Institution: University of Strathclyde

Unit of Assessment: 3

Title of case study: Economic and health benefits from use of the HemoSep auto transfusion system to reduce blood transfusions and related complications during open-heart surgery.

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

A low-cost, efficient, blood cell salvage technology (HemoSep) has resulted from research carried out at Strathclyde between 2008 and 2013. The novel technology has been patented and licensed to Brightwake Ltd., who manufacture the device in the UK and market it through a global distribution network. HemoSep has now been used in clinical centres across Europe, North America, and South Africa since its commercial launch in late 2012. The use of the device has been shown to reduce the need for donor blood transfusions in open-heart surgical patients by at least 1 unit (450 ml) with an associated reduction in transfusion related complications such as heightened inflammatory response and bleeding. The reduction in blood transfusions associated with the use of HemoSep has a considerable cost benefit to healthcare providers (in North America blood costs up to $1600 per unit). In addition, commercialisation of HemoSep has led to the creation of new manufacturing, marketing and sales jobs in the UK and overseas.

2. Underpinning research (indicative maximum 500 words)

Context:

Conventional donor transfusion in patients undergoing major surgery has been shown to be both costly and to carry risks of inappropriate and heightened immune responses. Over the past 20 years, auto-transfusion, or re-transfusion of the patient's own blood, spilled during the course of major operations has become a standard technique in complex surgery such as open heart surgery and major vascular and orthopaedic surgery. This approach has been shown to considerably reduce the need for donor blood and given that the patient's own blood is being recycled, minimises associated risks of transfusion reactions. This technique has to date required very complex machinery, including large centrifuge and pumping apparatus and skilled personnel. These issues have restricted the uptake of auto-transfusion in some clinical sectors. However, with open-heart surgery currently amounting to over 1 million procedures annually, and blood increasingly assuming a direct cost to healthcare providers (up to $1600 per unit in the USA), auto-transfusion provides both cost and health benefits over the use of donated blood. This work focused on the development of a simple, safe and cost- effective alternative auto-transfusion technology that provided benefits over the large, complex and technically demanding centrifugal devices.

Key research findings:

In response to expressed clinical need, staff at the Department of Biomedical Engineering, University of Strathclyde, undertook the development of a new approach to auto-transfusion using membrane controlled superadsorber technology that removes the liquid (plasma) component of blood by a rapid "wicking" process rather than conventional centrifugation and pumping.
Studies were carried out to establish that this process was viable through testing of hand- built prototypes (2008-2009). These studies, using bovine blood in the laboratory, confirmed process viability and highlighted the critical factors governing performance; membrane pore size, membrane composition, superadsorber configuration and the need for agitation to avoid membrane fouling. This early research determined that the auto-transfusion system should comprise both disposable and hardware elements. The disposable element consists of the superadsorber/membrane system contained within a blood bag, and hardware in the form of a fixed rate agitation system capable of ensuring movement of blood cells across the membrane surface. These studies formed the basis for the device design file and the patent filed by the University in 2009. Subsequent to this technology development phase, prototype devices were constructed by the University's technology licensee (Brightwake Ltd) and clinical trials were initiated with the world-leading University of Kirikkale Medical School in Ankara, Turkey under the direction of Professor Serdar Gunaydin, Professor of Cardiovascular Surgery and an international key opinion leader in the field of extracorporeal devices for open-heart surgical deployment. These

clinical studies, carried out in over 100 open-heart surgical patients, confirmed that the use of the HemoSep technology resulted in a reduction in the need for donor blood and diminished inflammatory response and post-operative blood loss in patients undergoing HemoSep supported surgery when compared with other transfusion modalities.

Key researchers:
Terry Gourlay – Professor of Biomedical Engineering at University of Strathclyde at time of research from 2008 to present.

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

1. Gunaydin S, Gourlay T. Novel ultrafiltration technique for blood conservation in cardiac operations. Annals of Thoracic Surgery, 2013, 95(6), 2148-51. DOI: 10.1016/j.athoracsur.2013.03.048.

2. Gunaydin S, Gourlay T. Clinical evaluation of a novel ultrafiltration technique for circuit salvage in high-risk patients undergoing coronary revascularization. Presented at CREF (cardiac research and education foundation) Cardiothoracic Surgery Session. San Diego California, February 29th 2012. http://crefmeeting.com/wp-content/uploads/2012/10/CREF12GunaydinSlides.pdf

3. Gunaydin S, Gourlay T. Clinical outcome of transfusion processed by ultrafiltration in patients undergoing coronary bypass. Poster Presentation at European Society for Artificial Organs. Rostock September 2012. Abstract in International Journal for Artificial Organs, Vol. 35, Issue 8, p 602 http://www.artificial-organs.com/article/xxxix-annual-esao-congress--26-29-september-2012-rostock-germany--posters

4. Gourlay T, Gunaydin S. A novel ultrafiltration device for circuit salvage in high-risk CABG patients. Oral Presentation at European Society for Artificial Organs. Rostock, September 2012. Abstract in International Journal for Artificial Organs, 2012, Vol. 35, Issue 8 p. 561 http://www.artificial-organs.com/article/xxxix-annual-esao-congress--26-29-september-2012-rostock-germany--oral-presentations

Other evidence for quality of research:
The main findings are published in the Annals of Thoracic Surgery, which is the leading international peer reviewed journal in the cardiothoracic surgical sector. The research has been disseminated at leading international conferences, all of which are peer reviewed, with a number of further presentations planned for the coming year, including a keynote lecture at the forthcoming Canadian Institute for Military and Veterans Health Research Congress to be held at Queen's University, Edmonton, Canada in November 2013.

This work was internally funded in the first instance, followed by funding in the region of £500k through the technology licensee, Brightwake Ltd, as the project approached commercialisation. The research led to the filing of 2 patents (The HemoSep University of Strathclyde/Brightwake Ltd - (WO/2009/141589), 2009. Bag-in-a-bag Brightwake Ltd – (US 2012/0175319 A1)), one covering the core technology and the second a novel manufacturing process for forming the bag-in-bag element of the device that emerged from the manufacturing development process.

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

Process of impact generation from research:
Brightwake Ltd worked closely with the Strathclyde University team to develop a commercially viable and clinically suitable device, resulting in significant outcomes beyond the basic research stage. The relationship with Brightwake Ltd is enduring with continued interaction regarding the development of HemoSep derivatives and other devices. A Knowledge Transfer Account fellow was appointed to further exploit some of these opportunities (Dr Alasdair Walker, Oct. 2011-Sept.2012) and Brightwake continue to explore commercial opportunities with the University. Development of the technology towards a clinically deliverable device started in 2010. Strathclyde University were fully engaged in this, providing laboratory test facilities and expertise. Novel technology for "bag-in-bag" manufacture techniques emerged from this research with a patent filed

by Brightwake Ltd in 2012. In 2011-2012 independent verification of the performance and safety of the technology was carried out with the Department of Biomedical Engineering, University of Strathclyde providing advice on protocol development and analysis. The successful conclusion of these studies led to Brightwake Ltd investing in excess of £500k in infrastructure to manufacture devices for clinical trial as part of the CE marking process and subsequent clinical sales.

Types of impact:

Results of clinical trials show reduction in need for donor blood

A key opinion leader (Source B) was identified in July 2011 through the Strathclyde Institute for Medical Devices to lead the clinical trials. In 2011, a study protocol and post study analysis designed to meet CE mark requirements, was drafted by Strathclyde in association with SGS Ltd. Subsequently (2011-2012), studies were carried on high risk heart surgery patients with a focus on clinical outcomes relating to blood transfusion and fluid balance issues. This work confirmed that the device was effective in concentrating salvaged haemodiluted blood back to normal values in terms of all critical factors. Importantly, the HemoSep technique was shown to return ***all*** blood cell species back to patients, rather than simply red blood cells, a factor that considerably enhances the benefits of auto-transfusion in these challenging patients. The clinical investigators engaged in the early clinical trials expressed the view that HemoSep is "the simplest to use Auto-transfusion device available for open-heart surgery" and subsequently confirmed that the use of HemoSep "results in a reduction in donor blood usage of the order of 1 unit per open-heart patient" (Sources B and C).

Formation of new company

Having licensed the HemoSep device from the University, Brightwake Ltd formed a new company, Advancis Surgical to market this and other medical devices to the cardiovascular and other medical communities. Subsequent to granting of the CE mark, manufacture and marketing was scaled up. The commercialisation and clinical studies were funded directly by the commercial partner Brightwake Ltd. Brightwake Ltd have fully engaged in the commercialisation of the HemoSep technology and have worked closely with the University of Strathclyde in its continued development and delivery.

Commercial adoption of new and improved technology

The HemoSep technology has all the advantages of conventional centrifuge based auto-transfusion systems in terms of process time, but occupies around 10% of the space commonly required for a conventional system and can be operated by relatively non-specialist staff. These features have resulted in global interest in this device leading to rapid growth in sales. At the present time Brightwake has, through a distributor business model, established distributorships for HemoSep in Canada, Germany, Thailand, Italy, Australia, New Zealand and South Africa, and have already submitted for FDA approval for access to US markets. Orthopaedic and paediatric derivatives of HemoSep were launched in July 2013 and are undergoing clinical trials in UK and Canadian hospital sites.

Investment and jobs

The company have invested over £1.5 million in the manufacture and marketing of the HemoSep technology and have created 11 new jobs in the UK in the manufacturing and marketing of the device, together with other new jobs overseas in its international distribution network (3 full time sales staff in Canada, 2 in Thailand, 3 in Italy). A total of 25 new jobs associated with the HemoSep device had been created internationally by March 2013. (Source A) In addition to new jobs, the HemoSep technology has resulted in Brightwake investing in new plant and manufacturing technologies at its Nottingham headquarters. These include a dedicated clean room for device assembly and unique manufacturing technologies for the bag-in-bag device assembly (Source A provides confirmation of the investment details and progress with HemoSep to July 2013).

Sales

Brightwake made the first sale of HemoSep, and therefore established a new income stream, in September 2012. As of May 2013, less than 1 year after CE marking, Brightwake Ltd has sold

HemoSep hardware and disposables into Canada, Italy, Germany, UK, Thailand, South Africa, and Australia. The Director of R&D Brightwake/Advancis Surgical Ltd (Source A) states that "since we launched Advancis Surgical Ltd to develop and sell this and other medical device technologies, uptake of HemoSep has been very good….UK clinical trials are ongoing at a number of NHS centres and we anticipate considerable growth in the coming year."
Total sales of the disposable element of the HemoSep system are in the many thousands of units across these territories. Contracts for distribution in other territories are in negotiation at the present time. The critical market for HemoSep will be the USA, where there is a real focus on the cost and risks of conventional donor blood transfusions. Brightwake has recognised this as an opportunity and have already filed for FDA approval for this product. Sales in the USA are anticipated to exceed sales in the totality of other territories (Source A).

Benefits to patients
A number of patient benefits have been confirmed through clinical deployment of the HemoSep system to date. The large-scale clinical trial of HemoSep carried out in Turkey has demonstrated that the system results in a reduction in the need for donor transfusion by around 1 unit (450ml) per patient. This represents around a 50% reduction when compared to patients undergoing surgery without the HemoSep system. In addition, these studies have demonstrated a consistent reduction in the inflammatory response and bleeding known to complicate the post-operative recovery of these patients, leading to reduction in time spent in the intensive care setting after invasive surgery (see published results reference 1, Source B, and the statement on Advancis website, Source C)
The sparing of all blood cell species by the HemoSep system, rather than just red blood cells as is the case with conventional centrifugal systems, is the reason for these major benefits. This overall reduction in risk of transfusion reaction, blood loss and use of donor blood goes some way to rendering open-heart surgery a safer procedure for patients undergoing these complex procedures.

Summary
There are a number of beneficiaries from the HemoSep development. Healthcare providers will benefit from reduced costs of delivery of open-heart surgery resulting from the saving of donor blood and reduced complications in recipient patients. The shareholders and employees of the licensee company will benefit from the greater stability and the financial return that comes from launching a new and innovative product with genuine downstream development potential into a technologically receptive marketplace. Patients will benefit from reduced complications associated with donor blood transfusions and improvements in clinical outcome related to the preservation of all cell types when the HemoSep technology is employed during their surgery. Strathclyde University will benefit financially from the income generated through the license agreement with Brightwake Ltd and from the new and close relationship we have with the company in developing new medical devices.

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

A. Statement from Brightwake Ltd on current status of HemoSep program.

B. Statement from Professor of Cardiothoracic Surgery University of Kirikkale on clinical experience with HemoSep

C. Website for confirmation of HemoSep status and new developments - www.advancis.co.uk.