

<b>Institution:</b> Imperial College London
<b>Unit of Assessment:</b> 01 Clinical Medicine
<b>Title of case study:</b> Development of Novel Technologies for Radiofrequency Assisted Surgical Resection
<p><b>1. Summary of the impact</b> (indicative maximum 100 words)</p> <p>Based on clinical studies at Imperial College that radiofrequency energy can seal blood vessels, EMcision Limited was formed. The Company specialises in the research, development and marketing of medical and surgical devices that use RF energy to treat/palliate cancers in organs and tissues. The first product from the Company, the Habib™ 4X, has revolutionised the technique of liver surgery and has generated more than \$48 million in sales worldwide. The second most successful product, the Habib™ EndoHPB, generated \$1 million in revenue in 2012.</p>
<p><b>2. Underpinning research</b> (indicative maximum 500 words)</p> <p>Key Imperial College London researchers:  Professor Nagy Habib, Professor of Hepatobiliary Surgery (1991-present)  Mr Long Jiao, Reader in Surgery, Division of Surgery (1994-present)  Dr Robert Dickinson, Senior Lecturer, Biomedical Engineering (1992-present)  Joanna Nicholls, Research Manager, Division of Surgery (1994-present)</p> <p>Surgical resection is the gold standard for treatment of primary and secondary liver tumours. However, due to the vascular nature of the liver it is a complex procedure with a high risk of complications including severe blood loss, which has been shown to be an important factor correlating with morbidity and mortality in liver surgery. Frequently the site of the tumour renders surgical removal impossible without causing additional postoperative risk of deranged liver function due to the removal of large portions of the liver. In 1999, Professor Habib and Imperial colleagues were one of the first to report the use of RF ablation to treat unresectable liver tumours (1). When applied to tissue, RF energy causes ionic agitation leading to cellular destruction from dehydration of the cell. The “Eureka” moment occurred in 2002, when Professor Habib observed that RF energy could ablate not only tumour tissue, but could seal small and large blood vessels in the liver and that a complete blood-less resection could be achieved provided the scalpel severed only ablated tissue (2). However, the only device on the market used monopolar RF energy rendering the technique slow and laborious, with the added disadvantages of the risk of skin burns at the site of the patient contact pad and long anaesthetic times. Professor Habib designed, tested and manufactured a new bipolar, hand held, disposable RF device, the Habib™ 4X, via EMcision Limited to overcome these disadvantages. The device has carefully positioned probes which when connected to a RF generator deliver a precise amount of heat. This RF technique of liver resection was subsequently used to resect non-anatomical tumours in the liver, also tumours in the gall bladder, spleen and at laparoscopic liver resection with good results.</p> <p>EMcision was formed in 1999 with seed fund investment of £45K from the commercial arm of Imperial College London, Imperial Innovations, which funded patent filing and initial <i>in vitro</i> research and development. Additional funding from private investors of £1.3M was raised to support <i>in vivo</i> work and manufacturing costs. The work was performed both at Imperial College London (prototyping, breadboard, design, bench testing, etc) and out-sourced to niche UK suppliers for electrical safety testing, electromagnetic testing, and to manufacturers of the various parts. The first Habib™ 4X devices were manufactured in the UK at Wesley Coe, Cambridge, following grant of CE Mark in 2004.</p> <p>In 2003, an application was made to the BUPA Foundation for a grant to fund a small exploratory clinical study at the Hammersmith Hospital to assess the performance of the Habib 4X device. Of the 33 patients recruited only one patient required blood transfusion and none were admitted to ICU post operatively. Our group reported significantly lower blood transfusion rate (26% vs 53%,</p>

P=0.04); significant reduction in both ICU admission (6% vs 92%,  $P<0.0001$ ) and post op stay (10 vs 17 days,  $P<0.004$ ) with a substantial saving of £5185 per patient when comparing RF assisted liver surgery to the conventional technique (3). Professor Habib published a series of 604 consecutive patients who underwent liver resections with the RF assisted technique (4). The data was compared with published data of large series from 8 renowned liver centres where conventional surgical techniques were used. The Habib series was shown to have one of the lowest rates of blood transfusion (12.6% vs 23 – 49%), smallest amount of blood loss (median 155 mL vs 600 – 750 mL), and a 30-day mortality rate of 1.8% vs 3 - 5% (5).

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

- (1) Jiao, L.R., Hansen, P.D., Havlik, R., Mitry, R.R., Pignatelli, M., Habib, N. (1999). Clinical short-term results of radiofrequency ablation in primary and secondary liver tumors. *American Journal of Surgery*, 177, 303-306. [DOI](#). Times cited: 182 (as at 8<sup>th</sup> November 2013 on ISI Web of Science). Journal Impact Factor: 2.51
- (2) Weber, J-C., Navarra, G., Jiao, L.R., Nicholls, J., Jensen, S., Habib, N.A. (2002). New technique for liver resection using heat coagulative necrosis. *Annals of Surgery*, 236, 560-563. [DOI](#). Times cited: 144 (as at 8<sup>th</sup> November 2013 on ISI Web of Science). Journal Impact Factor: 6.32
- (3) Ayav, A., Navarra, G., Basaglia, E., Tierris, J., Healey, A., Spalding, D., Canelo, R., Habib, N.A., Jiao, L.R. (2007). [Results of major hepatectomy without vascular clamping using radiofrequency-assisted technique compared with total vascular exclusion](#). *Hepatogastroenterology*, 54, 806-809. Times cited: 2 (as at 8<sup>th</sup> November 2013 on ISI Web of Science). Journal Impact Factor: 0.77
- (4) Pai, M., Frampton, A.E., Mikhail, S., Resende, V., Kornasiewicz, O., Spalding, D.R., Jiao, L.R., Habib, N.A. (2012). Radiofrequency assisted liver resection: Analysis of 604 consecutive cases. *European Journal of Surgical Oncology*, 38:274-280. [DOI](#). Times cited: 4 (as at 8<sup>th</sup> November 2013 on ISI Web of Science). Journal Impact Factor: 2.61
- (5) Li, M., Zhang, W., Li, Y., Li, P., Li, J., Gong, J., Chen, Y. (2013). Radiofrequency-assisted versus clamp-crushing parenchyma transection in cirrhotic patients with hepatocellular carcinoma: A randomized clinical trial. *Digestive Diseases and Sciences*; 58:835-840. [DOI](#). Times cited: 1 (as at 8<sup>th</sup> November 2013 on ISI Web of Science). Journal Impact Factor: 2.26

#### Key funding:

- BUPA Foundation grant (2003-2005, £161,904) Principal Investigator, N. Habib. Radiofrequency bipolar bloodless liver resection device

#### Patents:

- <http://www.faqs.org/patents/assignee/emcision-limited/>
- <http://www.patentbuddy.com/Company/Profile/EMCISION-LIMITED/55773>

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

Impacts include: commercial, practitioners, health and welfare

Main beneficiaries include: patients, practitioners, Industry

Following European CE and US FDA approvals of Habib™ 4X, an exclusive licence was negotiated with Rita Medical Systems, USA, now known as AngioDynamics Inc, USA to market the device worldwide. The total number of units sold (2005 -Q2 2013) is 23,723 accruing \$48 million in revenues for AngioDynamics. Since the US launch of the Habib 4X it has captured 85% of the US hepatic RF resection market and has captured 30% of the total US hepatic resection market. Similarly, a smaller device, the Habib™ 2X, introduced in 2007, has captured 20% of the partial kidney resection market in the USA. More recently, the Habib™ 4X Laparoscopic device,

developed by the Imperial team and marketed by AngioDynamics, is being sold to urology surgeons performing keyhole kidney surgery.

The Habib 4X overcomes the well-established difficulties of significant blood loss encountered when removing tumours from organs with a propensity to bleed profusely. Initially, the device was developed to improve outcomes in liver surgery, but the device has been successfully deployed in other vascular tissues such as kidney, spleen, pancreas, uterus and lung.

An independent published randomised clinical trial comparing radiofrequency assisted parenchymal transection with the traditional clamp-crushing technique showed a reduction in blood loss and lower morbidity using the radiofrequency assisted resection [1]). Other publications have also shown similar reduction in blood loss. Two recent independently UK published data leads us to believe that the use of the Habib 4X improves outcomes: (i) UK Cancer Information Service 2011 recorded Imperial as having the best one and two year relative survival of liver patients of the London Cancer Networks (Figure 1); (ii) Dr Foster Intelligence Data showed that Imperial has the lowest in-hospital 30 day mortality risk for patients undergoing liver resection in England and Wales which is probably due to the use of the RF assisted technique (Figure 2). These results led the premier liver surgery unit in the UK to now use exclusively the Habib 4X for liver resection surgeries.

**Figure 1: Relative survival of liver patients (ICD-10 C22) by cancer network**

	One year relative survival 2006-2008 FU to end of 2009		Two year relative survival 2005- 2007 FU to end of 2009	
	Persons		Persons	
Cancer Networks	Number	%	Number	%
North West London CN	366	36.89	373	26.06
North London CN	328	33.56	338	24.21
North East London CN	364	25.04	338	15.59
South East London CN	325	29.97	324	19.3
South West London CN	304	27.27	276	15.94

(Source: UK Cancer Information Service; February 2011)

[image removed for publication]

**Figure 2:** [text removed for publication]

EMcision receives a royalty stream from the Habib™ 4X and Habib™ 2X revenues linked to which is all ploughed back into R&D resulting in a further 8 radiofrequency devices being developed, approved by regulatory bodies, manufactured and sold by the same team of researchers from Imperial College London, using UK niche contractors.

Since 2008, the following devices have been developed, CE approved (FDA 510[k] approval has also been obtained for the Habib™ EndoHPB [2009]) and generated revenue [2, 3]:

- Habib™ EndoHPB (for palliation of biliary and pancreatic tumours in the common bile duct and liver): CE mark approval in 2009; income to date £998,807
- Habib™ Percutaneous HPB (a percutaneous RF catheter for rapid ablation of solid tumours): CE mark approval in 2009; income to date £177,747
- Habib™ VesOpen (for vascular remodelling and opening of vessel that have become stenosed or occluded): CE mark approval 2009; income to date £5,5587
- Habib™ RF Duo (to cauterise and coagulate tissue in the liver and pancreas): CE mark approval 2013; income to date £114,918

In light of the success of EMcision, PROFIT magazine ranked the company as 14<sup>th</sup> on its 'Hot 50'

definitive ranking of Canada's Top New Growth Companies for 2013 (two-year revenue growth, 1067%) [4].

The Habib™ EndoHPB has also recently been reviewed at the NICE Interventional Procedures Committee [5]. NICE will report following publication of randomised clinical trial outcomes. A recent retrospective study reporting "impressive" stent patency and median survival outcomes in 58 patients with malignant biliary obstruction following RF application with the Habib™ EndoHPB.

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

- [1] Dolak, W., Schreiber, F., Schwaighofer, H., Gschwantler, M., Plieschnegger, W., Ziachehabi, A., Mayer, A., Krame, L., Kopecky, A., Scrutka-Kolbl, C., Wolkersdorfer, G., Madl, C., Berr, F., Trauner, M., Puspok, A. (2013). Endoscopic radiofrequency ablation for malignant biliary obstruction: a nationwide retrospective study of 84 consecutive applications. *Surgical Endoscopy*, 44, 1012-1020. [DOI](#)
- [2] Corroboration of revenue generated can be provided by the EMcision Sales Director.
- [3] [FDA and CE marked products](#) ([archived](#) on 8<sup>th</sup> November 2013)
- [4] PROFIT Magazine Top 50 <http://www.profitguide.com/microsite/profithot50/2013> ([archived](#) on 8th November 2013)
- [5] Habib™ EndoHPB discussed by NICE Interventional Procedures Committee on 11<sup>th</sup> April 2013: <http://www.nice.org.uk/media/CF2/99/IPACFinalAprilAgenda.pdf> ([archived](#) on 8th November 2013)