Institution: University of Bath

Unit of Assessment: 9: Physics

Title of case study: Medical microwave treatments for menorrhagia and cancer

1. Summary of the impact

Microsulis Medical Ltd was founded in 1997 by the University of Bath to commercialise Professor Nigel Cronin's invention of a device for microwave endometrial ablation (MEA) for use in treating excessive menstrual bleeding (menorrhagia). This minimally invasive therapy has a success rate exceeding 80% and remarkably short treatment and recuperation times. It has been used to treat over 20,000 patients worldwide since 2008. In Feb 2011 Microsulis sold the rights to its MEA device for $3m to a US company in order to concentrate on another application of Cronin's microwave technology, namely microwave tissue ablation (MTA) for use in treating cancer. Microsulis MTA systems are in place in over 100 hospitals worldwide and have been used in over 5000 treatments of tumours of the liver, lung, kidney and bone, including otherwise inoperable cases. In Feb 2013, the company was bought by AngioDynamics (a major international provider of healthcare devices) for $15m. This acquisition is expected to provide a major boost to both the reach of the life-saving MTA technology and global sales. Currently Microsulis employ around 20 people at their base near Portsmouth, producing and developing their MTA devices. Their sales revenue since 2008 totals over £11m.

2. Underpinning research

The fundamental idea of the underlying research is to destroy diseased or unwanted tissue by locally heating it using microwaves. There are two key aspects of the methodology. The first is the design of the microwave devices. The central challenge here is to deliver the microwave power to the tip of the probe, from where it radiates into the surrounding tissue, without the probe itself becoming hot. For example, with the percutaneous (through-the-skin) microwave tissue ablation (pMTA) device, 180 W of microwave power at 2.45 GHz is delivered to the tip of a needle-like probe with a diameter of 1.8 mm. This produces a highly controlled heating over a large enough volume to destroy a tumour. To keep the probe cool, water is circulated at high speeds under 4 bar of pressure. Cronin (Professor, Department of Physics, 1982-2011), and his Medical Physics group (including PhD students Clegg, Hardie, Feldberg) have been at the heart of this development since its initiation in 1994. They have designed, built and patented the microwave probes [1].

The second aspect is to understand the effects of microwave irradiation on various tissues, for example, investigating how the heating effects depend on frequency and the ways in which heat is dissipated via blood flow, etc. Experimental [2,3] and modelling studies [4] of these aspects led to clinical trials [2,5,6]. Cronin and his group have also been heavily involved in these experimental and clinical studies. Without their work, the MEA, MTA and pMTA devices developed and marketed by Microsulis during the REF period would not exist.

The University of Bath has actively supported Microsulis over a period of 13 years, initially providing the company with their own laboratory space on campus and by granting Cronin substantial periods of secondment to the company to further the collaboration. Though recently retired from the University (2011), Cronin remains their Chief Scientist. His research has also been supported by substantial contracts with Microsulis [7], and joint grants between Microsulis and the University, funded by the Department of Health/EPSRC Health Technology Devices Programme [8].

3. References to the research

[1]. N. Cronin, *Microwave applicator*, patent num. WO 1999056642 A1, filed May 1999.

[2](*) AD Strickland, PJ Clegg, NJ Cronin, B Swift, M Festing, KP West, GSM Robertson and DM Lloyd, *Experimental study of large-volume microwave ablation in the liver*, British Journal of Surgery, **89**, 1003-1007 (2002). doi:10.1046/j.1365-2168.2002.02155.x

[3](*) AU Hines-Peralta, N Pirani, P Clegg, N Cronin, TP Ryan, ZJ Liu and SN Goldberg, *Microwave ablation: Results with a 2.45 GHz applicator in ex vivo bovine and in vivo porcine liver*, Radiology, **239**, 94-102 (2006). doi:10.1148/radiol.2383050262

[4](*) D Hardie, AJ Sangster and NJ Cronin, *Coupled field analysis of heat flow in the near field of a microwave applicator for tumour ablation*, Electromagnetic Biology and Medicine, **25**, 29-43 (2006). doi:10.1080/15368370600572953

[5]. DA Hodgson, IB Feldberg, N Sharp, N Cronin, M Evans and L Hirschowitz, *Microwave endometrial ablation: development, clinical trials and outcomes at three years,* British Journal of Obstetrics and Gynaecology, **106**, 684-694 (1999). DOI: 10.1111/j.1471-0528.1999.tb08368.x

[6]. AD. Strickland, PJ. Clegg, NJ. Cronin, Mosheir Elabassy and David M. Lloyd *Rapid Microwave Ablation of large hepatocellular carcinoma in a high-risk patient*. Asian J Surg. **28**, 151 (2005): doi:10.1016/S1015-9584(09)60282-7

[7]. *Microwave Ablation of Bone Tumours*, Microsulis Medical Ltd, £871,896. (1/08/2007 - 31/07/2010).

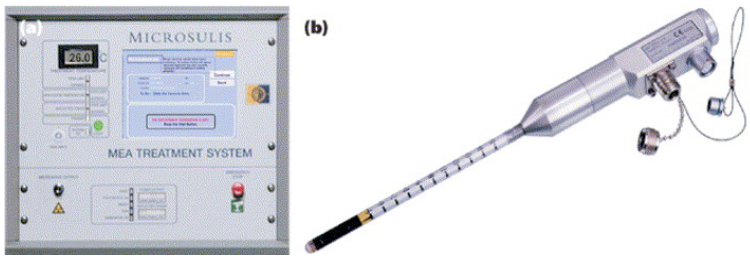
[8]. *Microwave Coagulation Therapy for Liver Cancer*, EPSRC Grant GR/R27853 £161,317 (01/09/2001-31/08/2004); *Percutaneous Microwave Ablation of Bone Tumours*, Department of Health, £177,197 (01/11/2009-31/10/2012).

(*) Best indicators of research quality

4. Details of the impact

Microwave Endometrial Ablation

In 1997, The University of Bath founded Microsulis Medical Ltd to commercialise Professor Nigel Cronin's invention of a device for microwave endometrial ablation (MEA). Endometrial ablation is a treatment for severe cases of menorrhagia (heavy menstrual bleeding) as an alternative to hysterectomy. Following clinical trials [5], Microsulis' MEA device was approved by the National Institute for Clinical Excellence (NICE) [9], the U.S. Food and Drug Administration (FDA) [9] and gained the European kite mark. The device underwent further development over the past 15 years and since 2008 has been widely used to treat menorrhagia.



Microsulis MEA system, showing the microwave probe (right)

In summary the impact from the MEA system is:

- There are over 400 systems in hospitals worldwide and about 20,000 patients have been treated during the REF period in the UK, USA, Canada, Australia, South Africa and New Zealand [10].
- The treatment is fast and safe and can treat all areas of the uterus [9,11]. It removes the danger of death (0.1%) [12] associated with hysterectomy.
- A success rate of over 80% in dramatically reducing or stopping menstrual bleeding [9,11,13].

- Treatment only takes three minutes and because it is minimally invasive, patients usually go home the same day [9]. This compares with the 3-6 days hospital stay associated with a typical hysterectomy, followed by recuperation time of anything up to two months [11,12].
- Accordingly there are huge savings in time for doctors and patients alike. Additionally, because the uterus remains intact, there are also major psychological advantages for the patient. This all translates into massive cost savings for health care providers. [9]

In February 2011, Microsulis sold the rights to its MEA device to Novasure of Massachusetts for $3M [14]. The sale provided funding for Microsulis to develop ground-breaking devices for microwave tissue ablation (MTA) and percutaneous microwave tissue ablation (pMTA) based on Cronin's research.

Microwave Tissue Ablation

The idea behind MTA is to use microwaves to produce a highly controlled, localised and rapid heating that destroys cancerous tumours. Initial development work concentrated on liver tumours [3-6]. Secondary liver tumours are common in cases of bowel cancer and, if they are controlled, there is a good chance of preventing further spread of the cancer. An MTA device for use in open surgery has been developed and following successful clinical trials [3,6] obtained CE mark and United States FDA approval [15]. Since its launch in 2008, over 100 MTA systems have been installed in hospitals around the world and nearly 700 treatments have been completed, with high success rates [10,16].

A needle-like (percutaneous) MTA device has also been developed and gained European CE mark, ETL safety accreditation and United States FDA approval [15] in 2010. The device has the great advantage of being applied through the skin, rather than requiring open surgery. This has a number of advantages for patients, doctors and hospitals alike:

- It gives surgeons the option to treat *previously inoperable* patients with tumours in inaccessible locations [6,17].
- A recent international review of clinical effectiveness [16] found that of 250 ablated tumours in 135 patients, local recurrence was observed at only 5% of ablated sites
- The treatment costs approximately £2,500 per session and it can be repeated. Surgery costs up to twice this amount and there is less chance it can be repeated [18].
- The procedure is less invasive than open surgery, meaning less time in theatre, fewer medical complications and shorter recuperation times [19].
- Increased patient throughput and reduced operating and patient stay costs and staff costs, leading to higher revenues in private healthcare settings.

The Microsulis pTMA device

Initial use of the pTMA device has been for liver tumours [16], but lung [18], kidney, pancreas and bone treatments are being performed [10]. Although only released in late 2010, pMTA is already in use at over 80 surgical and radiological centres [10]. Over 5000 patients have been treated with MTA/pTMA since 2008 and the number of new treatments is more than doubling year on year [10]. Whilst there are many competing companies and devices in the oncology arena, Microsulis are well ahead of their competitors in terms of device performance and ease of use. Commenting on the Microsulis system, the consultant radiologist at Oxford University Hospitals Trust states "This is

a fantastic development. It will kill small tumours in minutes and we are examining how it can improve survival by reducing cancer mass in larger tumours….. We believe it could save - thousands of lives a year." [18]

Microsulis employ around 20 people at their Portsmouth base, from where they produce and sell their third-generation MTA and pMTA devices [10] (jobs in the medical instruments sector carry a high output multiplier of ≈2.5 [20]). They have recently invested £250k in a new in-house production and packaging facility, increasing its manufacturing capacity. Microsulis's sales revenue in the REF period totals over £11m [10]. The company was named 'Innovator of the Year' at The News Business Excellence Awards in 2012 and also claimed the runner up prize in the 'Exporter of the Year' category [14].

In February 2013, Microsulis was acquired by AngioDynamics of Albany (New York) - a leading international provider of medical devices. The sale for $15m [21] is expected to provide new impetus for global sales of the pMTA device (which is being marketed as "Acculis MTA"), and further improve patient access to this lifesaving technology.

In summary, Professor Cronin's invention of new technologies for medical treatments has revolutionised healthcare outcomes for tens of thousands of patients and created substantial economic impact both directly via the turnover of Microsulis Ltd and indirectly via savings to healthcare providers.

5. Sources to corroborate the impact

[9] FDA: http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/DeviceApprovalsandClearances/Recently-ApprovedDevices/ucm082313.htm; NICE: http://guidance.nice.org.uk/TA78 ; (accessed 16/4/13)

[10] Data supplied by Chief Executive Officer, Microsulis Medical Ltd. http://www.microsulis.com. Note that following their recent acquisition by Angiodynamics the Microsulis website may be subject to change.

[11] Microwave Endometrial ablation: http://publications.nice.org.uk/microwave-endometrial-ablation-ipg7/the-procedure - indications (accessed 22/4/13)

[12] Encyclopedia of Surgery http://www.surgeryencyclopedia.com/Fi-La/Hysterectomy.html (accessed 16/4/13).

[13] J.M. Cooper, et al, J. Am. Assoc. Gynecol Laparosc 11(3) 394 (2004).

[14] http://www.businesswire.com/news/home/20110204005902/en/Microsulis-sells-Microwave-Endometrial-Ablation-MEA-Hologic

[15] For FDA approval see: http://www.fda.gov/ (accessed 16/4/2013)..

[16] D.M. Lloyd *et al*, HPB **13** 579 (2011). doi: 10.1111/j.1477-2574.2011.00338.x.

[17] N. Bhardwaj, A.D. Strickland, F. Ahmad, M. El-Abassy, B. Morgan, G.S.M. Robertson, D.M. Lloyd, European Journal of Surgical Oncology **36**, 264-268 (2010) http://dx.doi.org/10.1016/j.ejso.2009.10.006

[18] Consultant radiologist quoted in Sunday Express newspaper article: "*It's fantastic. Docs cooked my Cancer*" , Nov 27, 2011.http://www.express.co.uk/news/uk/286269/It-s-fantastic-Docs-cooked-my-cancer (accessed 16/4/13**)**

[19] C. Jones, S.A. Badger, G. Ellis, The Surgeon, **9**, 33 (2011).

[20] *The Economic Impact of UK higher education institutions*, report by Universities UK. (2007). http://www.universitiesuk.ac.uk/highereducation/Pages/EconomicImpact3.aspx (accessed 15/4/2013)

[21] http://www.bizjournals.com/albany/news/2013/02/01/angiodynamics-drops-15m-on-another.html (accessed 22/7/13).