Institution: University of Aberdeen

Unit of Assessment: UoA1: Clinical Medicine

Title of case study: Creating innovative technologies and products for the treatment of bone defects

Period when the underpinning research was undertaken: 2005 - present

Details of staff conducting the underpinning research from the submitting unit:

Name(s):	Role(s) (e.g. job title):	Period(s) employed by submitting HEI:
Prof Iain Gibson	Professor in Medical Sciences	2002 – present
Prof Jan Skakle	Professor in Physics	1995 – present
Prof Richard Aspden	Professor in Orthopaedic Science [Emeritus]	1990 – 2016 [2016 – present]

Period when the claimed impact occurred: Aug 2013 - present

Is this case study continued from a case study submitted in 2014? No

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

Over 500,000 spinal fusion surgeries requiring a bone graft substitute are carried out each year in the US alone. However, traditional synthetic materials mean that, in at least 20% of cases, the materials fail to achieve successful fusion, resulting in poor clinical outcomes. Research at the University of Aberdeen has resulted in new approaches for the development and production of synthetic materials that overcome these limitations, leading to 3 patents and commercial exploitation via a spin-out company. Since August 2013, this new company has used the underpinning research to fuel its expansion, attracting GBP6M in financing between 2014-2020, which led to an GBP8.4M acquisition in 2020 by an international company, increasing company headcount to deliver economic impact. The company has also created new products that fill unmet clinical needs.

2. Underpinning research (indicative maximum 500 words)

Trauma or disease requiring bone to be replaced can be grafted by surgeons. In fact, in the US alone, there are over 500,000 spinal fusion surgeries requiring a bone graft substitute every year. However, commercial synthetic bone graft substitutes have been typically synthesised using either ceramic-based approaches or melt-derived glass approaches. These traditional materials are dense, unlike bone mineral, and have had limited clinical success both due to generation of fibrous tissue growth around the material, rather than new bone, and lack of resorption into the body. These failures account for around 20% of cases, leading to significant implications on patient health, quality of life and ability to return to work, with concomitant socio-economic costs to society. Even with these limitations, the current annual share for synthetic substitutes represents almost a third of the USD3.2 billion bone graft global market. Research started in 2005 at the University of Aberdeen – supported first by an EPSRC Advanced Research Fellowship awarded to Professor Iain Gibson (**P1**) and then a Scottish Enterprise Proof of Concept Grant (**P2**) – sought to address this problem by developing a novel synthetic bone graft substitute using a different approach to synthesise the materials. This multi-disciplinary research project was carried out within the Institute of Medical Sciences and the Department of Chemistry (with co-applicants Skakle and Aspden), and included pre-clinical assessment managed through sub-contracted collaborators.

The research aimed to develop a synthetic approach that produced a bone graft scaffold material that exhibited chemical and morphological similarities to bone mineral, based on the hypothesis that such a scaffold architecture would support faster bone repair and be capable of cell-mediated resorption. If successful this would address two unmet clinical needs: an off-the-shelf synthetic

bone graft substitute that would perform as well as or better than autograft (the clinical gold standard, but an approach that is accompanied by longer patient healing time, and postoperative pain at the autograft harvest site); and a synthetic material that would eventually be fully remodelled and replaced by host bone.

The research involved the development of both a novel composition of silicate-containing calcium phosphate material and the process of making it into a new synthetic bone graft substitute material. [**R1**, **R2**] The resulting material was designed to have a crystal morphology and size that is closer to that of the bone mineral crystals in bone, compared to other synthetic bone graft materials, with crystal dimensions ranging from approximately 50 nm to 150 nm. The processing of the composition into a granule bone graft resulted in a similar amount of total porosity to common macroporous bone grafts (>75% total porosity), but the size of the pores is significantly smaller (sub-micron sized), rather than macropores (100-500 microns), meaning that the resulting material has a high surface area. The hypothesis of this material design was that making a bone graft with much smaller crystal sizes and a high surface area would result in a bone graft that would provide a surface that supports bone repair and would be more readily remodelled than current 'ceramic' synthetic bone graft substitutes. Further research identified specific microstructural features in calcium phosphate materials, and methods to produce these, that led to an osteoinductive property in the material [**R3**]. Pre-clinical testing of this material showed that the rate of bone formation was significantly faster than observed for one of the leading synthetic bone graft substitutes on the market, using a challenging model of spinal fusion. This study also showed that the graft material was remodelled and slowly replaced by host bone.

Following the completion of the Proof-of-Concept project, the technology and intellectual property formed the basis of a spin-out company from the University of Aberdeen in 2011 (SIRAKOSS Ltd.), who continue to commercialise the technology.
Research and development of the underpinning research continued through a Royal Commission for the Exhibition of 1851 Industrial Fellowship funded PhD project at the University of Aberdeen, supervised by Professor Iain Gibson from 2013 to 2016.

Building on the underpinning research, a recent study by SIRAKOSS demonstrated the efficacy and safety of the final developed product in a regulatory pre-clinical study, leading to 100% fusion success after 26 weeks, which further validated the Aberdeen-led research [**R4**].

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

Research outputs

R1. Patent: "Silicate-substituted hydroxyapatite", Gibson, I.R. and Skakle, J.M.S. US Patent no. 8,545,895 (Granted 1st October 2013, Priority date 8/1/2009)
R2. Patent: "Bone Graft System", Gibson, I.R., Skakle, J.M.S., Conway, J.C., Annaz, B. US Patent No. 9,492,591 (Granted 15th November 2016, Priority date 25/6/2010)
R3. Patent: "Calcium Phosphate Material", Gibson, I.R., Skakle, J.M.S., Conway, J.C. US Patent No. 9,492,585 (Granted 15th November 2016, Priority date 23/12/2011)
R4. Conference abstract: "235. Evaluation of a nanosynthetic silicated calcium phosphate putty in a posterolateral rabbit spinal fusion model" (2020) Walsh, W., Oliver, R., Wang, T., Wills, D., Conway, J., Buckland, T. and Gibson, I.R. The Spine J., 20;9:S116 (https://doi.org/10.1016/j.spinee.2020.05.646)

Research Grant Funding (to the University of Aberdeen)

P1. EPSRC Advanced Research Fellowship and Associated Research Grant – "*Enhancing the performance of calcium phosphate implants by accelerating blood vessel formation (angiogensis)*" (GBP331,713) – Dr Iain Gibson (PI) – 2005-2009;
P2. Scottish Enterprise Proof of Concept 8 Grant – "*Smart materials that guide new bone formation - novel scaffolds for tissue engineering applications*" (GBP210,597) – Dr Iain Gibson (PI) with Dr J. Skakle and Prof. R.M. Aspden – 2007-2010

Evidence of the quality of the research

Grant P1 was peer reviewed within the EPSRC Peer Review College and included interview. Grant P2 was peer reviewed by Scottish Enterprise.

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

The SIRAKOSS technology, underpinned by the Aberdeen research, addresses the unmet clinical needs for bone graft substitutes by creating an off-the-shelf synthetic bone graft that accelerates bone formation and repair so that the graft is fully remodelled and eventually replaced by new bone. The technology has enabled the growth and expansion of a spin out company, attracting equity investment, company led research funding, creating new employment and created 2 new products that fill unmet commercial needs.

Growth of a spin-out company, attracting investment, creating employment and winning awards

Since spinning out from the University of Aberdeen, SIRAKOSS has raised significant investment and grant funding for an early-stage medical device company, securing a total of approximately GBP6M in financing, which lead to an GBP8.4M acquisition within the REF period [**S1**].

SIRAKOSS was acquired by OssDsign in November 2020, enabling the new partnership to market innovative products in the USA and Europe, the two major territories for this technology. The OssDsign deal of GBP8.4M to acquire SIRAKOSS yielded GBP3.8M to investors and other shareholders in November 2020, with final payments due in 2021 with additional future milestone and royalty payments agreed. [**S2**]

The growth of SIRAKOSS led to an increase in headcount during the REF period, growing from 2 FTE to 7 FTE. Professor Gibson continues to work with SIRAKOSS/OssDsign on a 0.4FTE basis. The expansion also supported a range of subcontracted services by the company, including finance, IP, regulatory, IT and marketing/branding, all to UK-based companies [**S3**].

OssDsign anticipate product launches based on the SIRAKOSS acquisition, starting in 2021. Completion of milestones to date, along with achieving major projected commercial milestones during the REF period, supported a significant increase in company valuation and a growth in company size, increasing the headcount significantly. These activities enable SIRAKOSS/OssDsign to market innovative products in the two major territories for this technology, in a bone graft market worth over USD3 billion. The next stage of growth anticipated in 2021, based on this acquisition, will be to build commercial sales in the USA and to capture clinical evidence.

Investment has been supported by industry recognition of the SIRAKOSS technology, through a number of awards. In 2014, the technology was awarded the Venture Prize from The Worshipful Company of Armourers and Brasiers [**S4**]. The company has been shortlisted twice in the Scottish Enterprise Life Science Awards, first for the Investment of the Year (2016) and then for the Innovation Award (2020) [**S5**].

Creating 2 new products that fill unmet commercial needs

The SIRAKOSS technology has led to the development of 2 new products, all of which address unmet clinical needs, namely the availability of a synthetic bone graft substitute material with a similar efficacy to biologics but with a lower cost and reduced risk. A CE Mark for the first product, Osteo^3 Granules, was awarded in 2019 [**S6**] and the second product, Osteo^3 ZP Putty, a formulation with ready-to-use intra-operative handling characteristics, was cleared by the FDA in the USA for use in trauma and spine surgery in 2020 [**S7**]. Current synthetic materials do not provide surgeons with a bone graft that performs at a level that reliably matches or exceeds that of autograft, or approach the efficacy of expensive biologics. A clear unmet commercial need exists for a synthetic material that achieves clinical outcomes that would meet or exceed autograft, and would approach the performance of biologics but at lower cost to healthcare providers. A US-based orthopaedic spine surgeon said "*the bone graft technology that has been developed by Sirakoss is very interesting and I found the existing data to be very compelling, demonstrating at a minimum an equivalent performance to autograft… I believe that these results will be of great interest to surgeons who rely on these types of bone graft substitutes. In summary, based upon my review, I believe that this novel material represents an exciting advance in synthetic bone graft technology*" [**S8**].

At the time of acquisition SIRAKOSS was a pre-revenue company but the acquirer, OssDsign, anticipate product launches in 2021. Innovation continues, including a new bone graft composition developed by SIRAKOSS in 2019-2020, with a patent application submitted in August 2020. This new composition will enable new clinical applications of the core science, extending into medical implants such as spinal cages.

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

S1. **Investment**: Written testimonial from Series A investors; press articles on investments http://www.bbc.co.uk/news/uk-scotland-scotland-business-30291998; https://epidarex.com/sirakoss-series-a/ (Dec 2nd 2014);

S2. **Acquisition**: Written testimonial from OssDsign; press article on acquisition https://news.cision.com/ossdsign-ab/r/ossdsign-completes-acquisition-of-the-scottish-bone-graft-company-sirakoss,c3233866 (Nov 9th 2020)

S3. **SIRAKOSS CEO**: Written statement

S4. **Awards**: Artificial bone wins major award https://www.nature.com/articles/sj.bdj.2014.629 (July 25th 2014)

S5. **Awards shortlist**: https://www.abdn.ac.uk/news/8481/ (Dec 1st 2015); https://www.lifesciencesscotland.com/news/finalists-announced-scotlands-life-sciences-awards-2020 (Jan 24th 2020)

S6. **CE Mark**: Jan 2019 Press release

S7. **FDA clearance**: June 2020 Press release

S8. **Orthopaedic Spinal Surgeon**: Written testimonial