Institution: University College London

Unit of Assessment: 15 – General Engineering

Title of case study: Health and economic benefits resulting from the development of non-invasive growing prostheses

1. Summary of the impact

A team of biomedical engineers at UCL has developed a non-invasive growing implant that improves the health and quality of life of young patients who have suffered from certain bone cancers. The prosthesis avoids the costly and invasive surgical interventions of previous treatment. Instead, the prosthesis can be lengthened in a quick and pain-free procedure conducted at an outpatient clinic. As a result, it reduces the costs of bone reconstruction and growing by around £19,000 per patient, as well as reducing the risk of infection and subsequent treatment. Since 2008, more than 400 devices have been sold; in addition to the cost savings indicated above these devices have generated more than £6 million income for UCL spin-out company Stanmore Implants Ltd, which was sold for £10 million in 2008.

2. Underpinning research

The standard treatment for bone tumours is surgical removal followed by replacement with either a transplant or a fixed metallic implant, usually incorporating a joint replacement device. In children, however, the use of fixed-length prostheses can result in different limb lengths, as the continued skeletal growth in healthy bone fails to be matched in a limb with a metallic implant. Modular and invasive extendible implants allowing growth of the affected limb have been developed since the 1970s in response to this problem. The first-ever growing prosthesis was extended invasively; this device was superseded by a number of other commercial invasive devices. For example, a device developed at UCL in the 1990s involved inserting larger and larger spacers to extend the prosthesis. Whilst these invasive prostheses allow affected limb lengthening, they require repeated surgical procedures in order to induce it. Moreover, despite providing good functional and psychological outcomes, these invasive extendible endoprotheses were associated with a high risk of complications including joint stiffness, nerve injury and aseptic loosening. Their use in children is also a risk factor for infection, with prosthetic lengthening subjecting children to increases in infection rates of up to 5% per procedure, depending on the site of the prosthesis.

Gordon Blunn, Professor of Biomedical Engineering at UCL's Institute of Orthopaedics & Musculoskeletal Science and a member of UCL staff since 1986, aimed to overcome these challenges and produce an endoprosthesis that could be lengthened within the body without the need for extensive surgery. To attain this goal, other UCL staff contributed expertise related to implant engineering design (Dr Meswania, Senior Research Fellow) and the measurement of forces acting on orthopaedic implants in vivo (Dr Steve Taylor, Senior Research Fellow), especially the development of instrumented versions of implants for measuring the forces acting across them in selected subjects. Surgeons at the Royal National Orthopaedic Hospital conducted the medical and surgical work required to put the research findings into practice.

UCL research published in 1998 measured and calculated the forces needed to distract invasive prostheses; those forces were found to be up to 1513 N [1]. This research led UCL staff to develop a prototype prosthesis, the design of which was based on an electric motor along with a super magnet and a high reduction gearbox, all contained within the prosthesis. Research published in 2006 provided a detailed account of the use and potential of the prototype implant in the first seven patients into whom it was implanted, who had a mean age of 12.1 years at the time of surgery [2]. It showed that forces exerted within the drive unit needed to be refined and that, to do so, the device's drive unit needed to be remodelled to provide greater electromagnetic force.

Subsequent research, published in a 2008 paper [3] detailed the refinements made to the prosthesis as it came closer to its current design. Magnetically coupled drive technology was used, including a synchronous motor with a gear-driven telescopic shaft. In this design, the stator was an external device used to extend the prosthesis remotely as the patient grew. This compact external drive produced a focused magnetic flux that did not require cooling and operated on a single-phase power supply. The extending mechanism was able to overcome up to 1300 N force, the force exerted by the soft tissues during the lengthening procedure. The force needed to overcome the

restraint of the soft tissues was measured during extension of the invasive devices in 20 patients.

In the implant the magnet turns a lubricated and sealed gearbox, which has 23 discrete parts and a reduction of 13,000:1. Due to space limitations, the gearbox and magnet used to extend the prosthesis fit within a cylinder measuring 20mm by 25mm. This is the diameter of the resected bone and allows for maximum extension. The gearbox turns a power screw, which extends the body of the implant. To ensure adequate strength, this device was further tested under a cyclic sinusoidal load producing a peak direct compressive load of 2,271 N, a peak medial bending of 56.8 Nm and torsion of 9 Nm. This simulated the loading conditions of an implant in a patient. The test was in Ringers' solution, at body temperature, for 10 million cycles. At every 1 million cycles the prosthesis was extended.

Critical to successful extension of the device *in vivo* – and essential to generate the required force – was the development of a unique gear with a missing tooth. That missing tooth meant that the rotation of the mechanism was slightly askew, enabling more powerful extension for the same amount of reduction.

Further articles building on this work were published between 2009 and 2012 and showed the need for comprehensive pre-clinical testing of the device before its installation, in order to ensure lower failure rates once in patients following trials in larger patient cohorts [4, 5].

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

[1] Meswania JM, Walker PS, Sneath RS, Grimer RJ. In vivo distraction forces in extendible endoprosthetic replacements – a study of 34 patients. Proc Inst Mech Eng H. 1998; 212(3):151-5. http://doi.org/b9jvkt

[2] Gupta A, Meswania J, Pollock R, Cannon SR, Briggs TW, Taylor S, Blunn G. Non-invasive distal femoral expandable endoprosthesis for limb-salvage surgery in paediatric tumours. J Bone Joint Surg Br. 2006 May; 88(5):649-54. http://doi.org/csxfvc

[3] Meswania JM, Taylor SJ, Blunn GW. Design and characterization of a novel permanent magnet synchronous motor used in a growing prosthesis for young patients with bone cancer. Proc Inst Mech Eng H. 2008 Apr; 222(3):393-402. http://doi.org/fbv68r

[4] Sewell MD, Spiegelberg BG, Hanna SA, Aston WJ, Meswania JM, Blunn GW, Henry C, Cannon SR, Briggs TW. Non-invasive extendible endoprostheses for limb reconstruction in skeletally-mature patients. J Bone Joint Surg Br. 2009, Oct; 91(10):1360-5. http://doi.org/cdm28j

[5] Picardo NE, Blunn GW, Shekkeris AS, Meswania J, Aston WJ, Pollock RC, Skinner JA, Cannon SR, Briggs TW. The medium-term results of the Stanmore non-invasive extendible endoprosthesis in the treatment of paediatric bone tumours. J Bone Joint Surg Br. 2012 Mar; 94(3):425-30. http://doi.org/ptx

References [1], [3] and [5] best indicate the quality of research

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

The research presented in section 2 was vital to the development of a licensed implant which now forms part of the Stanmore Juvenile Tumour System – a customised endoprothesis for use in children after massive bone removal. The implant has benefited paediatric patients and healthcare providers around the world, while also having a significant commercial benefit for the licence holder, Stanmore Implants Worldwide (SIW).

Development and commercial adoption of a new technology, with wide-ranging subsequent economic benefits: A full UK and US patent on the technology was granted in 2001 [a]. A licence to manufacture the device was granted to Stanmore Implants by the tech transfer company at UCL in 2007. Stanmore Implants, originally a UCL spinout company, was then sold for £10 million in February 2008 [k]. In 2011, the device received FDA approval for use in the USA [b]. In the USA the market for this product is estimated to be worth over $30 million. The device has now been

used in 15 countries worldwide, including the US. More than 400 devices have been sold around the world since 2008. This has provided Stanmore Implants Ltd., a UCL spin-out company set up to commercialise the research, with an income of over £6 million [d].

A recent US study assessed the cost of a non-invasive lengthening procedure at $267, compared with approximately $8,000 if surgery is required [b]. On average, a patient with an invasive device would have six surgical interventions over the course of their growth period and the calculated saving would be over $46,000. In the UK, the cost to the NHS of performing a single invasive lengthening procedure – including the costs of a two-night stay in hospital and the operation is £3,500. On this basis alone, using the non-invasive implant, which in the UK costs £18,000, produces a saving of around £19,000 per patient. If we factor in freeing up operating facilities and surgeon time then the saving increases even more. In a number of patients who would have had an invasive prosthesis there would been an increased infection risk with a even greater cost implication. Given that about 50 children require this procedure in the UK each year, the use of the non-invasive technology therefore allows UK health service savings of over £10m per annum, the "hidden" savings including the cost of in-patient care, rehabilitation and the inconvenience associated with invasive lengthening for both the patient and their family.

Provision of a superior surgical device: In a study presented to the American Academy of Orthopaedic Surgeons (AAOS) 2012 Annual Meeting, the Stanmore endoprosthesis compared favourably to other mechanical prostheses on the market with a higher MSTS (Musculoskeletal Tumour Society) score than other available devices, with a score of 27.4 (out of 30). The score is an internationally recognised method of evaluating endoprostheses, with the system assigning numerical values (0-5) for each of six categories: function and emotional acceptance, pain, walking and gait quality for lower limbs, functioning in upper limbs, demographic information and patient satisfaction.

Likewise, only three implants failed to extend, out of a series of 44 patients followed up for between 22 to 104 months [output 5, above]. The UCL research team developed a programme of testing for each individual device before they were implanted and there have been just 12 failures of the 400 devices that have been sold since 2008. These implants have been sold over the entire world [d].

Describing the UCL growing prosthesis, the President of the British Orthopaedic Association said: "as an orthopaedic surgeon who specialises in sarcoma treatment and working in a world-renowned centre for bone cancer surgery, this innovation has changed the way I treat these patients." [h] Certainly, the prosthesis developed by Professor Blunn and his team demonstrates reproducibility and reliability superior to other implants extendable *in situ*. It has a much lower failure rate than mechanical lengthening prostheses: in one clinical trial of a rival device, mechanical failure affected 7 of 15 implanted devices [c]. In comparison, in a series reported in 2011 from the Royal National Orthopaedic Hospital in London, of 55 children aged between 5 and 16 who underwent reconstruction with the UCL prosthesis, 10 of the 11 patients (20%) who were skeletally mature at follow-up had equal leg lengths and nine had a full range of movement of the hip and knee. Such is the superiority of the UCL growing prosthesis, in fact, that a number of the devices supplied by Stanmore Implants have been used to revise competitor implants that have a high failure rate.

Improved health, welfare and patient wellbeing: In direct comparison to surgical treatment, the use of the UCL-developed prosthesis reduces, by an average of six per patient, the number of surgical interventions – with all their attendant risks of infection and additional trauma – required. Additionally, after insertion, the prostheses can be extended more gradually than other invasive expandable implants and for this reason nerve palsies, stiffness and pain is reduced [f, g]. The reduced pain and trauma, as well as the reduced risk of infection associated with this new technology is particularly welcome given its use to treat young patients. Each year in the United Kingdom, approximately 50 child sarcomas necessitate limb salvage surgery for children who need an extendable implant able to be lengthened periodically to keep pace with the growth in the opposite limb. The UCL-developed prosthesis delivers a good functional outcome and numerous patient benefits in comparison with both standard treatment and other non-invasive implants. Since

200, it has been the standard UK treatment for children with these bone cancers, although some minimally invasive devices are still used. Using electromagnetic induction, the prosthesis allows for gradual, painless controlled extension that can be undertaken in the clinic, reducing the need for repeated surgeries with the attendant increased risks of infection and the inconvenience and distress of hospitalisation for the patient. Furthermore, after the initial implantation surgery, no anaesthesia is required for the lengthening process. The device also has wider applications than paediatric patients: 1-2% of the implants using it have been to treat skeletally mature patients with shortening after failed joint replacement surgery [e].

The Macmillan Nurse Consultant & Lead Cancer Nurse in charge of the day-to-day care of paediatric patients at the Royal National Orthopaedic Hospital indicates that: "Patients no longer have to fear repeated surgery and more scars from surgery. It increases patient participation and ownership in their physical recovery and rehabilitation. The lengthening procedure is now coordinated and undertaken in a nurse-led clinic. This has resulted in reduced hospital stays, consultant surgeon and anaesthetist time and physiotherapy requirements. The lengthening procedure is completely painless for the patient and many patients have reported this time as being therapeutic as they sit and talk with the nurse. In conclusion, the non-invasive growing implant provides multiple patient benefits and improved patient outcomes whilst also reducing clinical risks and financial costs related to hospitalisation." [i]

The mother of a teenage patient said: "The implant is remarkable. It means that as long as the cancer stays away, she can grow gradually without having regular follow-up surgery… Until five years ago, Sophia would probably have had to have her leg amputated." [j]

5. Sources to corroborate the impact

[a] US Patent, Surgical Distraction Device; publication number US6849076. Publication date; 1 Feb 2005. Inventors: Gordon Blunn, Justin Cobb, Jay Meswania, Hilali Noordeen, John Perry. http://assignments.uspto.gov/assignments/q?db=pat&pat=6849076

[b] For confirmation of FDA approval and cost of the procedure versus surgery, see: http://www.stanmoreimplants.com/press-release-jts-extendible-implant-fda-approval.php

[c] For the failure rate of rival devices, see: Failure Rate Varies With Expandable Femur Prostheses, http://bit.ly/16FEcJY

[d] Correspondence from Stanmore Implants, confirming the number and value of sales since 2008, and the cost of the device. Available on request.

[e] Sewell MD, Spiegelberg BG, Hanna SA, Aston WJ, Meswania JM, Blunn GW, Henry C, Cannon SR, Briggs TW. Non-invasive extendible endoprostheses for limb reconstruction in skeletally-mature patients. J Bone Joint Surg Br. 2009 Oct;91(10):1360-5 http://doi.org/cdm28j

[f] For corroboration of the emotional acceptance of the procedure by children and their parents, see page 251 of Ruggieri P, Mavrogenis AF, Pala E, Romantini M, Manfrini M, Mercuri M. Outcome of expandable prostheses in children. J Pediatr Orthop. 2013 Apr-May;33(3):244-53. http://doi.org/n5r

[g] For corroboration of painless lengthening in children, see page 267 of: Hwang N., Grimer R. J., Carter S. R., Tillman R. M., Abudu A., and Jeys L. M. Early results of a non-invasive extendible prosthesis for limb-salvage surgery in children with bone tumour J Bone Joint Surg Br 2012 94-B:265-269 http://doi.org/n5s

[h] Statement from President of British Orthopaedic Association corroborating the change in clinical practice. Available on request.

[i] Statement from Macmillan Nurse Consultant & Lead Cancer Nurse, Royal National Orthopaedic Hospital corroborating benefits to patients. Available on request.

[j] For the quote from a patient's mother, see "The £20,000 bionic bone that will let Sophia's leg grow", Daily Mail, 7 June 2010: http://dailym.ai/1avGGyJ

[k] "UCL Business concludes £10 million sale of Stanmore Implants Worldwide", February 2008 http://www.ucl.ac.uk/media/library/Stanmore