Institution: King's College London

Unit of Assessment: UoA3 - Dental

Title of case study: Development of spin out company OSspray Ltd to investigate treatment of dental hypersensitivity

1. Summary of the impact (indicative maximum 100 words)

Dental hypersensitivity is a major problem for over half the population in the developed world. Researchers at the Dental Institute of King's College London (KCL) have developed a system to use bioactive glass powders to clean, seal and desensitize teeth, thus alleviating dental pain. As a result, a spinout company – OSspray – was formed in 2004 to develop and commercialise the system for dentists and hygienist to spray-clean teeth. Over £4.5 million of funding has been raised to date from institutional and venture capital investors and three product lines have been launched in the past 24 months. The products developed by the KCL/OSspray team have treated over 700,000 patients across the EU, USA and Asia. The knowledge gained by the KCL-based founders of OSspray has been used to train students in Innovation Technology.

2. Underpinning research

Background: An epidemiological study in the UK indicated that up to 57% of people questioned suffered from dental hypersensitivity. The aetiology of the condition is multi-factorial although it has been demonstrated that the structure of dentine in the affected areas is altered. Research into approaches to the treatment and prevention of dental hypersensitivity at Kings College London (KCL) Dental Institute has been led by Prof Timothy Watson (1989-present, Head of Biomaterials Department), Dr Ian Thompson (2002-present, Senior Lecturer), Dr Richard Cook (2002-present, Senior Lecturer) and Prof Avijit Banerjee (1995-present, Director of Integrated Clinical Care & Conservative Dentistry).

KCL Researchers develop a novel treatment for dental hypersensitivity: Currently there are two main approaches for the treatment of dental hypersensitivity: 1) tubule occlusion, where open conduits that connect the tooth's nerve and the outside environment of the mouth are re-sealed, and 2) blocking nerve activity through direct ionic diffusion. Over the last decade, KCL has focussed on the first approach by treating the tooth with a chemical or physical agent that creates a layer which mechanically occludes the exposed dentinal tubules. As such, the team has developed a novel cleaning and desensitising prophy-powder based on bioactive glass technology, called Sylc. The material (calcium sodium phosphosilicate) closely resembles natural tooth mineral and is applied to the tooth via an air polishing system, with the powder carried in a gentle airstream. This results in a simultaneous cleaning, desensitising, re-mineralising and whitening of teeth in just one application, eliminating the need for powerful bleaching agents and repeated trips to the dentist. The group applied for a patent in 2000 with initial funding to validate the hypothesis from an EPSRC grant in 2002.

Properties of Sylc are defined by KCL researchers:
A number of studies on the properties of Sylc have been conducted and published over the past 7 years. Initially the focus was on the clinical effect of air abrasion - a more vigorous form of air-polishing that can cut tooth tissue because of the hard powders that are used – and associated techniques. In one study, KCL researchers showed that air abrasion cutting of tooth tissues could be imaged in real time using video-rate confocal microscopy, for the first time allowing comparisons to be made between air abrasion cutting and the more destructive traditional dental drills (Cook RJ, et al. 2001). In another study, KCL researchers showed different reductions of dentine permeability (an *in vitro* indicator of dentine sensitivity) based on the type of prophylaxis product employed. They analysed this using sensitive measures of permeability followed by morphological assessment with scanning electron microscopy. Sylc bioactive glass was the most effective in reducing dentine permeability and the air-polishing procedures performed with Sylc created a dentine surface devoid of exposed dentinal tubules due to the presence of a compact multi-layered smear layer (Sauro S, et al. 2011a). A further study evaluated dentine remineralization. Here, compared to currently used treatments, Sylc was the only substance able to reduce dentine permeability after immersion in re-mineralising solutions and the only one to show hydroxycarbonate apatite precipitation as evidence of dentine remineralization (Sauro S, et

al. 2011b).

Clinical use of Sylc by KCL researchers: The team have focussed efforts on simple replacement of incumbent air polishing powders for dental prophylaxis by utilising the more therapeutic potential of bioactive glass. In a comparison of prophylaxis therapies, the air-polishing procedures performed with Sylc bioactive glass powder created a dentine surface resistant to citric acid attack thereby reducing the potential development of tooth wear (Sauro S, et al. 2010). While these lab-based studies confirmed the physical effect of Sylc, clinical trials in patients were carried out by KCL researchers to determine the effects on the feelings of dental hypersensitivity. One, which included 50 patients who underwent prophylactic treatment with Sylc or sodium bicarbonate, showed a significant 42-44% decrease in dental hypersensitivity with Sylc compared to control teeth both immediately and 10 days later. They also found that Sylc offered a more effective stain removal system and better whitening effect compared to sodium bicarbonate and that the treatment provided a more acceptable clinical experience for patients (Banerjee A, et al. 2010).

KCL researchers expand the use of air polishing to tackling dental decay: The program was expanded in 2009 to include research into alternative uses of bioactive glass air abrasion/polishing. The team moved the treatment modality of air polishing into minimally invasive dentistry. Hitherto, removal of dental decay has been achieved with overly invasive approaches, but use of tailored bioactive glass particles has led to expanded applications of the team's initial Intellectual Property submissions. This showed that use of Sylc could reduce the over removal of dental tissue during cavity preparation by having self-limiting cutting properties (Banerjee A, et al. 2011), developing the potential for safe caries removal using a less skilled workforce.

3. References to the research (indicative maximum of six references)

Banerjee A, Hajatdoost-Sani M, Farrell S, Thompson I. A clinical evaluation and comparison of bioactive glass and sodium bicarbonate air polishing powders. J Dent 2010;38(6):475-9. Doi: 10.1016/j.jdent.2010.03.001 (12 Scopus citations)

Banerjee A, Thompson ID, Watson TF. Minimally invasive caries removal using bio-active glass air-abrasion. J Dent 2011;39(1):2-7. Doi: 10.1016/j.jdent.2010.09.004 (5 Scopus citations)

Cook RJ, Azzopardi A, Thompson ID, Watson TF. Real-time confocal imaging airing active air abrasion - substrate cutting. J Microsc 2001;203(Pt 2):199-207. Doi: 10.1046/j.1365-2818.2001.00934.x (6 Scopus citations)

Sauro S, Watson TF, Thompson I. Dentine desensitization induced by prophylactic and air-polishing procedures: An in vitro dentine permeability and confocal microscopy study. J Dent 2010;38(5):411-22. doi: 10.1016/j.jdent.2010.01.010 (19 Scopus citations)

Sauro S, Watson TF, Thompson I. Ultramorphology and dentine permeability changes induced by prophylactic procedures on exposed dentinal tubules in middle dentine. Med Oral Patol Oral Cir Bucal 2011a;16(7):e1022-30. Doi: http://dx.doi.org/doi:10.4317/medoral.17397 (1 Scopus citation)

Sauro S, Thompson I, Watson TF. Effects of common dental materials used in preventive or operative dentistry on dentin permeability and remineralization. Oper Dent 2011b;36(2):222-30. Doi: 10.2341/10-225-L (8 Scopus citations)

Research Funding to KCL

- 2002-5. Engineering and Physical Sciences Research Council. Air Abrasion PI: T F Watson. £240,000
- 2005-6. Guy's & St Thomas's Charity. Bioactive glass processing. PI: I Thompson. £236,000
- 2008. OSspray Ltd (KCL-OSS1 -001). Clinical trial of air polishing powders. PI: I Thomson. £15,000
- 2008. OSspray Ltd (KCL-OSS1 -002). Caries Removal. PI: I Thompson. £6,600
- 2008. OSspray Ltd (KCL-OSS1 -003). Orthodontic Cleaning. PI: I Thompson. £12,600
- 2008. OSspray Ltd (KCL-OSS1 -004). Surface retention of bioactive glass. PI: I Thompson.

£3,600
- 2010-11. i4i (II-3A-1109-10046). Operative Caries Management. PI: TF Watson/I Thompson. £99,796

4. Details of the impact (indicative maximum 750 words)

KCL Researchers Form OSspray

The initial concept of bioactive glass air polishing therapies was developed in 2002 as a collaboration between Prof Timothy Watson and Dr Richard Cook of the Dental Institute, King's College London (KCL) and Prof Larry Hench and Dr Ian Thompson at Imperial College London. The hypothesis was that bioactive glass particulates could be tailored to allow selective removal of dental tissues, i.e. enamel, dentine and decay. This concept was filed as two patent applications in 2002 (1a, b). Intellectual Property from the project was granted in 2004 and the spin out company, OSspray Ltd, was formed by Dr Ian Thompson with seed funding from a government scheme (2a). Dr Thompson then moved from Imperial College London to KCL to catalyse the movement of the technology from concept to clinic. A series of minor investment rounds between 2004 and 2008 resulted in a clinical trial based at Guys Hospital London (part of the King's Health Partners network) (published as Banerjee 2010). This trial verified the additional claims around the product, principally faster cleaning and desensitisation of dental tissues, allowing regulatory clearance in the USA and EU in 2006 (2b).

Launch of Sylc and Development of Second-Generation Powders

OSspray's first major investment round in 2008 from Imperial Innovations, Yorkshire Fund Managers and NESTA resulted in the first product, Sylc, to be launched in early 2009 (3a-c). Sylc is marketed as having several uses including dental hypersensitivity treatment; fast removal of extrinsic stains; surface preparation prior to bonding and sealants; before and after scaling and root planing procedure to reduce sensitivity; plaque removal prior to fluoride treatments and for pre- and post-whitening treatments. These claims are backed-up in promotional material for Sylc by the above-discussed KCL research (3d).

The continued collaboration between KCL and OSspray has resulted in a prestigious i4i award in 2010. This new funding has allowed the research team to complete the search for a second generation of prophy powders which will take the clinical technique into a minimally invasive self-etching system, thereby making the process a more general therapy treatment for dental decay. This second generation powder was patented by the KCL/OSspray team in 2009 (1c).

International Use of Sylc and Sale of OSspray

OSspray continued to expand from 2008 to 2012, with rented premises on the KCL estate. The company employed 12 people and supported a number of KCL-based research projects that utilise its core technology, Sylc. By mid 2012 the KCL-based technology treated its 700,000th patient with a turnover of £500,000 per year (3e). By July 2012 OSspray was supplying products to all European countries (for instance, in Italy [4a] and Germany [4b]), as well as to North America (4c), the Middle East and Australasia, with independent professional trade articles both in the UK and abroad highlighting the clinical importance of the technology in treating dental hypersensitivity. For instance, in an article from the UK magazine 'Dental Hygiene and Therapy,' aimed at dental professionals, it is recognised that Sylc "uniquely repairs dental tissues and brightens teeth" (4d). The US magazine RDH (Registered Dental Hygienist) uses Sauro 2010 and Banerjee 2010, to illustrate how "bioactive glass is a more effective desensitizer than sodium bicarbonate in both good and poor oral hygiene groups" (4e).

In December 2012 OSspray sold the Intellectual Property and 'know how' assets to Denfotex Research Ltd (DRL). DRL is a UK-based company with over 10 years experience in the dental market. It has continued to grow the OSspray Sylc technology by moving the technology into China and Japan. Their website contains a number of details of Sylc including development and use, aimed at dental healthcare professionals. These are backed-up by the use of many of the KCL references discussed above (3d).

Further Impact

The skills developed by the academic staff, particularly Dr Ian Thompson, during the development of OSspray as a spin-out company has allowed the KCL Dental Institute to run an Intercalated BSc programme in Innovation Technology. This course has been run by Dr Thompson for the past 4 years and has graduated over 40 students who have specialised in the innovation process and gained the knowledge required to translate technologies from academic projects to clinically approved devices/treatments (5).

5. Sources to corroborate the impact (indicative maximum of 10 references)

1) Patents
- a) EP1372574B, US7329126, Canada 2,442,471. Use of Bioactive Glass. Hench L, Thompson I, Cook R, Watson T. Applicants: Imperial College Innovations Limited, King's College London: http://www.google.com/patents/EP1372574B1?cl=en
- b) EP1372574B, US7040960, Canada 2,442,492. Use of Bioactive Glass for Cutting Bioactive Glasses. Hench L, Thompson I, Cook R, Watson T, Robinson P. Applicants: King's College London, Imperial College Innovations Limited: http://www.google.co.uk/patents/US7040960
- c) WO 2009141611 A3. Abrasive agents, Cook R, Watson TF, Thompson ID. Applicant: King's College London: http://www.google.com/patents/WO2009141611A3?cl=en&dq=Thompson+Watson+Cook&hl=en&sa=X&ei=Na3NUfnIGYSp0QWm6IDQAw&ved=0CD0Q6AEwAQ

2) OSspray
- a) Registration of Osspray Ltd: http://wck2.companieshouse.gov.uk//compdetails
- b) FDA regulatory clearance: http://www.accessdata.fda.gov/cdrh_docs/pdf6/K062502.pdf

3) Sylc
- a) Angel News: http://www.angelnews.co.uk/company.jsf?companyId=349
- b) Imperial Innovations: http://www.imperialinnovations.co.uk/news-centre/news/imperial-innovations-increases-stake-osspray/
- c) KCL business success stories: http://www.kcl.ac.uk/innovation/business/success/spinout/spray.aspx
- d) Denfotex Research Ltd:
  - Website: http://www.denfotexresearch.com
  - Sylc reference base. Prophy Powder: http://www.denfotexresearch.com/index2.htm
  - Sylc reference base. Caries Removal Powder: http://www.denfotexresearch.com/index2.htm
- e) Letter of Professional Corroboration from OSspray available on request to confirm these numbers

4) Use of Sylc
- a) Italy: http://www.dentalica.com/it/Prodotti/Sylc/OSspray_Polvere_Sylc.aspx
- b) Germany: http://www.dentocare.de/Nach-Marke-Hersteller/Osspray/Sylc-Prophylaxepulver.html
- c) Canada: http://www.oralscience.ca/en/products/inno_sylc_nsk.html
- d) Dental Hygiene and Therapy. 9.5.2012: http://dentalhygienetherapy.co.uk/oral-health-news/4231/
- e) RDH magazine http://www.rdhmag.com/articles/print/volume-30/issue-11/features/air-polishers.html

5) Intercalated BSc programme in Innovation Technology: http://www.kcl.ac.uk/medicine/study/ug/intercalated/a-z/regenerativemed/index.aspx