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in BioInnovation, Dublin City University.

Department of

BioMedical Diagnostics Unit

Dublin City University

Research Supervisor

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“FROM UNMET CLINICAL NEED TO COMMERCIALISATION -THE BIOINNOVATE IRELAND
PROCESS”

Honesty Declaration

I hereby certify that this material, which I now submit for assessment on the programme of study leading to the award of Master of Science in BioInnovation, is entirely my own work, that I have exercised reasonable care to ensure that the work is original, and does not to the best of my knowledge breach any law of copyright, and has not been taken from the work of others save and to the extent that such work has been cited and acknowledged within the text of my work.

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Abstract

BioInnovate Ireland is a specialist training program in medical device innovation and product design. It is modelled on the Biodesign Fellowship programme which has been offered at Stanford University, Palo Alto, California since 2001.

The objective of BioInnovate Ireland is the training of students in a systematic approach to needs finding as well as invention and implementation of new biomedical technologies. This thesis explores the methods and processes utilised by the BioInnovate Ireland Dublin team in the first year of the programme as they identified a number of unmet clinical needs and developed concepts for these needs. One project which I personally championed and which was brought forward to the concept development stage is discussed in detail. The project activity decision with regard to the viability of bringing the project forward to business plan is analysed and the lessons which can be learned from the process are also discussed.

This thesis offers a personal perspective and reflection on the BioInnovate process and the potential that it holds for the innovation process within the Irish medical device industry.

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Chapter 1

Introduction

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1.1 Introduction

The aim of this chapter is to provide a background to the BioInnovate Ireland Fellowship and an outline of the various stages it involves.

1.2 The Medical Device Sector in Ireland

The medical device sector is of great importance to the Irish economy. Successive Irish Governments have attempted to promote Ireland as a location for foreign direct investment (FDI). This has included a heavy focus on the medical device sector.

IDA Ireland has made Ireland the location of choice for international life science and healthcare companies. Attracting FDI and the establishment of R&D facilities has required the provision of manufacturing and operations facilities, retention of attractive taxation rates and provision of a highly educated and skilled workforce.

Apart from the attraction of multi-national medical device companies, there have also been a number of successes in the generation of indigenous spin-out and start-up companies operating within the Irish medical device sector. In this way, Ireland has developed a strong reputation as a leading medical device industrial cluster.

Examples of this include the fact that:

- The global leader in the drug – eluting coronary stent market was researched, developed and commercialised in Ireland. (Irish Venture Capital Association).
- 30 Million People (25% of world’s population) who have diabetes rely on an injectable device made in Ireland. (Irish Medical Devices Association Yearbook - Driving Innovation through Collaboration – 2011).

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- Ireland exported medical technologies worth 7.2 billion in 2010 – up 14% on 2008. (IMDA Website).
- Ireland is the second largest exporter of medical products in Europe. (Enterprise Europe Network – Medical Devices Sector in Ireland 2010)

1.3 The decision to establish the BioInnovate Ireland Programme

Forfas is Ireland’s policy advisory board for enterprise and science. In a 2010 report, it underlined the belief that research development and innovation initiatives will be key drivers for future growth of the Irish economy.

Another key impetus for BioInnovate was the report of the Innovation Taskforce which was also published in 2010. The report outlined the importance that innovation holds for Ireland. The stated aim of the taskforce was to ensure that by 2020, Ireland would become home for a number of world-leading innovation-intensive companies and that these companies would be either Irish-owned or be headquartered here. This was thought to be possible through the creation of an innovation eco-system in which a number of key elements interacted and provided support for each other. One of the underlying principles of this idea was that the state should actively accelerate flagship projects and prioritise the provision of excellent infrastructure to facilitate innovation.

As a direct result of the above reports, five higher education institutes (National University of Ireland Galway, University of Limerick, Dublin City University, University College Cork and the Royal College of Surgeons in Ireland) took the novel step of combining their collective resources and expertise by agreeing to develop a medical device innovation programme (BioInnovate Ireland). This venture was to be supported by a number of

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stakeholders including Enterprise Ireland (EI) and the Irish Medical Device Association (IMDA).

1.4 A brief summary of the BioInnovate Process

As previously stated, BioInnovate Ireland is a specialist training program in medical device innovation and product design. It is modelled on the Biodesign Fellowship program which has been offered at Stanford University, Palo Alto, California since 2001.

Each year, two multi-disciplinary Fellowship teams are recruited. Each team comprises four Fellows from either a medical, engineering, business, legal or technical graduate background. Over the course of a 10 month period, the two teams carry out their work in a number of distinct phases.

- Identification of unmet clinical needs;
- Inventing solutions to satisfy unmet needs; and
- Implementing or commercialising some of the solutions identified.

The 2011/2012 Dublin Fellows and their respective backgrounds were as follows

Dublin BioInnovate Team

Dr. Liam Mullins BE PHD

Liam graduated with a degree in Mechanical Engineering from NUI, Galway in 2002. He worked as a manufacturing engineer before starting a PhD in orthopaedic biomechanics at NUI, Galway in 2003. In 2005 he attended UC, Berkeley as a visiting scholar where he

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continued his research. Throughout his PhD Liam conducted analysis and testing of medical devices and materials for industry. Liam published four articles from his PhD research and has continued research into the behaviour of Nitinol devices.

Upon completion of his PhD research in 2007, Liam joined start-up Veryan Medical in Galway where he played a central part in the design of technologies to treat vascular disease. He has held roles with responsibilities in device design, animal trials, clinical trial design and biostatistics, finite element analysis, fatigue, manufacturing, patenting and market analysis. Liam is an inventor on four filed patents.

He has also consulted for a number of medical device companies and clinicians on the design and analysis of medical devices.

Dr. James McGarry BE, MB BCh BAO, MRCS, PhD

James was interested in the application of engineering to medicine that began as an engineering student with an award-winning thesis on the biomechanics of cardiovascular stents. He subsequently undertook a PhD at the Trinity Centre for BioEngineering with research periods in nanoscience, cell biology and bioengineering laboratories. Convinced that dual training in engineering and medicine would yield a unique and valuable platform for innovation in healthcare, he chose to study medicine following completion of his PhD.

James gained clinical experience in surgical posts, and was awarded the Membership of the Royal College of Surgeons examination. As a doctor and bioengineer, the BioInnovate Ireland Fellowship was a unique opportunity to utilise his prior training, but also yielded a

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new range of skills in the process of medical device innovation that were invaluable to his long-term goals.

Ms. Vicky McGrath BE MSc MBA

Vicky McGrath is a seasoned business professional with 15 years' experience in the medical device and diagnostics industry. She was co-founder and head of business development at Argutus Medical where she was responsible for fund raising, strategy, planning, development and commercialisation efforts. Prior to Argutus, Vicky worked in operational and consulting roles at Abbott Labs, Biotrin International and Sabratek Corporation. Vicky holds a BE in Mechanical Engineering from UCD, an MSc in Biomedical Engineering from Boston University and an MBA from the Smurfit Business School.

Mr. Kevin Moore B.Comm LL.B

After completing a B. Comm and then an LL. B. degree at NUI Galway, I spent seven years working with MG. Ryan and Co. Solicitors. During that time I advised a large number of firms and drafted and negotiated many commercial agreements on behalf of corporate clients including start -up companies. I have practical experience of the most critical issues facing start-up companies particularly in the healthcare and life-science sectors including reimbursement, regulatory and intellectual property matters. During my career, I have regularly advised in the areas of incorporation, corporate structure, company secretarial matters, intellectual property rights, corporate governance and private and venture capital funding. I regularly advised on a number of commercial agreements. I have also completed the Professional Practice Course at the Law Society of Ireland.

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Personal Decision to apply for the Fellowship: The opportunity to have a positive impact on patient care was a particularly compelling reason to apply for the Fellowship. However, the Fellowship also offered me the opportunity to actively participate in the innovation process and to develop my interest in innovation, technology transfer, entrepreneurship and commercialisation. It therefore meant that I would have a unique understanding of the medical device industry as a whole and would be better placed to form part of the ecosystem and support network envisaged for the medical device sector in Ireland.

1.5 The Phases of BioInnovate

1.5.1 Identification of unmet clinical needs

Fellows are afforded the opportunity to make observations in a clinical setting for a period of eight weeks. This process involves observing patients and healthcare professionals in a range of clinical settings including: specialist diagnostic clinics, surgical and interventional procedures, post-operative care and rehabilitation. Challenges faced within the clinical setting are documented. In this way, problem statements are defined and subsequently refined into needs statements which should adequately reflect unmet clinical needs.

Needs are then filtered according to acceptance criteria which are designed by the Fellows. Typically, the top needs are validated through ongoing consultation with practitioners and relevant professionals.

1.5.2 Inventing Solutions to satisfy unmet clinical needs

A number of needs are then selected by the Fellow's for this phase which involves 'Ideation' or the process of creating new concepts or ideas in order to provide solutions to one or more

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well-defined unmet clinical needs. A key aspect of this phase is brainstorming. The ideation is carried out utilising group creativity and the diverse backgrounds and experiences of the Fellows are utilised to propose solutions overcome the challenges faced.

1.5.3 Implementing or commercialising some of the solutions identified.

This is perhaps the most complex of the stages in the process and it involves taking steps to bring a new product to market. Valid needs are subjected to scrutiny in a number of areas to ensure that the solution is capable of being implemented by being brought to market.

Among other things, this involves careful consideration of

- Intellectual property landscape and strategy;
- Reimbursement situation;
- Regulatory affairs; and
- Basic Business Strategy - marketing, sales and distribution.

The Fellows bring concepts through to business planning, pitching to venture capitalists, early stage development planning and in some cases commercialisation.

1.6 Conclusion - Can BioInnovate assist in fulfilling the vision of the Innovation Taskforce?

As previously outlined, the innovation taskforce outlined a number of key steps which needed to be taken in order to fulfill its vision. The BioInnovate Ireland programme addresses a number of these directly.

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1. Supporting Innovators and Entrepreneurs – BioInnovate recruits a multi-disciplinary team of entrepreneurs who are funded and assisted for 10 months in their attempts to identify unmet clinical needs and propose solutions which are capable of commercialisation. These individuals are generally recruited from industry and take time out of their chosen profession. Without the support provided by BioInnovate most of the Fellows would not have the opportunity to explore their talent for innovation.
2. Ensuring that our education system promotes education and innovation – A key part of the programme is a five-week ‘bootcamp’ in which the Fellows are given an insight into all of the important aspects of medtech innovation e.g. reimbursement, regulatory, intellectual property landscapes etc. In addition, a BioInnovation class is held each week. This is attended by the Fellows as well as a post-graduate class who are mentored by the Fellows. Both the Fellows and the post-graduate apply this knowledge in developing novel medical devices. This method of learning marks a new departure for the education system.
3. Strengthening linkages between education and industry –Many of the sponsors and contributors to the programme are successful medical device companies such as Creganna -Tactx, Medtronic, Boston Scientific. These companies have a vested interest in the technologies which are produced as a result of BioInnovate. However, the benefits of collaboration go far beyond this. Sponsors also benefitted from learning about the innovation process adopted by the Fellows. In turn, the Fellows also benefitted from the advice, direction and real-world experience of some of the most established medical device companies in the world.

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4. Ensuring we have a world-class infrastructure - Perhaps the most important aspect of the programme is its ability to directly contribute to the med-tech infrastructure. On a number of occasions during the Fellowship, presentations were made which were attended by researchers, clinicians, medical device companies, serial entrepreneurs, venture capitalists, reimbursements specialists, regulatory experts, legal advisors and intellectual property specialists. All of these supports are vital for a successful medical device eco-system as envisaged by the Innovation Taskforce. The importance of the fact that they are all available and are keenly aware of the role that they play cannot be over-stated if Ireland is to remain attractive as a medical device hub and is attractive for foreign direct investment. In addition, the programme produces Fellows educated in medical device innovation who will commercialise technologies or who will work directly within the industry.

The following chapter documents the path taken by the Dublin BioInnovate team as they began the process of the identification of unmet clinical needs.

Chapter 2

Needs Identification

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2.1 Introduction

As documented in Chapter 1, the team were given generous access to some of Ireland's leading hospitals. However, the decision of how best to use this opportunity was a matter for the Fellows. Thus, the process utilised would be critical to the outcome of the project.

2.2 Mission Statement

Prior to commencing clinical immersion, the Dublin BioInnovate team prepared the following Mission statement.

‘To develop innovations that have a positive impact on patient care while reducing system cost.’

It was important at the outset to identify what the team wished to achieve within the year and to reduce this to writing. In this way, when the Fellows began the BioInnovate process they would be under no illusions what they should be looking to achieve during clinical immersion and beyond.

2.3 Locations for Clinical Immersion

Needs identification took place on site in a number of hospitals. The teams were permitted to observe procedures and meet with clinicians, nurses, radiographers, staff and patients when required. Access to daily rounds and staff meetings was also permitted. However, the primary focus was on documenting observations which, in the eyes of the Fellows, appeared to present a problem for physicians. In effect, what is required by this stage is an objective perspective on work practices, procedures, processes and treatments which are not often subject to such scrutiny. It is important that validation takes place at a later date and that the

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Fellows are not simply led by the opinions of third parties. Good observations should then provide the basis for well-described needs.

The team were kindly permitted to make observations at the following locations:

Dublin

- St James Hospital
- Beaumont
- Blackrock

Galway

- UCHG
- Galway Clinic

Cork

- Cork University Hospital
- Mercy Hospital
- Bon Secours Hospital

It was felt important to make observations in different healthcare settings. The rationale for the Fellows was that if a problem was restricted to a particular institution, then it could not be said to represent an unmet clinical need.

An effort was made to ensure that observations were made which spanned the cycle of care. An example of this involved interviewing a particular patient while they awaited a procedure. Arrangements were made to attend the procedures and the patient was interviewed following

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the procedure in the intensive care unit and then on the cardiology ward as he continued his rehabilitation.

It was decided by the Dublin team that every opportunity should be taken to observe as many procedures as possible and not simply to restrict the observation to the area of Cardiology. This reflected a belief on the part of the team that Cardiology is an area which has been the subject of a large amount of innovation in recent years. It was felt that taking every opportunity to observe all clinical areas possible would yield the best possibility of uncovering unmet clinical needs. Therefore, observations were made in the following clinical areas:

- Cardiology
- Cardiothoracic surgery
- Vascular Surgery
- Neurology
- Obesity Management
- Urology

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2.4 Recording Observations

Observations to Needs (from 1,200 to 185 unmet needs)

What (was the observation)?	Where was observation and what physician involved?	When	Procedure	Not a problem=0; A problem=1; Further work=2	Identifier
2-3% chance of rupturing an aneurysm when coiling	Beaumont, Dr John Thornton	18-Oct-2011	Conversation with JT	1	2
6.6% of coiled cerebral aneurysms require re-treatment, and DSA is still more sensitive (but less safe) than MRA in detecting residual flow within the aneurysm (MRA may be better at 3T)	RCSI, faculty of radiology annual scientific meeting 2011	22-Sep-2011		1	2
Coil embolization of small aneurysms with small					
What (was the observation)?	Where was observation and what physician involved?	When	Procedure		
2-3% chance of rupturing an aneurysm when coiling	Beaumont, Dr John Thornton	18-Oct-2011	Conversation with JT		
endo is better than clipping for most patients.	Dr John Thornton	18-Oct-2011	aneurysms	1	2

Needs Statement: A more effective and safer way to treat cerebral aneurysms with less recurrence

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Figure 2.1: A typical observation noted during clinical immersion

Observations were documented at the end of each day and Google Docs was utilised for this purpose. This was a painstaking process, part of which involved reviewing observations of other Fellows to ensure that similar observations from the same procedure were only recorded once. Similar observations from different procedures or conversations were recorded separately in order to highlight issues that posed a problem across institutions and for many different patients or physicians.

As detailed in **Fig 2.1** above, Fellows were required to record the following in the initial stages:

- A brief description of the observation;
- A note of where the observation was made i.e. was in it a procedure or in conversation;

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- The date of the procedure;
- The name of any physician involved.

At the end of the eight weeks of clinical immersion, the Dublin BioInnovate team had compiled over 1,200 observations.

2.5 Conclusion

The willingness of medical professionals to engage with the BioInnovate process is obviously crucial. It was found that, without exception, clinicians were willing to engage with the process when they understood that the end goal was the advancement of patient care. Until this fact was pointed out, clinical immersion was a less fruitful exercise. A useful method would have been to present an overview of the process at a staff meeting early in the clinical immersion.

At the outset, the Dublin Fellows had set a goal of obtaining over 1000 observations during the clinical immersion phase. It has been generally accepted within previous Biodesign Fellowships that over the course of two months of clinical observation, 1000 observations is a legitimate target and moreover, is a necessary target required in order to eventually produce the unmet clinical needs required. Observations will not always represent legitimate problems and even legitimate problems will not always represent unmet clinical needs which are worth pursuing. The decision to observe procedures across a variety of clinical areas played a vital role in achieving this target. Had the focus been restricted to the Cardiology department, the likelihood is that there would have been downtime in waiting to see relevant procedures or to speak to clinicians. In addition, it is rarely possible to facilitate four observers into an

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operating theatre or a clinic. The strategy to avoid these difficulties meant that the Fellows were rarely left without an opportunity to make observations.

However, this also meant that the observations were obviously drawn from a wide number of areas and this would have implications for filtering the observations and translating them into unmet clinical needs. This process is explored in the following chapters.

Chapter 3

Translating observations into unmet clinical needs

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3.1 Introduction

The needs filtering process was perhaps the most challenging aspect of the BioInnovate process. This chapter explores the reasons for eliminating various problems identified in order to arrive at a list of the top 10 unmet clinical needs.

3.2 Filtering phases

At the beginning of this process, the Dublin team began with over 1,200 observations/ problem statements which reflected the difficulties that had been observed.

By the end of this process, the Fellows hoped to become experts on a chosen few unmet clinical needs. There was a realisation that this could not be done on a large number of needs. At the outset therefore, there was recognition that a number of filtering mechanisms would need to be applied.

There was agreement between the Fellows that filtering would be an ongoing process but that it should be divided into a number of phases:

- **Phase 1:** Needs (roughly defined based on clinical immersion observations) were to be initially be filtered based on:
 - 1) Impact on patient care;
 - 2) Propensity to reduce costs; and
 - 3) Market size.
- **Phase 2:** A more detailed assessment of criterion 1-3 in Phase 1 was performed. Clinical feasibility which is discussed below in terms of the burden of proof for potential solutions was also considered. A deep-dive fact -based assessment was performed on each rough

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need in areas including disease state, epidemiology, market analysis, pathogenesis, causes, risk factors, presentation, diagnostic tests, current medical management, current surgical or interventional management, key clinical outcomes/endpoints, current effectiveness of treatments, trial duration, potential for cost reduction and market size/growth. The rough needs were then appraised and changed or deleted accordingly.

- **Phase 3:** This took place concurrently with brain-storming and included further clinical validation and input from seasoned clinicians, med-tech and business professionals. A thorough competitor analysis, stakeholder analysis and assessment of the current reimbursement situation were performed. Regulatory burden, IP concerns, and technological feasibility which were not addressed in detail in Phase 2 were to be assessed.

The following figures set out the mechanisms by which Phases 1 and 2 detailed above were achieved.

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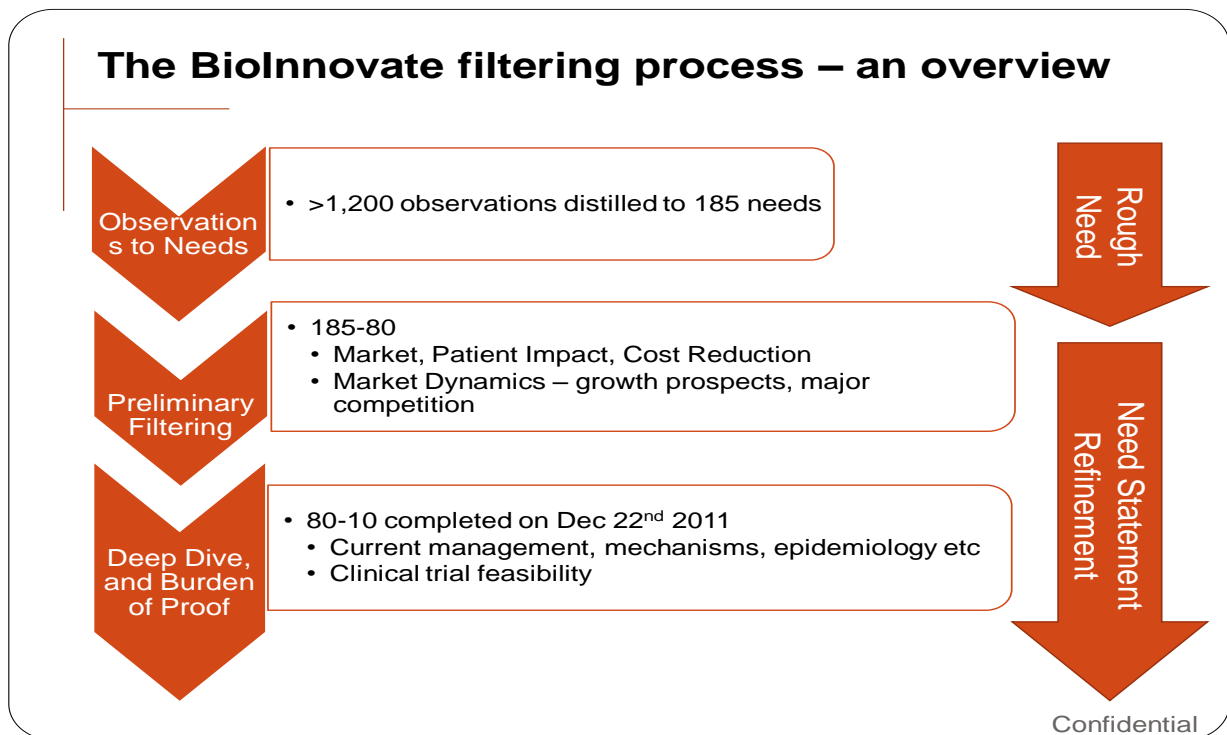


Figure 3.1: The BioInnovate filtering process – an overview

3.3 Observations to needs

The first step in this process required eliminating a number of observations. It was decided that observations under the following headings were outside the scope of what the team wished to achieve:

- Information Management or IT-only projects – During clinical immersion, a great many problems arose because of the fact that IT systems across institutions were not compatible. Even within hospitals, hand-written notes were often used when recording patient data and this would need to be inputted into the system later on or

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even utilised by other members of staff. It was felt by the Fellows that relevant technologies to meet these needs already existed so perhaps the will was not there to change systems. Also, within the team there was no I.T. expert and therefore it would be unlikely that the team would achieve solutions to these problems.

- Logistical issues - There were a number of difficulties with the flow of good medical products and patients. For example, on ward rounds, it often took a long time for doctors to locate their patients who had been placed in any ward where there was space. It was felt that dealing with these logistical matters would not bring about the improvements to patient care that the Fellows were looking to bring about.
- Ergonomics – There were a number of observations which arose out of sub-optimal working environments. For example, staff in hospitals had a great deal of difficulty moving patients onto and off beds on which they had been treated in various theatres. Once again, it was felt that dealing with ergonomics would not bring about the improvements to patient care that the Fellows hoped to achieve.
- Imaging – In a number of settings, including the catherisation lab, interventional radiology, vascular surgery and neurology, it was observed that the quality of imaging used by physicians to view positions within vessels were often quite poor. Many observations were made around the inability to confirm that treatment had been effective. Improved imaging and mapping has the potential to impact hugely on patient care. However, it was felt that the skills did not exist within the team to bring about improvements in the area and that the expertise of the large players in the market may prove too strong.

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After the elimination some observations as detailed above, every remaining observation was considered. As a group, the Fellows made a decision as to whether each observation represented a truly unmet clinical need or something that was simply less than ideal or a ‘nice to have’. Observations falling into the former category were assigned a ‘1’ and brought forward. The latter were assigned a ‘0’ and disregarded at that stage.

3.4 Need Statement Development

Concurrently, every problem statement was refined into rough need statement. Need statement development was a critical aspect in the process.

The aim was to clearly articulate a need so that the parameters would guide the development of concepts and potential solutions. It was felt critical that the needs statement would address what change in outcome was required and not how it would be addressed. Therefore, no potential solutions could be reflected in the need statement.

Additionally, Fellows were keen to define the scope of each need statement correctly, conscious that a narrowly defined statement could miss a potentially large market or that a statement which was too broadly defined would not articulate the need correctly.

3.5 Preliminary Filtering

It was next decided that the remaining 185 roughly drafted needs would need to be ranked. In this regards, the Mission Statement was utilised to develop the filters that adequately reflect what needed to be achieved. Essentially these meant that a number of parameters would need to be met before a project could be taken forward.

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Preliminary Filtering (from 185 to 80 unmet needs)	
Market Size 1: < 250 m 2: 250 m to 500 m 3: 500 m to 1 bn 4: 1 bn to 2 bn 5 : 2 bn	Potential for cost reduction 1: None 2: Minimal 3: Some 4: ... 5: Massive reduction in cost (e.g stroke)
Patient Impact 1: No change 2: Reduction in peri/ post-operative pain 3: Some change in clinical outcome 4: Change in QOL/ some reduction in deaths 5: Massive improvement in QOL, reduction in deaths	
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Figure 3.2 Preliminary Filtering (from 185 to 80 unmet needs)

Each need was allocated a figure based under each of the above headings and therefore received a ranking as outlined in Fig 3.3 below.

Preliminary Filtering (from 185 to 80 unmet needs)							
Need	Identifier	Market	Patient Impact	Cost Reduction	Total	Rank	Additional identifier
A need for a more convenient means of boosting cardiac output in an emergency or operative setting	159	5	4	4	39	7	
A way to more safely treat cerebral aneurysms and prevent recurrence, particularly at bifurcations	177	4	4	5	39	7	2, 47
A need for a more reliable long-term reversible less invasive alternative to gastrectomy or banding in managing obesity	161	5	4	4	39	7	162
A more effective and safer way to convert or ablate an ectopic source of atrial fibrillation.	166	4	4	5	39	7	
A way to prevent atrial or ventricular clot formation and migration in the presence of atrial fibrillation	167	5	4	4	39	7	66
A way to prevent complications due to reperfusion injury following delayed revascularisation in stroke	176	4	4	5	39	7	
A way to prevent complications associated with thrombolysis such as a ICH, GI bleeds, haemoptysis	1	5	4	3	36	32	71
A way to detect recurrence of atrial fibrillation in an at risk patient.	30	3	5	4	36	32	
A way to eliminate the need for a bypass pump during CABG/AVR	33	4	4	4	36	32	150, 117, 108, 105, 100, 106
A way to improve diagnosis and monitoring of patients with known ischaemic heart disease.	38	4	4	4	36	32	
A way to improve the precision and efficacy and reduce complications of renal denervation in treating hypertension.	43	5	3	4	36	32	28
Need	Identifier	Market	Patient Impact	Cost Reduction	Total	Rank	
A way to more safely treat cerebral aneurysms and prevent recurrence, particularly at bifurcations	177	4	4	5	39	7	
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Figure 3.3 Continued Preliminary Filtering (from 185 to 80 unmet needs)

The result of this process meant that the 185 needs were further reduced to a top 80 unmet clinical needs.

3.6 The Deep Dive

In arriving at the top 80 needs, time constraints meant that rankings needed to be allocated on the basis of limited information. For example, a cursory look at the current and projected future markets for cerebral aneurysms was used to allocate a figure for that market. There was a consensus amongst the Fellows that in order to make satisfactory progress, a more in-depth analysis of the needs would be required.

On that basis, all of the needs were grouped into relevant clinical areas e.g. peripheral vascular, obesity management or structural heart. Each of the Fellows were assigned clinical areas with responsibility for conducting an in-depth analysis of the disease state and how it is currently managed.

Detailed information was gathered under the following headings:

- Epidemiology
- Pathology
- Causes and Risk Factors
- Patient History/ Presentation/ Symptoms
- Diagnosis
- Current Treatment Guidelines
- Medical Management
- Surgical/Interventional Management
- Effectiveness of Treatment
- Perceived inadequacies of current management

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- Devices/Drugs/ procedures in the pipeline which might meet the current unmet clinical need

The breadth of clinical areas considered meant that the review took a number of weeks. The Fellows would present their findings back to the group and based on this and the discussions and further research that ensued, each need was assigned a mark under the various headings. This in- depth analysis of the disease state and its management allowed the Fellows to better understand each need as well as establish which needs presented a better opportunity e.g. if a need for a medical device was already served by medical management techniques this was seen as less of an opportunity than a need with no current solution

3.7 The burden of Proof

As detailed above, during phase two, the Fellows opted to include a Clinical Feasibility Filter. It was felt that in order to have a product that was capable of commercialisation, it would be necessary to be able to show an effect. Preferably quickly and easily. Therefore, in each area, current clinical trials which are ongoing were assessed and used to objectively predict the type of trial that a regulatory body would be likely to require before a product was brought to market. The headings used were as follows:

- Trial Duration: This heading addressed the time that would be required to show an outcome in a patient group. For example, if it might be possible to confirm that a particular need had been addressed peri-procedurally or in the hours thereafter, then the need would score highly. However, if some years were required to show that a patient's symptoms had reduced over time, then the need would not score well in this area.

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- **Endpoint:** Clinical endpoints are used to measure whether the target outcomes of a trial have been achieved. The ease with which these can be measured will go a long way towards assessing the success of the trial. For example, if the endpoint is a reduction in pain following thoracic surgery, this will not be easily measured. However, the ability to reduce the incidence of stroke after trans-catheter aortic valve implantation (TAVI) is more easily measured and would score higher in this area.
- **Difficulty in proving efficacy:** This points to the effort required to show that an improvement can be shown statistically. Essentially, the lower the desired improvement rate, the greater the number of patients which will be required to be recruited and therefore the cost of the trial may become prohibitive to the commercialisation process.

Predicting the type of trial which may be required before a concept has been generated is a difficult but very useful process. Each of the headings mentioned above have huge implications for the cost and difficulty of a clinical trial. Any start-up company looking for funding will be hindered in its efforts to secure funding if a trial is likely to be of too great a duration or the outcomes are uncertain. It was felt important to ensure that any product developed would be in an area where it was possible to show a clinical benefit quickly and expediently.

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	Stroke (acute)	Stroke (preventative)
Need statement(s)	<p><i>An easier and more effective safer way to remove a cerebral thrombus causing stroke (97, 179, 147)</i></p> <p><i>A way to prevent complications due to reperfusion injury following delayed revascularisation in stroke (176)</i></p> <p><i>A way to prevent cardioembolic stroke (68)</i></p> <p><i>A need for an improved method of preventing thrombus formation and migration (99)</i></p>	
Original Identifiers	97, 147, 176, 179	68, 99
Redefined need statement (if any change)	<p>A way to improve revascularisation, reperfusion injury and clinical outcome in acute stroke intervention.</p> <p>A way to prevent cardioembolic stroke</p>	
Clinical Trial Feasibility (0 to 15)		
Time Required to Show Outcome (5 <24hrs; 4<3mts, 3=6mts to 1yr; 2=1yr to 2yrs, 1>2yrs)	4	2
Endpoint is easily defined, measured, and has high specificity	5	5
Difficulty proving efficacy (statistically and ability to recruit, 5 > 50 patients, 4 > 100 patients, 3 > 200, 2 > 400, 1 > 500)	4	1
Total =	13	8
Market Size (0 to 15)	12	12
Patient Impact (0 to 15)	15	15
Cost Reduction (0 to 15)	15	15
Competitive Landscape		
Competition & Incumbents		
Overall total (out of 60) =	55	50
Rank	1	6

Figure 3.4: Snapshot of needs statements and scorings awarded in the area of Stroke after the Deep Dive.

3.8 The Top 20 Needs

After the assignment of final marks and the addition of a mark for clinical feasibility, the team was left with 20 top needs at the end of 2011.

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A need for a minimally invasive way to treat carotid artery disease, with reduced incidence of stroke
A more reliable and cost-effective way to close a femoral arteriotomy during an interventional procedure
A need for a more effective and efficient method for closure of a laparoscopic port site, particularly in the obese
An improved way to treat chronic total occlusions using interventional techniques
A more effective and less painful way to treat varicose veins
A way to prevent persistent air leaks due to lung resection
An improved way to recanalise ‘below the knee’ peripheral arterial disease
A more reliable way to seal a gastrointestinal anastomosis
A way to prevent or treat pressure ulcers in immobile patients
A need for a less invasive alternative to surgery in improving survival in severe COPD
A way to treat and prevent recurrent atrial fibrillation
A way to prevent seeding of carcinoma during percutaneous biopsy and treatment
A way to treat chronic venous insufficiency
A way to prevent stroke during and after transcatheter aortic valve implantation, during the high risk period
A way to prevent reperfusion injury following revascularisation in ischaemic stroke
A way to mitigate injury due to delayed revascularisation in ischaemic stroke
A way to treat complex cerebral aneurysms
A way to treat/prevent the complications associated with cirrhosis
A way to improve costs and outcomes in dialysis access
A way to prevent heart failure after myocardial infarction

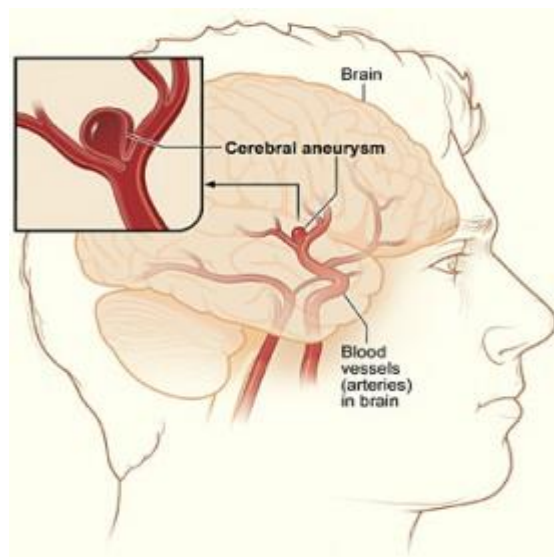
3.9 Conclusions

The ability to make informed decisions under time constraints is a critical skill. Distilling 1,200 observations to 185 unmet clinical needs in a number of weeks will provide a challenge for any team. Over-reliance on instinct will almost certainly lead to the elimination of key observations at an early stage. The selection of filtering criteria and the establishment of parameters by which each need is evaluated proved critical to the process utilised by the Dublin Fellows.

Furthermore, the concept of need statement development mentioned above cannot be understated. As stated above, good observations form the basis for well-described needs. For example, it is often said that a common mistake of previous Biodesign Fellows had been to incorporate elements of solution into a needs statement. While it is understandable to wish to reference potential solutions in these early stages of the process, the effect is to narrow the focus of the team and limits the possible opportunities explored in due course. The experience of the Fellows was that the description of needs evolved continuously as new information comes to hand during the deep dive. By constantly reviewing their work, the Fellows felt that the needs were properly described at the end of the process. The next chapter examines the background to one of the unmet clinical needs identified as well as the opportunity it presented. The remaining chapters explore the premise that a problem is half solved if properly stated.

Chapter 4

Project Profile: A way to treat complex cerebral aneurysms



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4.1 Introduction

This chapter gives a background from one of the unmet clinical needs which was investigated by the Fellows and brought forward to the brainstorming stage. It is a summary of much of the information which was uncovered during the ‘deep dive’ conducted by the Fellows and it is constructive in terms of the level of detail which was required for each of the top unmet clinical needs.

4.2 The observation

In general conversation with an interventional radiologist, Dr. John Thornton, it was noted that ‘the risk of rupturing an aneurysm when coiling is about 2-3%.’ This information prompted the Fellows to investigate cerebral aneurysms, arrange to view some interventional procedures and interview experts and key opinion leaders in the field.

4.3 The background - Cerebral Aneurysms

A cerebral or brain aneurysm is a disorder of the cerebral vasculature. In short, a weakness in the wall of a blood vessel of the brain, leads to dilation or a bulging outwards of the vessel. Small aneurysms are generally classified by physicians as less than 15mm in diameter.

In the event that an aneurysm grows larger physicians advise that this can lead to symptoms such as:

- severe headaches
- nausea
- loss of vision
- loss of consciousness

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- Vomiting.

However it is not uncommon for some patients with large cerebral aneurysms to remain asymptomatic.

From viewing medical procedures it became clear to the Fellows that cerebral aneurysms vary greatly in terms of size or shape which makes it difficult to predict how they are likely to develop and behave. The American Heart Association / American Stroke Association (the Stroke Association Website, November 2012) classify cerebral aneurysms through their size and shape as follows:

Size

- Small aneurysms are less than 5 mm (1/4 inch).
- Medium aneurysms are 6–15 mm (1/4 to 3/4 inch).
- Large aneurysms are 16–25 mm (3/4 to 1 1/4 inch).
- Giant aneurysms are larger than 25 mm (1 1/4 inch).

Shape

Aneurysms can be:

- Saccular (sac-like) with a well-defined neck
- Saccular with a wide neck
- Fusiform (spindle shaped) without a distinct neck

Over time, if aneurysms grow larger, the risk of rupture increases as the wall of the vessel becomes thinner.

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If this situation occurs, a subarachnoid haemorrhage can occur whereby blood leaks into the spaces surrounding the brain. In addition, a bleed directly into the brain causes haemorrhagic stroke. Damage to the brain typically occurs quickly and complications can include permanent neurological damage, hydrocephalus and vasospasm. The risk of mortality is extremely high.

Cerebral aneurysms are relatively common, with an estimated prevalence of 1 to 5% in the general population. Although 50 to 80% of all cerebral aneurysms do not rupture, when they do the results are devastating for patients. The estimated incidence in the US is 27,000 cases per annum). 30 day mortality is 45% and 30% of survivors have moderate or severe neurological deficits. (Brisman, J.L., Song, J.K., Newell, D.W. Cerebral Aneurysms. N Engl J Med 2006; 355: 928-39.) For these reasons, screening programs have been established to determine at-risk individuals, in particular those with a family history (two immediate relatives with intracranial aneurysms) or a diagnosis of polycystic kidney disease (the Stroke Association Website, November 2012).

The brain is particularly sensitive to bleeding and damage can occur very rapidly, often resulting in death. According to estimates, approximately 40% of those whose aneurysm rupture do not survive the first 24 hours, with about 25% dying from complications within 6 months (Patient Information Publications).

4.4 The current treatments

If a patient with an intracranial haemorrhage (ICH) is rapidly transferred to a hospital, they may undergo emergency surgery to stop the bleeding, provided by either a neurosurgeon, with clipping, or a neurointerventional radiologist, with coiling. The success of such

treatment will be highly dependent upon the amount of damage that has occurred. The consequences of an ICH are so serious and the outlook is so poor that aneurysms which are deemed to be at high-risk for rupture (in accordance with international treatment guidelines) may be treated electively before they ever rupture. In certain circumstances, particularly with critically ill patients, or really complex aneurysms surgical clipping may be required, although this approach is generally only used in a small percentage of any patient population.

4.4.1 Coiling

Coiling is the less invasive of the two treatments. However, it should be remembered that not all aneurysms are suitable for coiling. In either the emergency or the elective setting, endovascular coiling (‘coiling’) is the current treatment of choice and has existed for upwards of twenty years. Covidien, Johnson and Johnson, Stryker and Terumo are all examples of large corporations involved in the production of coils for use in neurovascular procedures.

Coiling is a minimally invasive procedure (under sedation at most). The tiny coils are delivered through a catheter that enters the arteries in the brain via an artery in the groin. Coils are inserted into the aneurysm one by one, through the catheter, until the sac is full of coils and causes a clot to form in the sac, thereby preventing additional blood from entering the aneurysm. When a thrombus has been caused to form and fill the sac, further expansion of the aneurysm is thereby prevented. Coiling has become widely used and has been shown to be superior to surgical clipping in the emergency setting, with reduced morbidity and shortened hospital stays (Brisman et al).

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As mentioned above, coiling works well for simple aneurysms (those with a narrow neck) because the coils are easily kept inside the sac without any need for further assistance. However, coiling has a number of limitations:

1. Very large, wide-necked or irregular shaped aneurysms are difficult to treat with coiling and interventionalists often have to use balloons (as a temporary platform) or stents (as a permanent platform) in the vessel, through which the coils are delivered. The platform provides the necessary support to prevent the coils from exiting the sac and causing a clot, or even occluding the parent artery. Using these additional tools requires tremendous skill and can be very time consuming. The techniques are used in an estimated 30% of all coiling procedures (Millenium Research Group. US Markets for Transcatheter Embolization and Occlusion Devices 2011.)

However, in a number of cases this is the only treatment option. In an emergency ICH situation only balloon assisted coiling can be used (stent-assisted coiling is contra-indicated in an ICH as patients with a stent must be put on medication that further increases the risk of bleeding), with limited success because of the time required to complete the procedure and thus stop the bleeding. It follows that the risk of neurological deficits increases significantly with continued bleeding.

2. The costs associated with coiling, both in terms of material costs and time, can be significant, particularly for large aneurysms that require multiple coils to fill the sac. Typically a single coil ranges in price from \$500 to \$3,000 (Cloft, 2009). Treating a large aneurysm that requires 10 or 20 coils, and possibly a stent (~\$5,000), can be extremely costly (Cloft, 2009). An analysis of a submission by Covidien in support of its Pipeline Embolisation Device to the National Institute for Health and Clinical Excellence (NICE) in

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the UK, details the costs associated with treatment of unruptured complex aneurysms as follows (NICE, 2011):

Intervention	Procedure cost
Pipeline embolisation device	£24,341
Stent-assisted coiling	£37,451
Neurosurgical clipping	£11,658
Conservative management	£10,352

4.4.2 Flow Diverters

As the name suggests, these devices are used to ‘divert flow’ away from an aneurysm. This is achieved by inserting a stent-like device into the lumen of a parent vessel which prevents the flow of blood into the aneurismal sac. In this way, the inter-saccular blood forms a thrombus thereby achieving the same result as the insertion of coils into an aneurysm.

Flow-diverters are particularly suited to treating rare fusiform aneurysm where bulging occurs along the circumference of the vessel and giant aneurysms with wide necks which may not be suitable for the retention of a coil.

Although flow diverters are often compared to stents, they are actually required to have much more material than a traditional stent to that they can achieve their aim of the prevention of blood flow into an aneurysm.

Flow diverters are currently extremely expensive. In the UK, average flow-diverter prices are estimated at (£10, 171) by Covidien, one of the main manufacturers: Nice: Medical

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Technology, Guidance assessment report overview - Pipeline embolisation device for the treatment of complex intracranial aneurysms 2011.

Through interaction with a number of clinicians who are key opinion leaders in this field, it was noted that there has been experience of a high rate of complications including rupture, migration, thromboembolic occlusions and blockages of other vessels (perforator branches). Flow-diverters also by their nature, lead to the introduction of large amounts of intra-luminal thrombogenic material into the vascular system, leading to long-term dual anti-platelet therapy.

Another restriction is that flow diverters do not permit a clinician to confirm peri-procedurally that occlusion has been achieved. They are therefore unsuitable for use in emergency procedures.

4.5 Future Competition

Through an analysis of the intellectual property landscape, two emerging technologies of note were identified:

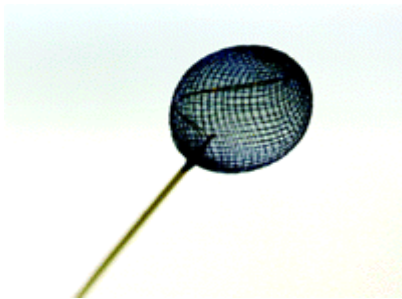
4.5.1 Sequent Medical Woven Endobridge II (Web II)



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This device consists of a mesh which is designed to occlude wider – neck saccular aneurysms of particular sizes. Devices have been made which are suitable for treatment of aneurysms between 5 and 11mm in diameter.

4.5.2 NFocus Neuromedical - the Luna Aneurysm Embolization system (Luna AES)



This device is another intra-saccular device. It is a self-expanding ovoid braided intra-saccular thrombogenic implant device that provides an attenuated mesh of metal across the neck of the aneurysm.

Benefits of the Sequent and Luna devices include their ability to be positioned within the sac, treatment of the aneurysm in a single step and faster occlusion times. The primary criticism is that pre-procedural accuracy in sizing is essential and if underestimated, blood may surround the device within the sac leading to recurrence, or parent vessel occlusion. If under-sized, the interventionalist has limited time to retrieve the device via the delivery catheter or the risk of a thromboembolism becomes critical.

4.6 Conclusion: The Unmet Need and Opportunity

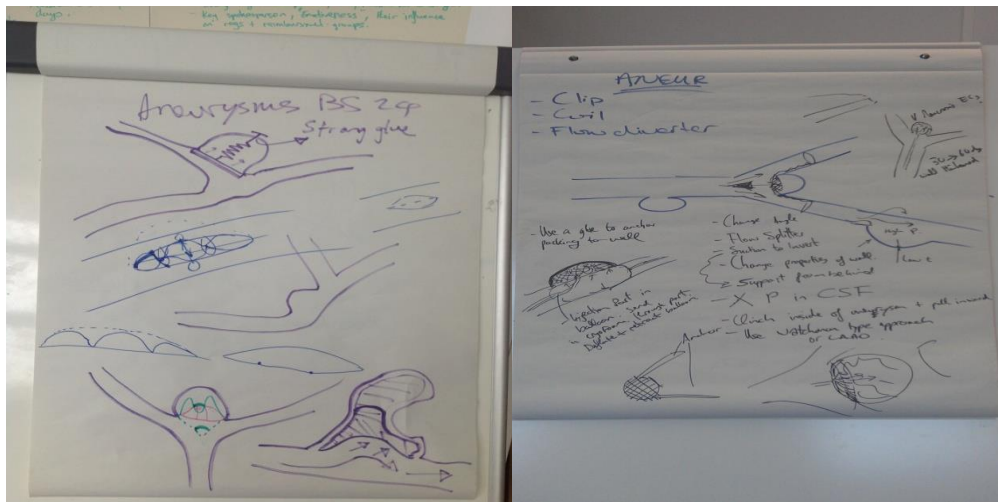
From speaking to clinicians and observing procedures and researching literature, it became obvious that the current treatment methods for dealing with complex cerebral aneurysms are not ideal. Apart from the risk of rupturing an aneurysm peri-procedurally, there were many other drawbacks. Therefore, there existed an opportunity to create an alternative to current treatment mechanisms. However, any solution would need to be

- Safer
- More effective
- Less expensive
- Less time – consuming.

The efforts made to identify a solution in this regard are detailed in the following chapter.

Chapter 5

Invent



5.1 Introduction

As detailed above, from the top twenty unmet clinical needs, eight needs were selected by the Fellows for brainstorming. This chapter details the process utilised and the solution proposed for the cerebral aneurysm referred to in Chapter 4.

5.2 Appraisal for brainstorming

Rather than selecting the tops needs, all needs were appraised as follows:

- Consideration of technological and clinical risk – If it was felt that working in a particular area was not technologically feasible then this would pose obvious difficulties. Clinical risk was seen as something which might always exist with any novel technology but it was a factor to be noted.
- Size of the project and the probable time to exit - If for example, the project was to involve the development of a heart valve, then the time to exit and cost of the project may prove prohibitive in securing funding as it would be an unattractive proposition for a venture capitalist.
- One opportunity suitable for licensing was to be brought forward – the goal of this project was to ensure that at least one project which was capable of commercialisation by the Fellows themselves would be produced. However, if one compelling solution was produced which was more suitable to be licensed externally to the group, then this would be considered.
- Skill set within the team - It was deemed important that the expertise to commercialise a solution was readily accessible within the group.

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- Fellow’s interest – it was a pre-requisite that passion and interest in the project was required in order to make it a success.

5.3 Ideation

As mentioned in Chapter 1, ideation was carried out utilising group creativity and the diverse backgrounds of the Fellows. Brainstorming was therefore conducted as a group and in a variety of locations to encourage creativity. All Fellows were encouraged to participate equally.

At the outset, all potential approaches, no matter how feasible were suggested and a list was compiled. Ideas were suggested in a rapid fire manner with the emphasis being on wild ideas and novel approaches.

After this process, the various ideas were presented visually and appraised for their possible clinical benefit and technical feasibility.

5.4 Continued interaction with clinicians

Contemporaneously with brainstorming, every opportunity was taken to meet with clinicians, venture capitalists and key opinion leaders to seek further information and opinions.

Typical examples of questions asked of physicians involved in the area of cerebral aneurysms included the following:

- What effect would reducing the blood flow have on the aneurysm?
- Will pipeline devices require antiplatelets beyond 6months?
- What causes the weakness in the wall of an aneurysm?

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- What is the weak point of the aneurysm? Is it at the neck or elsewhere and would strengthening of wall help?
- How many aneurysms remain untreatable despite the addition of Flow diverters to the toolbox of a neurovascular interventionalist?
- Do the flow diverters migrate much, and if so does this scare you?
- Is perforator occlusion a problem with flow diverters?
- How unacceptable is the use of anti-platelets in your experience?
- Are perforators actually staying patent with Flow diverters?
- Would a solution which cannot be assessed for technical success during a procedure be appropriate?
- Given the high rate of restenosis for stents, to what degree can the cerebral vasculature tolerate some kind of anchor?
- With less material in a device, is shorter interval of (or no) antiplatelets acceptable?
- Are there dangerous aneurysms out there being left untreated for want of a device that can be used in more complex aneurysms?
- Is peri-procedural confirmation of occlusion a 'nice to have' or seen as necessary?
- Is there always a follow-up procedure to evaluate progress?
- Does the shape of aneurysms vary greatly? Does this cause further difficulty in treatment?
- How often are these aneurysm monitored?
- Is coiling acceptable treatment for narrow-necked aneurysms or do you believe that coiling might be replaced by flow diverters?

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- Do you see a future role for stent assisted and/or balloon assisted coiling into the future?
- Do you think flow diverters on their own will be adequate or are you looking at a combination of diverter & coiling?
- What has the clinical experience been with 1) Onxy and 2) Trufill?
- How long does it take for Onyx and Trufill to cure?

5.5 In-depth analysis of Competition

Reference was made in the previous chapter to the emerging technologies which were briefly reviewed. In order to inform the brainstorming, more detailed analysis of those technologies was continued by the Fellows. A sample of the information compiles on the Sequent Web – Woven Endobridge Cerebral Aneurysm device is provided below:

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Sequent Web - Woven Endobridge Cerebral Aneurysm Device

First in Man study attempted to measure immediacy, degree and durability of aneurysm occlusion. Implanted in one unruptured MCA trifurcation aneurysm and one patient with an unruptured basilar tip aneurysm.

Results:

- Delivery and deployment of the WEB II device was technically straightforward and achieved without complications.
- Neither device required retrieval or repositioning after full deployment.
- There were no peri-procedural thromboembolic or hemorrhagic complications.
- In both cases, complete aneurysm occlusion was observed within minutes of device deployment.
- Short-term angiographic follow-up confirmed stable complete occlusion at 8 weeks.

Notes:

- The device is designed with a concave base to avoid the formation of thrombus on the device. Patients only required aspirin (100mg six months) and heparin (3 days).
- The structure of the WEBII was designed for large neck aneurysms. The device is indicated for the treatment of saccular aneurysms with a neck-to dome ratio of ≤ 1 and a neck length-to-width ratio of < 2 , where the neck length-to-width ratio is the ratio of the longest neck diameter divided by the shortest neck diameter.
- Devices available in varying sizes to treat aneurysms from 5mm to 11 mm in diameter.
- Series B funding received - \$15.5 Million.
- Series C funding received - \$26 Million.
- 6F catheter required. Standard 0.027 micro catheter used to deliver the device itself.
- Patient 1: 3 mins to device deployment after placing catheter in aneurysm. Stasis in aneurysm 10 mins after deployment.
- Patient 1: appears to have had a narrow neck but a high AR (5.5 width, 2.1 neck).
- Patient 2: Aneurysm measured 7×4.6 mm with a 3.35-mm neck.
- May be better than coiling - First, better at creating the endoluminal overgrowth of neointimal-neoendothelium at the aneurysm-parent artery interface. Which probably means greater rates of complete occlusion with lower rates of delayed re-canalization following treatment. Second, the amount of device manipulation within the aneurysm sac is reduced, particularly for large aneurysms.
- Has not yet been used in the most common aneurysms found. MCA bifurcation represent 20% of all cerebral aneurysms. Basilar Artery 7%.
- Patient 2: 13 mins to deployment from catheterisation of aneurysm.
- If the operator decides that the sizing or orientation is not favourable, the device needs to be immediately resheathed/removed/repositioned.
- If the device is over-sized relative, it could push out through the aneurysm neck (the path of least resistance).
- The neck cannot exceed the device diameter.

5.6 The Design Principles

From the information during the process, it was clear that a number of design principles would need to be established. These were as follows:

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- The invention needed to induce thrombosis within an aneurysm sac only;
- The risk of damage during and after the procedure had to be minimised;
- There could be no thromboembolic occlusion of the parent artery;
- The invention would ideally be inexpensive;
- The invention had to be capable of treating ‘hard to treat aneurysms’; and
- The inventions had to be capable of treating regular aneurysms.

The experiences of the Dr. Liam Mullins in previously designing medical devices and the experiences of Dr. James McGarry in previously using medical devices were invaluable in the establishment of these design principles.

5.7 The Proposed Solution (s)

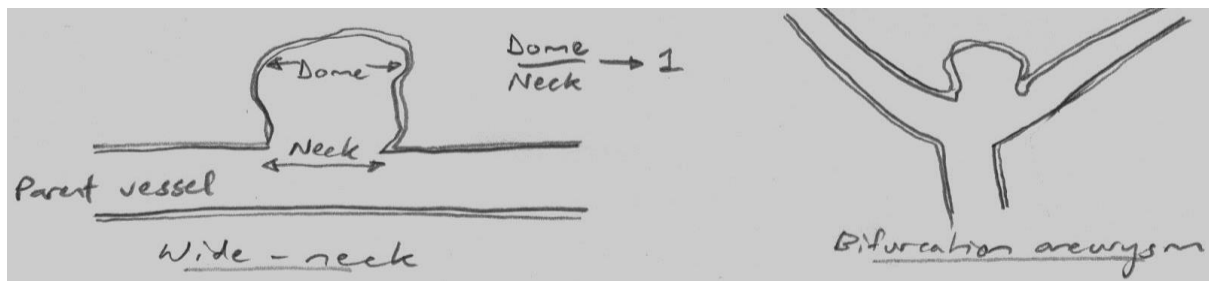


Figure 5.1: Sketches of complex cerebral aneurysms that may be difficult to treat by unassisted endovascular coiling.

Solution 1: Stabilising wings: To keep the occluding material in the sac, an expandable shape memory frame that sits on either side of the sac in the parent vessel was devised. This frame anchors the material in place by extending along the length of the parent artery and providing geometric stability. Unlike a stent, anchoring is achieved with minimum damage to the parent vessel wall. The area of contact and therefore endothelial injury will be far less

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with this design. The frame is symmetric with two wings and a central portion that attaches to a body within the sac, or to a lid over the sac. The lid design could therefore be used as an adjunct to coiling or as an alternative to stenting. A considerable advantage is that long-term antiplatelet therapy would not be required as endothelial injury would be minimal in attaining stability.

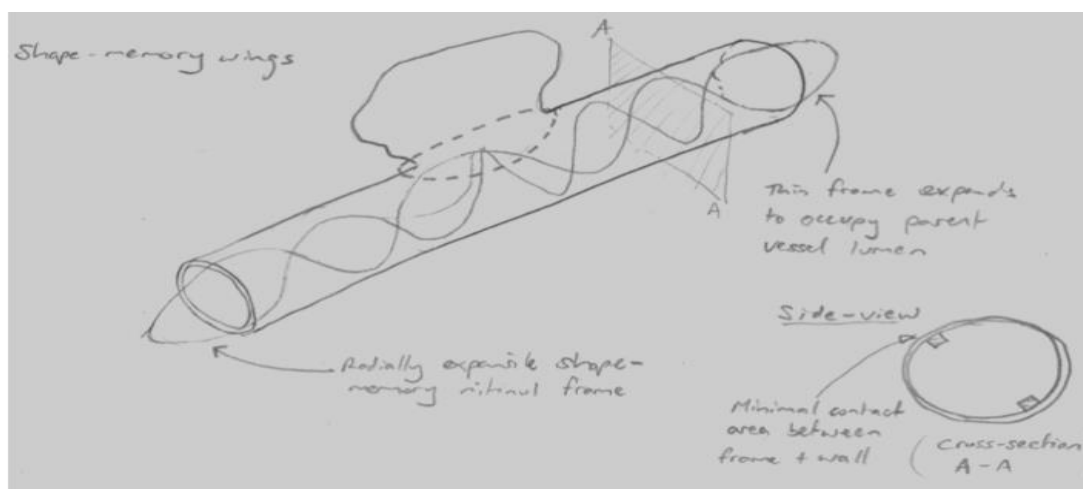


Figure 5.2: Stabilising wing sketches.

Expanding stabilising symmetric wings keep an intra-saccular component in position within the aneurysmal sac. (**Inset:** Sketch of a cross-section of parent vessel artery illustrating the typical degree of strut-wall area of contact, and therefore minimal risk of wall injury or thrombus formation in the parent vessel.)

Solution 2: Compliant intra-saccular bag. A compliant (possibly double-walled) bag is advanced in to the sac by catheter delivery and allowed to fill with, for example, blood. The bag is compliant and occupies the irregular aneurysm shape, becoming flush with the aneurysmal sac wall. The bag may be limited in size such that it does not fill the entire sac. A double-wall design would allow a thin layer of

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adhesive to be introduced in between the two walls of the bag. Perforations in that portion of the outer wall of the bag that lies within the aneurysmal sac would allow the adhesive exit the inter-wall bag space and cause the external surface of the bag to adhere to the inner wall of the aneurysmal sac. The surface of the bag forming a border with the parent vessel has no perforations, and simply hardens to form a solid surface. A supporting balloon or temporary lid may be used to provide the desired support and shape for the hardening bag wall along the parent vessel. The thrombus containing bag and any adhesive will be made of materials that are both biocompatible and are reabsorbed, such that with time and healing the treatment will be integrated into the vessel wall. Other embodiments of a similar principle include the use of foams with channels for transporting adhesive to the interface with the sac wall.

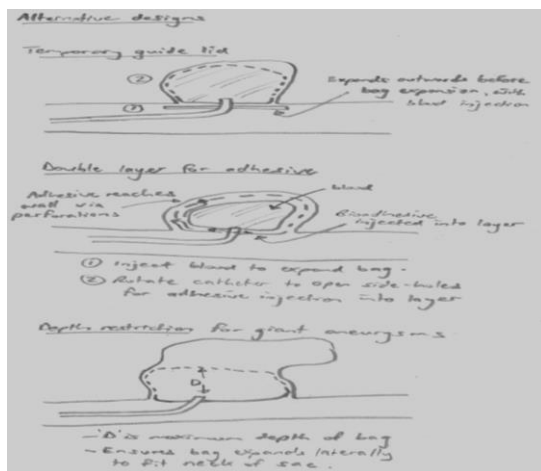


Figure 5.3: Compliant intra-saccular bag sketches

5.8 Conclusion

The process required the Fellows to, once again, delve further into the particular disease state during the invention stage. The result of this was a solution to an unmet clinical need. Traditionally, medical devices are invented or produced at which point it becomes necessary to begin work on distinguishing them from their competitors or establishing their novelty. By the nature of the process followed, much of this work had already been accomplished by the Fellows.

Chapter 6

Project Activity Decision and Conclusion

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6.1 Introduction

This chapter details the status of the project detailed in the foregoing chapter by the end of the process in May 2012. It also offers a reflection on the success of the process followed by the Dublin team.

6.2 Project Activity Decision

At the outset, it had been envisaged by the Fellows that an output of the programme would take the form of one or more business plans. Time constraints meant that it would not be possible to achieve this by the time the Fellowship drew to a close in May 2012. Therefore, it was deemed prudent to compile the basic elements of a business plan and include these in an invention disclosure form (IDF) which would be submitted to Dublin City University as owners of any intellectual property generated during the programme.

6.3 Final Conclusions and Lessons learned

It is submitted that the process followed by the Dublin Bionnovate team was a success in view of the fact that a novel solution to an unmet clinical need was created and disclosed in the form of an invention disclosure. It is acknowledged that the brainstorming, ideation and invention phases of the programme were more time consuming than originally envisaged yet the likelihood is that the additional time spent on these areas was necessary in order to produce a novel solution to an unmet clinical need. While it may have been prudent to work concurrently in sub-groups to ensure that all targets of the programmes were met, it cannot be said how this would have affected the quality of the solutions produced.

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While the output was most certainly a medical device which is capable of commercialisation, more work would be required with respect to topics such as reimbursement, regulatory matters and costs of product development as these had only been dealt with in a preliminary fashion. However, the primary building blocks and requirements for successful commercialisation of the device were in place by the time the Fellowship drew to a close. Given that the unmet clinical needs had been appraised objectively in the initial phases, it had been ensured that the solution was addressing an unmet clinical need in a large market that was capable of having significant patient impact, reducing cost to the healthcare sector and, was capable of proof in a clinical trial relatively easily. These facts, in addition to the fact that the actual solution proposed had the approval of key opinion leaders in the industry, sponsors of the programme and venture capitalists means that there is an increased likelihood of long-term success for the solution and a likelihood of sourcing commercialisation funding and seed capital required in the short-term future . It can therefore be said that the BioInnovate programme provides a template for future innovations in the medical device sector. In addition to this, the eight Fellows who participated in the programme were provided with a unique understanding of the industry as well as the fundamental issues facing start-up medical device companies. Therefore, in future years, BioInnovate Ireland can have a key role to play in the fulfilling the vision of the Innovation Taskforce. Furthermore, it is hoped the work done by the Fellows in terms of unearthing unmet clinical needs and researching these areas will be available for further research by future Fellows and industry partners in conjunction with the various higher education institutes.

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