolically active bone.

This retrospective case series involved surgeon and radiologist review of bone scan results in patients with SiCaP graft. The outcome of metabolic activity was determined by radiotracer uptake.

METHODS: Nine patients under the care of a single surgeon status post PLF with SiCaP graft underwent bone scans, which were sent to a core laboratory for analysis. Metabolic activity determined by radiotracer uptake were compared with radiographic findings on plain films and CT when available.

RESULTS: Bone scans were obtained at a mean follow-up of 12.6 months ± 4.3 months after surgery. All nine cases reviewed showed radiotracer activity in surgically implanted posterolateral bone with SiCaP graft. These findings indicate intact graft vascularity and the presence of viable osteocysts in each case examined. Radiotracer uptake in SiCaP posterolateral grafts was similar or greater than for normal bone and was present at various states of graft maturity.

While bone scans indicate viable graft in plain x-ray views where bone could not be seen, fusion status and graft maturity could not be determined on bone scan alone. There was complete agreement between bone scans and CT scans, indicating that CT scans afford the best method for determining fusion and graft maturity.

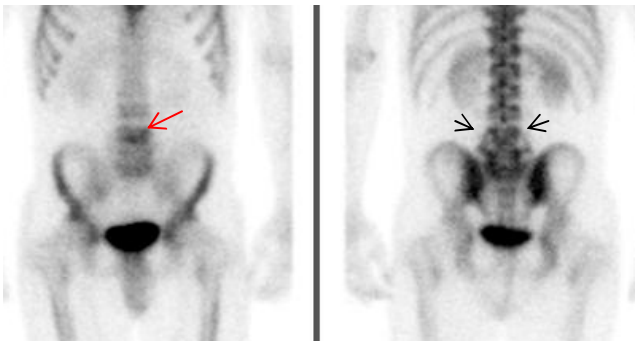

Fig. 1: Bone Scan at 18 Months Post-operative: Fusion masses demonstrate tracer uptake at L4-L5 bilaterally with intensity similar to normal bone (black arrows), corresponding to surgically treated levels. (Anterior view on left, posterior view on right)

CONCLUSIONS: This analysis of a small series of bone scan results in PLF patients support the continued use of SiCaP graft as a viable alternative to autogenous bone graft. This case series is secondary to a larger retrospective fusion cohort to determine radiographic and clinical success rates using SiCaP.

While bone scans can show biological activity within the graft material, they are not wholly suitable for determination of fusion or graft maturity.

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