Institution: University of Bath

Unit of Assessment:12: Aeronautical, Mechanical, Chemical and Manufacturing Engineering

Title of case study: Enhancing clinical materials and techniques in orthopaedic surgery through improvements in bone cement systems

1. Summary of the impact

Bone cement is widely used in joint replacement surgery, both for implant fixation and to enhance screw fixation in osteoporotic bone. Specific impacts include the development of two new orthopaedic cement systems by Summit Medical (Gloucester), also enabling that firm to obtain product approval and achieve significant new penetration of UK and international markets (UK bowl 70%; UK syringe 35%; US overall 15% – translating to total global sales 2009-2012 of £36M: 2012 = £9M).

Research outcomes have also impacted as a key element in the bid by Stryker Orthopaedics to obtain EU clinical approval and undertake US submission (ongoing) of injectable cements for augmenting bone screw fixation. Approval enabled the firm to establish *Hydroset* as a mainstream product with a cumulative total income of $180M since 2008 (income 2012 = $32M). The reach of these impacts also extends to improved clinical outcomes, resulting in improved quality of life and reduced healthcare costs.

2. Underpinning research

Key researchers

Professor AW Miles (Lecturer 1986-1992, Senior Lecturer 1992-1998, Reader 1998-2000 and Professor since 2000); Dr S Gheduzzi (Research Fellow 2006-2008, Lecturer 2008-2012, Senior Lecturer since 2012); Dr RC Phelps (nee Haynes) (Research Officer 1993-1996 and 2005-2006); and Dr RJ Eveleigh (Teaching Company Associate 1998-2000).

Context

These researchers are members of the University of Bath Centre for Orthopaedic Biomechanics, which has an international reputation for research into the mechanical properties of biomaterials and their clinical application in orthopaedic surgery. There are two major areas of research expertise relevant to this case study: (i) the biomechanical evaluation of the cement properties associated with different mixing systems and (ii) the protocols and optimization of the design parameters of mixing and delivery systems.

Summit Medical: bone cement mixing and delivery systems

A Teaching Company Scheme (TCS) with Summit Medical, based in Gloucester, ran from 1996-2000. The specific aim was to carry out research that would lead to the development of a commercial capability in novel bone cement mixing and delivery systems. The research investigated the use of mixing systems in a vacuum bowl to reduce cement porosity, as well as mixing directly in the delivery syringe. Previous underpinning research [1, 2] provided critical insights into the shortcomings of existing bone cement systems; it led to distinctive understandings of the rheology, mixing, handling and mechanical property issues of these cements, together with meeting the requisite clinical testing and evaluation protocols. This knowledge was directly transferable to the development, certification and launching of commercially-viable bone cement mixing and delivery systems [4].

Stryker Osteosynthesis: calcium phosphate cement for screw augmentation in cancellous bone

Dealing with the high incidence of fracture fixation in osteoporotic bone presents a significant clinical challenge when attaching fracture plates with bone screws, due to the poor structural integrity of the bone. The Centre's research reputation in screw fixation in orthopaedics [5] and experience in bone cements [3, 6] led to industrially-sponsored research with Stryker Europe

(2005-2006). The Senior Director, Biomaterials R&D and Technical Marketing, Stryker Osteosynthesis [section 5, B] indicates that '*The choice of this centre was because of their track record with analysis of implant screw failure ...*'. The aim was to determine the clinically relevant mechanical and rheological properties of an injectable calcium phosphate bone cement, *Hydroset*, marketed by Stryker (USA). The experimental results gave clear insights into the improvements to be expected when using injectable cements; a four-fold increase was obtained in pull-out strength in the *Hydroset*-augmented foam used to simulate osteoporotic bone without a cortical layer; in the presence of a cortical layer, augmentation led to a nearly fourteen-fold improvement. A major focus of the research was to align the testing procedures with the requirements of the statutory clinical licencing authorities.

3. References to the research (* references that best indicate quality)

1. RS Majkowski, AW Miles, GC Bannister, J Perkins and GJS Taylor. Bone surface preparation in cemented joint replacement, 1993, Journal of Bone and Joint Surgery, **75-B**, No 3, 459-463. DOI: 0301-620X/93/3565
2. RS Majkowski, GC Bannister and AW Miles. The effect of bleeding on the cement-bone interface: an experimental study, 1994, Clinical Orthopaedics and Related Research, **299**, 93-297. DOI: 10.1097/00003086-199402000-00040
3. JL Hailey, IG Turner, AW Miles and G Price. The effect of post-curing chemical changes to the mechanical properties of acrylic bone cement, 1994, Journal of Materials Science: Materials in Medicine, **5**, 617-621. DOI: 10.1007/BF00120342

4*. M Wilkinson, RJ Eveleigh, AJ Hamer, A Milne, AW Miles and I Stockley. Effect of mixing technique on the properties of acrylic bone cement: a comparison of syringe and bowl mixing systems, 2000, Journal of Arthroplasty, **15**, No 5, 663-667. DOI: 10.1054/arth.2000.6620

5*. RC Haynes, RG Poll, AW Miles and RB Weston. An experimental study of the failure modes of the Gamma locking nail and the Dynamic Hip Screw under static loading conditions: a cadaveric study, 1997, Medical Engineering and Physics, **19**, No 5, 446-453. DOI: 10.1016/S1350-4533(97)00003-9

6*. S Pina, SM Olhero, S Gheduzzi, AW Miles and JMF Ferreira. Influence of setting liquid composition and liquid-to-powder ratio on properties of a Mg-substituted calcium phosphate cement, 2009, Acta Biomaterialia, **5**(4), 1233-1240. DOI: 10.1016/j.actbio.2008.11.026

4. Details of the impact

The growing incidence of osteoarthritis and osteoporosis associated with the increase in the aging population presents a significant challenge in healthcare delivery. Bone cement is widely used in joint replacement surgery, both within the UK and internationally. In the UK, cement fixation (according to the UK National Joint Registry data) is used in around 50% of the 75,000 total hip replacements carried out each year and in over 80% of the 80,000 total knee replacements. Specific impacts of this research are:

- The development of two new orthopaedic cement mixing and delivery systems in association with Summit Medical (Gloucester), enabling that firm to achieve significant new penetration of UK and international markets [A].
- Incorporation of research outcomes on the mechanical enhancement of screw fixation in osteoporotic bone as a key element enabling Stryker Osteosynthesis to obtain clinical product approval of injectable cements and thus achieve significant new penetration of the global market [B].
- Improved clinical outcomes in orthopaedic interventions resulting in improved quality of life and reduced healthcare costs.

Summit Medical: bone cement mixing and delivery systems

The impact on Summit Medical through the Teaching Company Scheme as manifested in the 2008-2013 assessment period has been to gain new knowledge and capabilities in respect of bone cementing systems. Original collaborative research has contributed to two new commercial products – *Enhanced HiVac Bowl Bone Cement Mixing System* and the *HiVac Bone Cement Mixing and Delivery System*. The two *HiVac* systems are now in widespread use with cemented joint replacements. Market share is stated by Summit Medical as: UK vacuum bowl mixing systems 70%; UK syringe mixing systems 35%; US overall 15%. These figures translate into total global sales 2009-2012 of £36.1M (Summit Medical Ltd annual turnover at 31/03/2011 of £13.27M represents ≈ 50% of the Summit Medical Ltd turnover of £27.62M) [A].

The 2012 sales of £9.1M represent approximately 13% of the global market estimated at $100M (£70M). The *HiVac* systems also enjoy excellent clinical outcomes, as evidenced in National Joint Registries. These outcomes impact directly on improved quality of life for patients and reduced clinical costs. The development of testing and evaluation protocols during the collaboration contributed to the clinical adoption of these systems for their cemented implant portfolio by leading international orthopaedic companies (e.g. DePuy Orthopaedics, Zimmer, Wright Medical) [A].

Development of the *HiVac* systems has contributed to Summit Medical becoming a world leader in the supply of cement mixing systems. Additional research insights gained into the associated fields of wound drainage valve design and femoral seal have further positively impacted on raising the professional image of Summit Medical within a very technical and competitive commercial area. The quality of the collaboration between the University researchers and the company was acknowledged with a TCS Certificate of Excellence that awarded the programme '*... the highest grading by the TCS Grading Panel for its achievement in meeting ... TCS objectives*' in terms of transferring knowledge, providing industry based training and enhancing the partnership between the university and business [C].

Additional impacts for Summit Medical from the TCS activity with Bath are stated in [A] as:

'*TCS scheme helped establish a training structure for new graduates/ young engineers.*'

and the establishment of a product development department:

'*R&D Personal currently 5 persons at Summit Medical.*'

Stryker Osteosynthesis: calcium phosphate cement for screw augmentation in cancellous bone

It has been estimated that more than 40% of women and 14% of men over the age of 50 years will experience fractures related to osteoporosis. Dealing with these fractures is significantly complicated by poor bone quality. Stryker Osteosynthesis had developed *Hydroset*, an injectable calcium phosphate cement for use in bone void-filling designed to augment screw purchase in weak osteoporotic bone. Stryker sponsored research at Bath that led to new knowledge about the clinical benefits to be obtained from using *Hydroset* and indicating significant improvements in pull-out strength. The chief impact of this work was in generating the technical file compiled by Stryker to obtain EU regulatory approval and FDA submission (ongoing) for clinical use of this injectable cement in screw augmentation procedures. Approval was granted in 2008 and *Hydroset* is now a mainstream product of Stryker with an associated total income of $180M since 2008 (income 2012 = $32M) representing a market share in this field of greater than 20%. It is stated, [B], by the Senior Director, Biomaterials R&D and Technical Marketing, Stryker Osteosynthesis that:

'*The first ever regulatory claim for CaP cement augmentation of orthopaedic screws in cancellous bone was granted by the TÜV Rheinland LGA in 2008. This claim (the data submitted to the LGA) was substantially supported by studies done by the Centre for Orthopaedic Biomechanics, University of Bath. ….The added clinical value is significant ... Bath has been a key part of developing both the claim and enabling the commercial success of Hydroset. The Centre for Orthopaedic Biomechanics is considered a centre of excellence in this field by Stryker Corp ...*'

These products have also resulted in impact in terms of improved clinical outcomes, as evidenced by practitioner-generated publications:

'*This cadaveric study indicates that supplementation of angular stable screws with calcium phosphate cement for the fixation of proximal humeral fractures significantly reduces the risk of glenohumeral screw penetration and enhances resistance to failure.*' [D];

'*... augmentation with calcium phosphate cement (Hydroset) in the treatment of proximal humeral fractures with locked plates decreased fracture settling and significantly decreased intra-articular screw penetration.*' [E];

'*... We believe that injectable osteoconductive calcium phosphate bone cements may be a useful adjunct in treating osteolytic cysts around well-fixed knee-replacement components.*' [F].

In summary, in the case of the Summit Medical, the *Enhanced HiVac Bowl Bone Cement Mixing System* and the *HiVac Bone Cement Mixing and Delivery System*, and the Stryker *HydroSet Injectable Cement*, that the market shares are testament to their clinical adoption by practicing orthopaedic surgeons from around the world.

5. Sources to corroborate the impact

A. Corroborative statement from Head of Development, Summit Medical, 17 September 2013.

B. Corroborative statement from Senior Director, Biomaterials R& D and Technical Marketing, Stryker, 5 December 2012.

C. TCS Certificate of excellence awarded to the University of Bath/Summit Medical Ltd.

D. G Gradl, M Knobe, M Stoffel, A Prescher, T Dirrichs and H Pape. Biomechanical evaluation of locking plate fixation of proximal humeral fractures augmented with calcium phosphate cement, Journal of Orthopaedic Trauma, **27**(7), 399-404, 2013. DOI: 10.1097/BOT.0b013e318278c595

E. KA Egol, MT Sugi, CC Ong, M Ontero, R Davidovitch and JD Zuckerman. Fracture site augmentation with calcium phosphate cement reduces screw penetration after open reduction–internal fixation of proximal humeral fractures, 2011, Journal of Shoulder and Elbow Surgery, **21**(6), 741-748. DOI: 10.1016/j.jse.2011.09.017

F. HD Atkinson, VS Ranawat and RD Oakeshott **,** Granuloma debridement and the use of an injectable calcium phosphate bone cement in the treatment of osteolysis in an uncemented total knee replacement, 2010, Journal of Orthopaedic Surgery and Research, **5**(29), 1-6. DOI: 10.1186/1749-799X-5-29