Minimally Invasive Medical Devices Environmental Scan

Technology & Markets
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Life Sciences SCOTLAND

iti Life Sciences real possibilities

E-Scan Aim

- ITI Life Sciences recently released an environmental scan of the non-invasive medical device space. This highlighted four non-invasive technology applications, which are of interest given their market and innovation potential, namely wound management, drug delivery, non-invasive sensing and wearable monitors. Both drug delivery and wound management have now been progressed to full foresighting analysis and reports will be released in the coming months.

- However, it also became clear while analysing the non-invasive medical device space that opportunities relating to **minimally invasive** technologies may exist, where a reduction in invasiveness is sufficient to offer benefits over conventional technology despite a completely non-invasive solution not being achieved.

- As a result, ITI Life Sciences has now conducted an environmental scan to identify sectors where reductions in invasiveness of key technology could significantly impact the market.

- In this context, minimally invasive devices can be defined as those which require percutaneous techniques, minor incisions or insertion through a bodily orifice for diagnosis, monitoring or treatment of disease.

Strategic Analysis of the Minimally Invasive Technology Landscape

Scope

PROJECT SCOPE

EMERGING TECHNOLOGIES

MARKET DYNAMICS

- Size
- Growth
- Drivers, Challenges, Restraints

KEY PLAYERS

IP LANDSCAPE

TECHNOLOGY SCOPE

DIAGNOSTICS

MONITORS

THERAPEUTICS

OTHER DEVICES

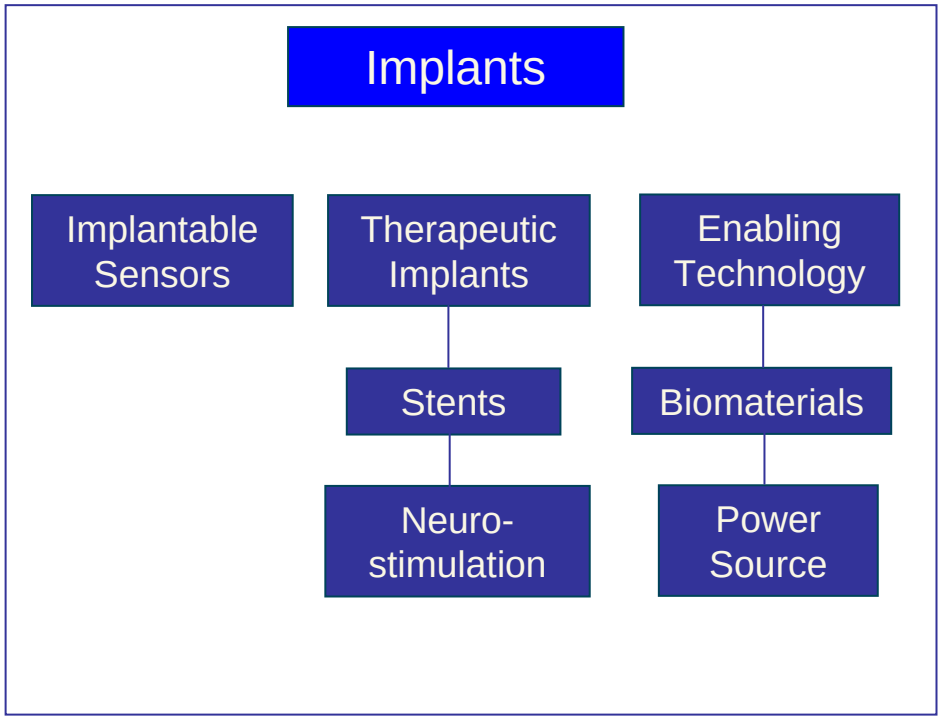
LIMITATIONS

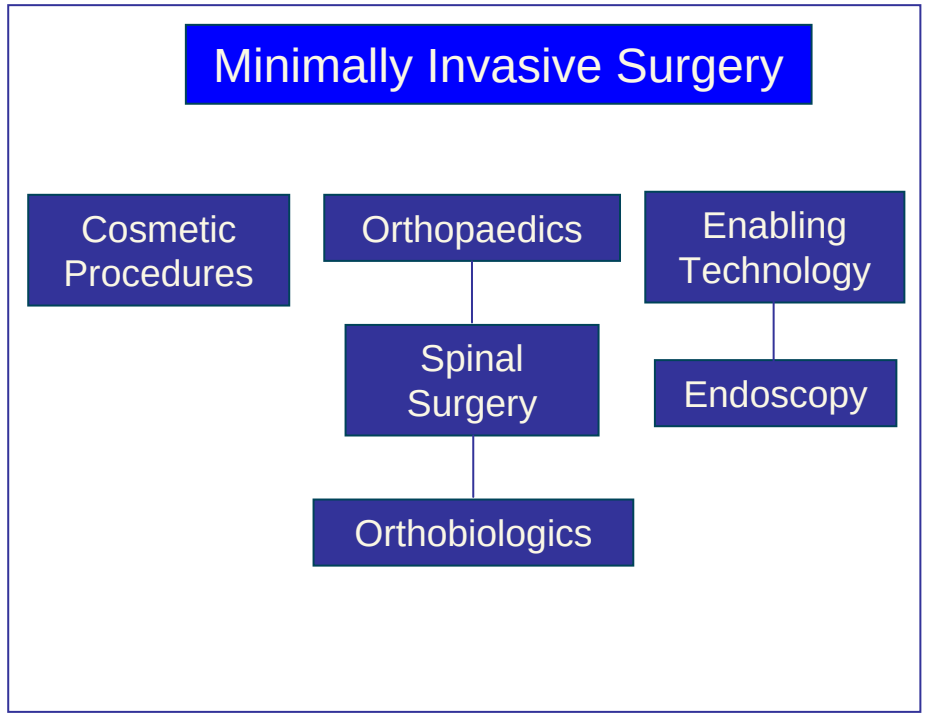
An environmental scan is designed to provide an insight into current market dynamics and technology advances. ITI believes in providing the most up-to-date information available and so readers will note that (i) patent activity during 2006-2007 is reported and (ii) a variation in the market examined (ie EU vs US vs global) with the most up-to-date and available market data reported.

This E-Scan is limited to technologies within the Life Sciences Sector and does not include imaging technology, which has been covered by recent foresighting activities

Leading Technology Applications

- 6 application areas and 3 associated enabling technologies were identified as having significant innovation and market potential.
- These can be grouped into 2 broad areas, namely implants and minimally invasive surgery, and will each be addressed in turn.





Implantable Sensors

Wireless Automated Implantable Sensors

MARKET SHARE

Global

Current market size (2006) - $980 million

CAGR (2006–2013) –11.4%

Potential market size (2013) – $2.09 billion

CHALLENGES

Price sensitivity of the industry

Strict regulatory provisions

Low rate of technology transfer

Dependent on physician recommendation

DRIVERS

Advances in nanotechnology encourages biosensor miniaturisation

High market demand for implantable biosensors for a number of applications

Demand for automated systems & remote disease management

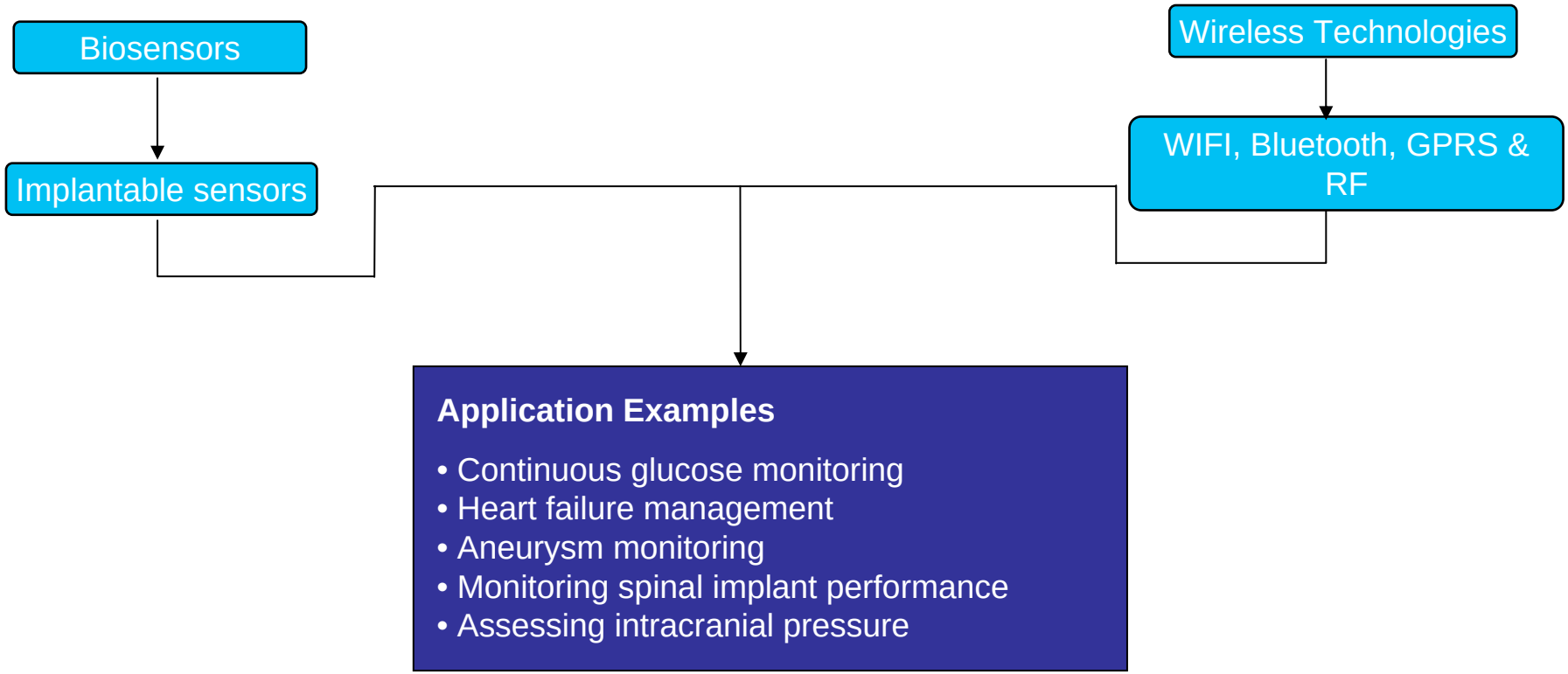
RESTRAINTS

High research and development expenses

Alternative technologies such as non-invasive sensors, POC tests and emerging biomarkers will create competition and may limit future demand

Long time lag between academic research and commercialisation

Implantable Sensor Technology

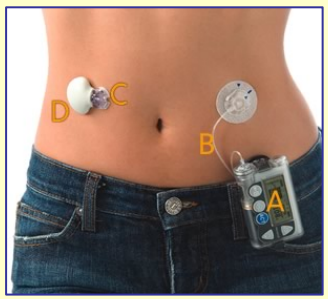


- Implantable sensor technology is viewed as having moderate potential to disrupt the existing implant market and significant potential to lead to incremental improvements in devices currently in the marketplace.

Continuous Glucose Monitoring

- Continuous Glucose Monitoring (CGM) has a number of benefits over conventional glucose monitoring technology:
  - Could provide a warning that the patient is moving towards a hypoglycaemic episode
  - Can alert the user that they are in hyperglycaemic state and so reduce the risk of associated complications
  - Enables patients & doctors to monitor trends in glucose levels and so aid disease management
  - Can be linked with an insulin pump to create a closed-loop system, where insulin is automatically dispensed in response to changes in blood glucose levels.
- There are currently 2 companies with FDA-approved devices on the market – Medtronic and DexCom. Abbott also has a device in development - the Freestyle Navigator. Both Medtronic and DexCom sensors suffer from a number of disadvantages, however:
  - Sensors have a short-life span and must be changed frequently (3 days or 7 days respectively)
  - They are approved as an adjunctive and not as a replacement device due to poor performance when glucose levels are low or rapidly changing
  - Still require calibration with a conventional finger-stick blood glucose device. The Medtronic device requires one finger-stick calibration point every 12hrs.

Medtronic
Alleviating Pain · Restoring Health · Extending Life



Insulin Pump **A** delivers insulin through an infusion set that has a cannula **B** that sits under skin for up to three days after being inserted.
Continuous Glucose Monitoring is made possible through a tiny glucose sensor **C**, which can be worn for up to three days at a time.
Both cannula and sensor are easily inserted using an automatic insertion device provided with the system.
Glucose sensor data is sent continuously to a small lightweight device **D** that attaches to the glucose sensor. The transmitter sends the glucose data to the insulin pump through advanced radio frequency (RF) wireless technology.

Source: www.medtronic.com

Continuous Glucose Monitoring

- There is a clear opportunity to improve existing implant technology, which companies such as SMSI are addressing.

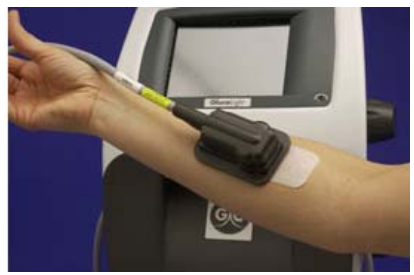
Sensors for Medicine and Science

- Developing a small implant, which is designed to be placed under local anaesthetic in either forearm or abdomen. Implant communicates to an external reader, which may take the form of a wrist-watch.
- Initial target of 6 months of use before sensor replacement.
- Early animal tests suggest good biocompatibility.
- Long road to development; SMSI is nearing completion of its pre-clinical studies after 10 years of development during which they raised a total of $45M.

- This technology sector could face competition from emerging non-invasive technologies such as those being developed by Glucolight and SpectRx though this technology is still some way from the marketplace.

SpectRx's continuous glucose monitoring device is based on laser microporation technology, which non-invasively accesses skin interstitial fluid (ISF).
The patch is worn on top of the skin and measures glucose levels in the ISF that has been drawn up by the patch.

GlucoLight's SENTRIS-100



Developing a hospital-based continuous, non-invasive blood glucose monitor based on Optical Coherence Tomography.

GlucoLight CORPORATION

iti Life Sciences real possibilities

Cardiovascular Applications

Medtronic

Reveal Insertable Loop Recorder: Revealing the cause of unexplained fainting

Implantable patient- and automatically-activated cardiac monitoring system that can record an ECG at the time of a syncopal episode to rule in or rule out life-threatening arrhythmias.
The device is placed under the skin in the upper chest through a small incision and can provide information for up to 14 months. When an episode occurs, the patient places a small hand-held activator over the device to record the ECG, although the device can also be programmed to record automatically.

On 2nd March 2007, FDA panel voted against the approval of Medtronic's implantable haemodynamic monitor (Chronicle), which was designed for patients with heart failure who may be at increased risk of decompensation. Chronicle continuously monitors intracardiac pressures through a sensor placed in the right ventricular outflow tract. The stored data can be transmitted by the patient to clinicians, who can increase the diuretics when they see elevations that signal impending volume overload. The clinical trial demonstrated a 21% drop in the composite rate of the primary end point after 6 months. However, FDA panel ruled that approval should not be given as statistical significance was not reached, thus suggesting that the ability to demonstrate that the diagnostic test is accurate and reliable in measuring what it's designed to measure is not sufficient for approval.

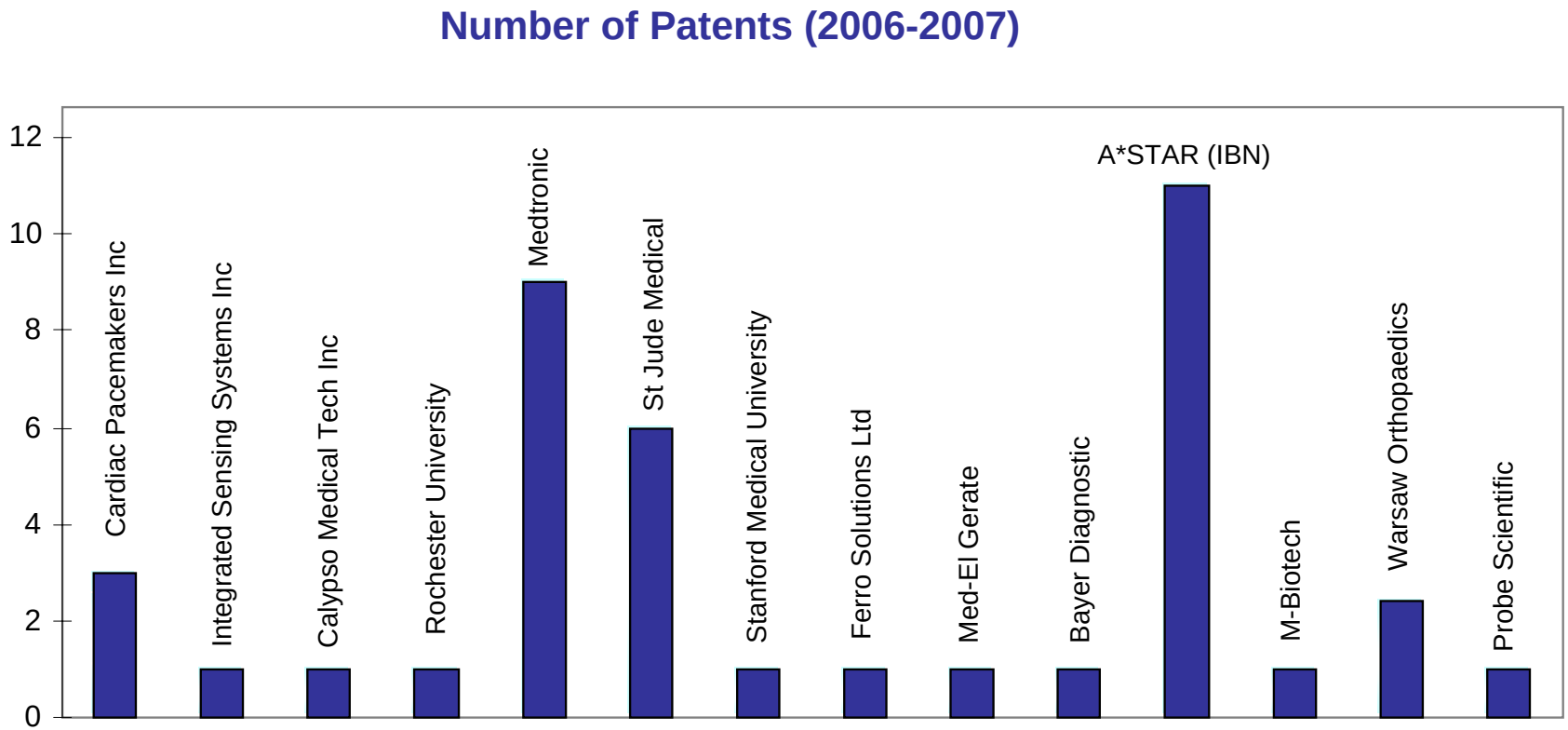
cardiomems™

CardioMEMS EndoSure s2™
Wireless Pressure Sensor

Implantable Pressure Sensor for Abdominal Aortic Aneurysms

Treatment of an aneurysm requires either traditional open surgery to remove the aneurysm or less invasive endovascular surgery, where a stent graft is placed inside the aneurysm sac to reduce pressure. However, current stent graft durability has been questioned and the procedure can also lead to the late development of endoleaks. As a result, endovascular repair requires long-term patient monitoring.
CardioMEMS has developed a wireless, battery-free, implantable sensor that is inserted during endovascular repair. Real-time pressure information is transmitted via RF to an external electronics module, which then communicates this information to the patient's physician.

Wireless Implantable Sensor IP Landscape



Therapeutic Implants: Neurostimulation

Neurostimulators

MARKET SHARE

Global

Current market size (2004) - $1 billion

CAGR (2004–2010) – 35%

Potential market size (2010) – $6.1 billion

CHALLENGES

Demonstrating sufficient cost-benefits compared to drugs to obtain reimbursement

Strict and stringent imposition of FDA regulation

Accompanying risk of infection

Development of nanoelectrodes

DRIVERS

Development of biocompatible materials

Emergence of new power source technology eg externally rechargeable batteries

RESTRAINTS

Complete biocompatibility

Technology Applications

- Neurostimulatory devices are implants, which are connected to electrodes placed in specific regions of the brain or central nervous system and designed to deliver precise patterns of electrical pulses via specific nerve pathways to treat a variety of conditions.
- They are considered to be an outgrowth of the pacemaker industry, where such implants are used to manage cardiac rhythm.
- Devices offer a number of advantages over traditional pharmaceutical therapies: side-effects are minimised as neurostimulatory action is site-specific; therapies are reversible; devices can be a treatment option for patients, who have no other therapeutic alternative. Admittedly, the cost of implantation is high. However, devices may still be more cost-effective in certain chronic conditions, where a lifetime of drug management is required.

Potential Applications:

- Deep Brain Stimulation
- Gastric Electrical Stimulation
- Sacral Nerve Stimulation
- Spinal Cord Stimulation
- Vagus Nerve Stimulation

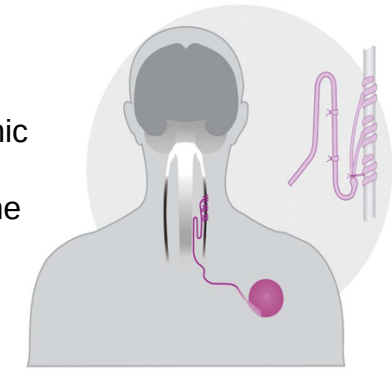
- Auditory Correction
- Depression
- Epileptic Seizure Control
- Incontinence
- Migraine
- Movement Disorders
- Pain Management
- Obesity
- Sleep Apnoea
- Spinal Cord Injury
- Stroke Therapy
- Visual Correction

Technology Snapshot

- Technology emerging in the neurostimulation field is considered to be potentially disruptive and provides device companies with an opportunity to tap into chronic disease markets such as pain and migraine management where patient populations number in the millions.

Cyberonics®

Treatment of Epilepsy and Depression



VNS Therapy is a non-pharmacologic treatment approved for pharmacoresistant epilepsy and chronic recurrent treatment-resistant depression.
A small generator is implanted under the skin in the left chest area with small wires running under the skin to the left vagus nerve in the neck. This delivers precisely timed and measured mild electrical pulses to the vagus nerve in the neck which in turn activates various areas of the brain. Physicians can adjust the timing and amount of stimulation the patient receives using an external programming system.

Boston Scientific

Precision Plus™ implant, remote control and charger

Treatment of Neuropathic Pain

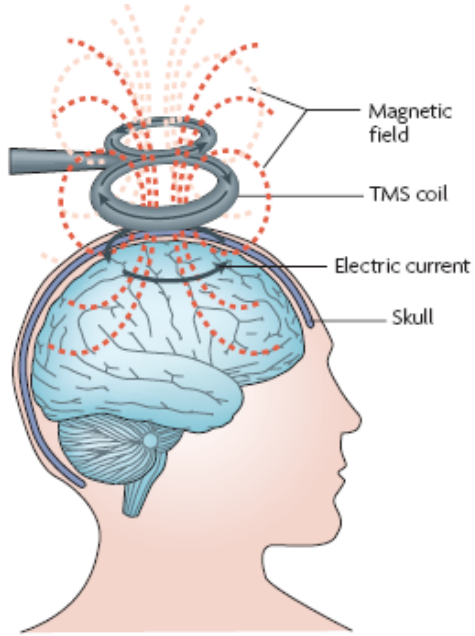
Spinal cord stimulation (SCS) therapy is used for treatment of neuropathic pain, a condition where the nerve fibers are injured or impaired and results in a change in nerve function causing severe pain. The treatment is FDA-approved and reimbursed by the majority of US health plans.

The newest system, Precision Plus, is designed to precisely and simultaneously target pain in up to four areas and adjusts for impedance changes that occur with physiological adaptation.

The system includes a patient joystick that allows patients to sculpt desired fields of pain relief and Precision Leads, which are designed to sculpt the electric field and eliminate ‘dead spots’. Advances in battery technology have also halved battery size and improved battery performance.

TMS – a non-invasive alternative?

- Transcranial Magnetic Stimulation is a pain-free method of stimulating the brain through the intact scalp. The stimulator produces a magnetic field similar in size to a MRI scanner but lasts only a millisecond. The field induces electrical currents and is thought to activate axons of neurons in the cortex and subcortical white matter.
- This technology has received considerable attention in recent years and has been used to explore therapeutic opportunities in an staggering array of conditions from stroke to addiction and OCD to depression. The quality of trial design is, however, variable and so efficacy remains questionable and mechanism of action is still poorly understood.
- Saying that, it is clear that TMS can cause changes in the brain that outlast the period of stimulation and can lead to small yet measurable changes in performance in healthy individuals. Although the technology is unlikely to repair or restore function to specific sets of synaptic connections damaged by disease or injury, it may still be possible to increase the ability of the brain to undergo compensatory changes and so help the brain restore itself. If so, the technology may be more successfully employed in addressing conditions such as stroke rather than depression.
- A number of early-stage companies such as Neuronetics and Neuralieve are focused on the development of non-invasive neurostimulators based on TMS technology. These target depression and migraine respectively.



Source: Nature Reviews Neuroscience 2007

Source: Neuronetics

Players

MAJOR PLAYERS (GLOBAL)

Medtronic Inc.

Boston Scientific Corp

St Jude Medical

Cyberonics

SELECT COMPANIES

BrainsGate Ltd.

NDI Medical

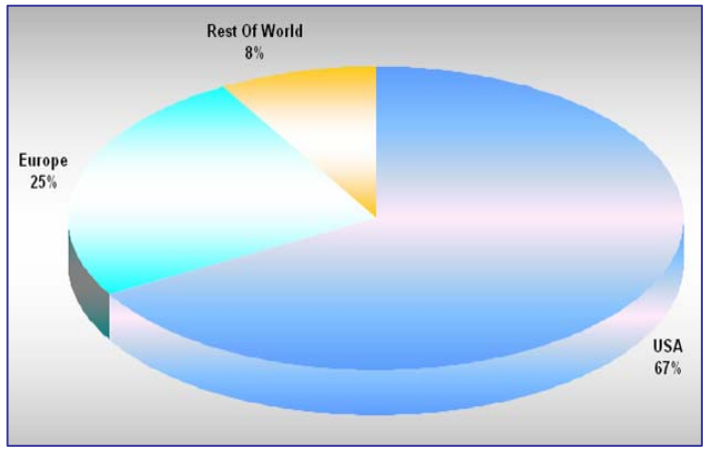
NeuroPace

NeuroVista Corporation

Northstar Neuroscience

Quallion

Second Sight



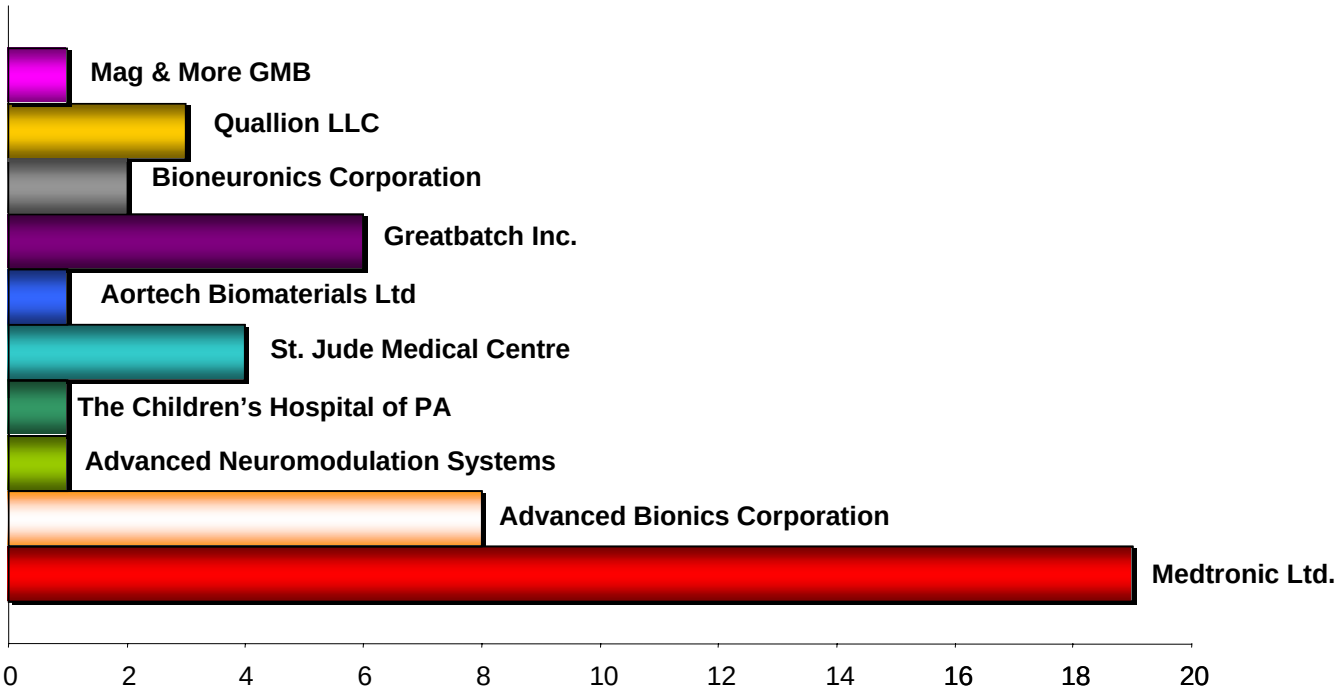
St Jude's Medical acquired Advanced Neuromodulation Systems in Nov 2005 for $1.3B.

Boston Scientific Corp acquired Advanced Bionics in June 2004 for $740 million in cash plus earn out payments tied to future performance milestones.
Boston Scientific recently sold interests in its auditory business and drug pump development program to former principals and shareholders of Advanced Bionics for $150 million (Jan 2008), while retaining sole management control of the Pain Management business.

Northstar Neuroscience saw its share price drop dramatically in January on release of data from its EVEREST pivotal trial. No improvement in hand and arm function in stroke survivors was noted.

IP Landscape

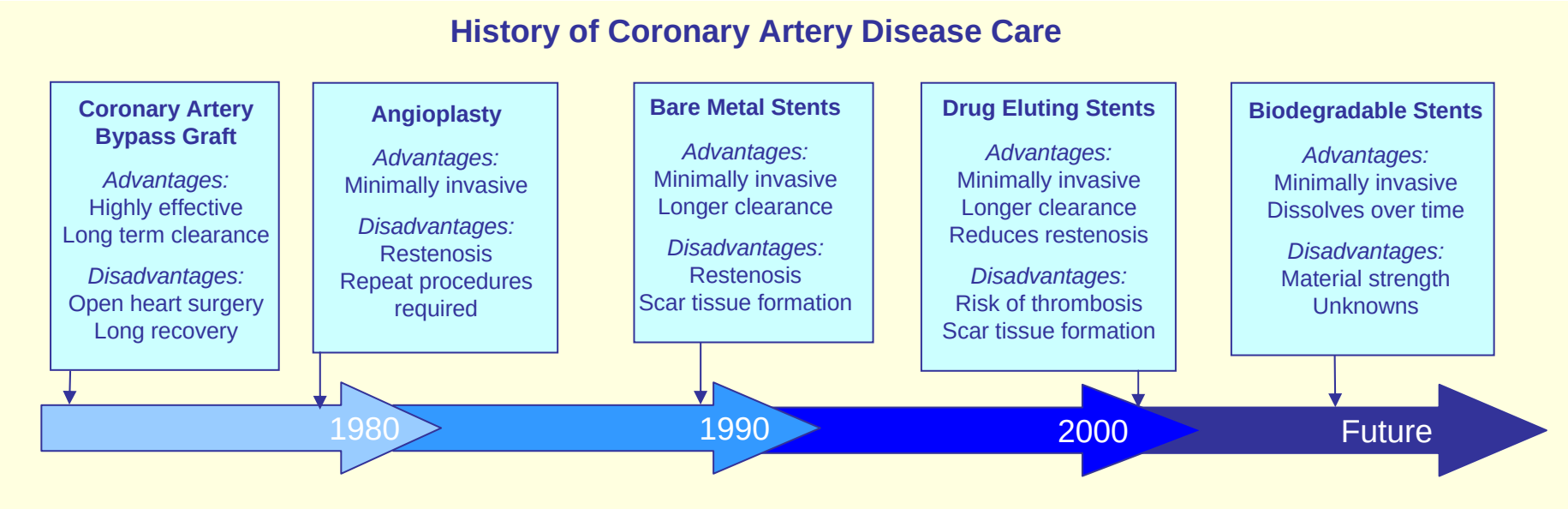
Number of Patents (2006-2007)



Therapeutic Implants: Stents

Treating coronary artery disease

- Achieving and maintaining optimal and rapid restoration of blood flow in the infarct-related vessel is the primary treatment goal for patients with acute myocardial infarction. The technologies developed to achieve this treatment goal have improved significantly since early 80's.



- A stent is a wire metal mesh tube used to prop open an artery during angioplasty. The stent is collapsed to a small diameter and put over a balloon catheter, which is then moved into the area of the blockage.
- When the balloon is inflated, the stent expands, locks in place and forms a scaffold, which holds the artery open. The balloon is deflated and removed and the stent stays in the artery permanently, holding it open and improving blood flow. The endothelium grows over the metal surface of the stent within a few weeks of the stent being placed.
- Drug (sirolimus or paclitaxel) eluting stents have revolutionized the area, significantly reducing restenosis and revascularisation rates compared to bare metal stents.
- Stents can also be used to treat peripheral arterial disease (PAD) where angioplasty and stenting of small vessels below the knee, for example, are now successfully staving off amputation among older patients with PAD.

Market: Coronary Stents

MARKET SHARE

U.S

Total Revenue (2006) - $2.8 billion

CAGR (2007-2013) - 6.0 %

Projected Revenue (2013) - $4 billion

CHALLENGES

Safety concerns of current drug eluting stents

Entrenched market leaders and low degrees of current product differentiation

DRIVERS

Accelerated obesity rates in certain population segments heightens physician demand for percutaneous coronary intervention

Improved clinical efficiency shifts market demand for minimally invasive catheter-based surgery

Imaging developments improve accuracy of implantation and surgical procedure, boosting confidence in approval of therapy

The next generation of DES could expand device applicability and lower safety concerns

RESTRAINTS

Market saturation combined with new market entrants leads to price erosion

Negative press on the stent market has tempered usage of drug eluting stents

Spiraling healthcare costs, particularly for CVD, is causing providers to adopt a more econometric-based approach to decision making

Market: Peripheral Stents

MARKET SHARE

Europe

Total Revenue (2006) - $160 million

CAGR (2007-2013) - 12.9 %

Projected Revenue (2013) - $376 million

CHALLENGES

Lack of trained surgeons increases the complexity of endovascular surgeries and reduces product success

Lack of reimbursement results in patients opting for surgical procedures

Stent placement malfunctioning

DRIVERS

Increase in R&D to improve quality of products

Improved diagnosis of PAD and awareness among patients has increased procedure rates

Improving clinical trials show better results compared to alternate treatments

Increase in emboli protection devices results in better surgery

Cost effectiveness and advantages of being minimally invasive

RESTRAINTS

Limited applicability of stents as PAD treatment strategy curbs usage

Brand loyalty affects acceptance of new products; Boston Scientific captured nearly 70% of market within a year of introducing TAXUS

Variation in product performance (eg stent fracture), risk associated with surgeries (eg restenosis, stroke), and concerns over safety

Lack of centres to perform these surgeries results in long waiting lists and unmet potential

Troubled times

- Drug Eluting Stents (DES) are widely viewed as the device industry's only true blockbuster product – a fusion of pharmaceutical and device technology that heralded a new era of drug-device hybrids.
- Rapid adoption of DES technology was observed with usage among interventional cardiologists peaking during 2006 at around 90%. Approximately two-thirds of all DES were implanted for off-label indications.
- However, a series of clinical trial results has now significantly eroded confidence in this product.

Study	Outcome: SAFETY & EFFICACY CONCERNS
BASKET-LATE (2006)	Reported DES to result in higher rates of mortality and myocardial infarction compared to bare-metal stent (BMS), which was largely attributable to late stent thrombosis.
Meta-Analyses (2006)	Observed DES patients to have a higher late mortality compared to BMS.
SCAAR (2006)	Reported patients in the DES arm to experience higher 3-year mortality than those with BMS.
COURAGE (2007)	Reported no benefit of percutaneous coronary intervention (PCI) compared to optimal medical therapy in patients with stable angina. However, nearly 70% of PCI is performed for Acute Coronary Syndromes (unstable angina or acute MI).

- As a result, DES usage in US dropped from 90% to approx 60% in 2007 and, in fact, the sector witnessed a resurgence in BMS (a rare example of reversion to prior-generation technology).
- Industry responded by highlighting the design flaws of these studies, including the relatively small sample numbers, and pointed towards other studies with more positive outcomes.

2007 slightly more upbeat

- FDA also reviewed the evidence and at the end of 2006 concluded that:
  - DES are associated with a small increase in stent thrombosis but this was not associated with increased risk of death of MI compared to BMS
  - DES are not associated with increased rate of all-cause mortality compared to BMS
  - Concerns about thrombosis do not outweigh benefits of DES compared to BMS when DES are implanted within limits of their approved indications for use
  - Off-label use of DES is associated with increased risk of stent thrombosis, death or MI compared to on-label use
  - Data on off-label use are limited and additional studies are need to determine optimal treatments for more complex patients.

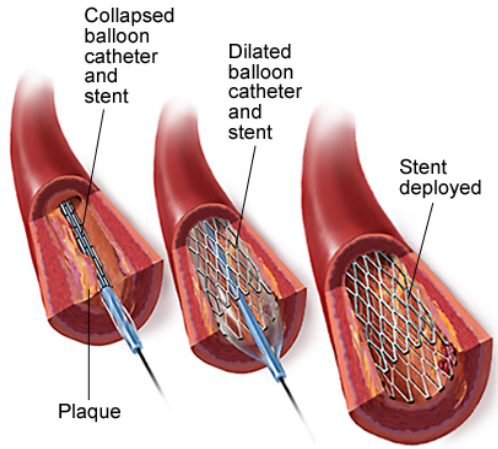
- Trial results reported towards the end of 2007 were also slightly more upbeat.

Study	Outcome: SAFE & EFFICACIOUS
SCAAR (2007)	Reported an increase in adverse events after six months for patients treated with DES but, unlike the earlier SCAAR report, the latest analysis found no overall increased risk of death for patients treated with DES as compared with bare-metal stents. Significantly lower risk of restenosis noted.
COURAGE (2007)	Subset analysis found PCI to be superior to medical therapy in patients with ischaemia.

- Boston Scientific have also announced that additional studies are being conducted to demonstrate safety and efficacy of TAXUS stent in extended uses.

Innovation Potential

- There is still clear scope for significant innovation in this segment given the concerns over current technology.
- There are 4 key attributes of drug eluting stent technology, which could be the focus of a development program:
    1. Efficacy
    2. Safety
    3. Deliverability
    4. Durability
- First generation DES (Taxus & Cypher) are already demonstrably superior to bare-metal stents but only in terms of efficacy. Therefore, safety, deliverability and durability each represent a promising area for future stent innovation. Safety, in particular, could prove to be a key product differentiator given recent events.
- Decreasing the risk of late stent thrombosis (LST) is key to improving product safety. Early discontinuation of anti-platelet therapy, delayed endothelialisation, polymer hypersensitivity and strut thickness are all thought to increase the risk of LST. Optimisation of these device attributes should improve product safety.

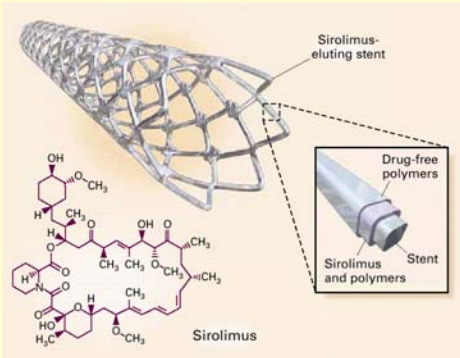


http://www.taxus-stent.com

Innovation Potential

Scope for Innovation (near-term & long-term)

- Reducing strut thickness & improved radiopacity
- Improved deliverability
- Biostable polymer refinements
- Reduced drug dosing and optimal release kinetics
- Bioabsorbable polymers and polymer-free systems
- Surface modification approaches
- New stent platforms
- Fully bioabsorbable stents
- Stents coated with antibodies or gene therapy agents



Cordis Cypher Sirolimus-Eluting Coronary Stent

- The next generation products – Medtronic's Endeavor and Abbott's Xience – begin to address some of these issues.

Endeavor Resolute

- Combines an advanced stent platform (thin strut) with the drug zotarolimus (a Sirolimus analogue) and a biocompatible polymer (phosphorylcholine), which is designed to simulate the outside surface of a red blood cell.
- Offers a safety profile similar to bare metal stents
- Has superior reduction in restenosis compared to BMS and comparable clinical outcomes to Taxus.
- The cobalt-alloy stent has a low profile, with a strut thickness of 0.0036 inches (91 µm), designed to improve tracking and crossing in tortuous anatomy.

Bioabsorbable Stents

- The therapeutic need for stenting is temporary; they have no utility once healing and re-endothelialisation has taken place. Indeed, their presence may actually lead to late thrombosis and chronic inflammation. They also prevent the lumen expansion associated with late favourable remodelling and pose as artefacts with modern imaging techniques.
- Bioabsorbable stents have the advantage of leaving behind only the healed natural vessel once the stent is bioabsorbed so removing the need for prolonged anti-platelet therapy and reducing the likelihood of LST. These stents would also be suitable for complex anatomy where stents impede vessel geometry and are prone to crushing and fractures. They could also be used as a delivery device, transferring drugs to the site of interest or genes (such as those that code key regulatory pathways of cell proliferaton) inside cells of the arterial wall.

Bioabsorbable stents should have:

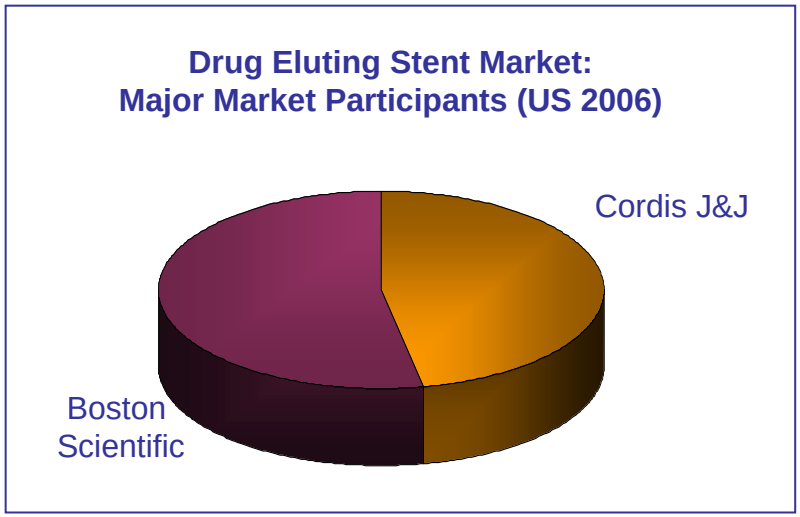
1. Sufficient strength to avoid recoil
2. Controlled rate of degradation and corrosion
3. Biocompatibility with vessel wall
4. Lack of toxicity

There are 2 types of material currently used:

1. polymeric based – such as poly-L-lactic acid (PLLA) and polyglycolic acid (PGA)
2. metallic based – iron and magnesium

- However, the polymeric biodegradable stents currently in development do exhibit several limitations. They are associated with local inflammation, bioabsorption is slow and stents are radiolucent and so impair accurate positioning. They tend to have lower material strength and so require thick struts that impede delivery. Metal bioabsorbable stents have the potential to perform similarly to current metal stents though their biocompatibility will depend on their solubility and released degradation products.
- As a result, it is clear than significant R&D is required to bring biodegradable stents to the marketplace.

Players

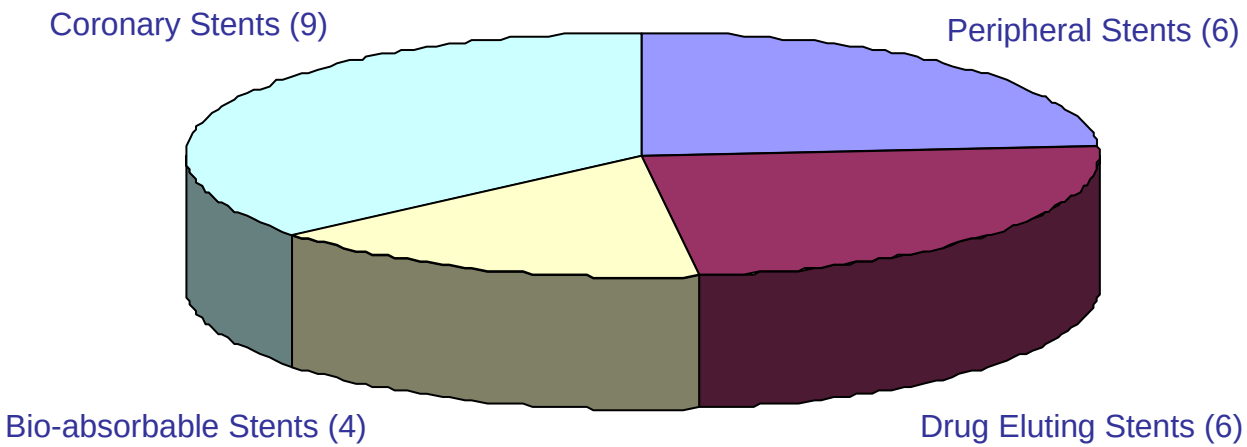


KEY DES PLAYERS (GLOBAL)

- Boston Scientific
- Cordis Corp (J&J)
- Medtronic
- Abbott Laboratories
- Conor Medsystems (acquired by J&J in 2007)
- Xtent Inc.

- Two new entrants to US market are expected in 2008. FDA has already approved Medtronic's Endeavor. This was the first drug-eluting stent to be authorised for US market entry since Taxus (Boston Scientific) was approved in March 2004. Abbott Labs are widely expected to gain FDA approval for its Xience stent shortly and so join the US market by second quarter of 2008.
- The market is currently dominated by big cardiovascular players. Indeed, DES are one of the few cardiovascular device segments that didn't emerge largely on the back on VC funding. However, recent events may serve to open up the market to new entrants.
- The cost of bringing new DES to market is, however, likely to rise. Current estimates are that a new DES start-up will require more than $100M in financing and 5-7 years of product development time before achieving FDA clearance.

IP Landscape



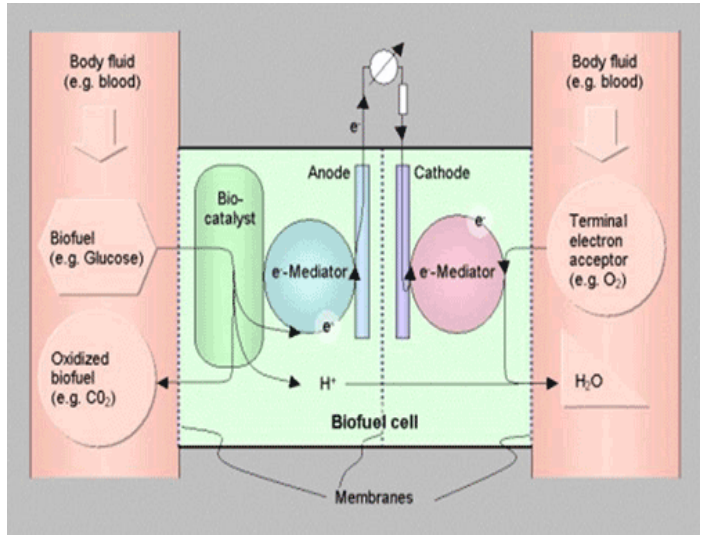
Implant Enabling Technologies

Enabling Technologies

Long-lived Batteries

- An increasing number of sensing implants are placed for long-term use. However, the limited life-span of current implant batteries often necessitates surgical replacement. It is estimated, for example, that around 100,000 cardiac pacemakers are replaced annually at cost of approx. $10K each.
- Several groups are tackling this issue. For example, participants within the Healthy Aims Framework 6 programme are working towards the development of a battery-independent sustainable power source – the implantable Biofuel Cell. Such fuel cells could be used as a sustainable power supply, harvesting the body's natural energy through conversion of chemical energy (in the form of circulating glucose) to electrical energy.

BioFuel Cell



Biocompatible Materials

- A major challenge for implant development is prevention of implant rejection. The body typically rejects the implants as foreign objects, eliciting an immune response and causing proteins and fibrotic tissue to grow over the implants, so interfering with their ability to function.
- This issue is being addressed with the development of biocompatible implant coatings. Biocompatible materials or biomaterials can be defined as systemically and pharmacologically inert substances designed for implantation within or incorporation with living systems and include materials such as nitinol, PEEK and titanium. Ideally biocompatible coatings should not give rise to an immune response and also be flexible, able to conform to the surface of irregularly shaped devices, be impermeable to avoid ingress of biological fluids and show good adhesion to the underlying device.

Biocompatible Surface Coatings

MARKET SHARE

U.S.

Present (2005) - $2.4 billion

CAGR (2005-2012) - 5.3%

Potential (2012) - $3.5 billion

CHALLENGES

Demand for clinical proof against the use of traditional alloys

Long-term material performance

Difficulty in obtaining FDA approval

Complete biocompatibility and high cost

DRIVERS

Active lifestyle of people

Increased reimbursement levels benefit implant market

Biomaterials Access Assurance Act of 1998 reduces litigation risk for material suppliers

Better understanding of polymer structure and compatibility issues

RESTRAINTS

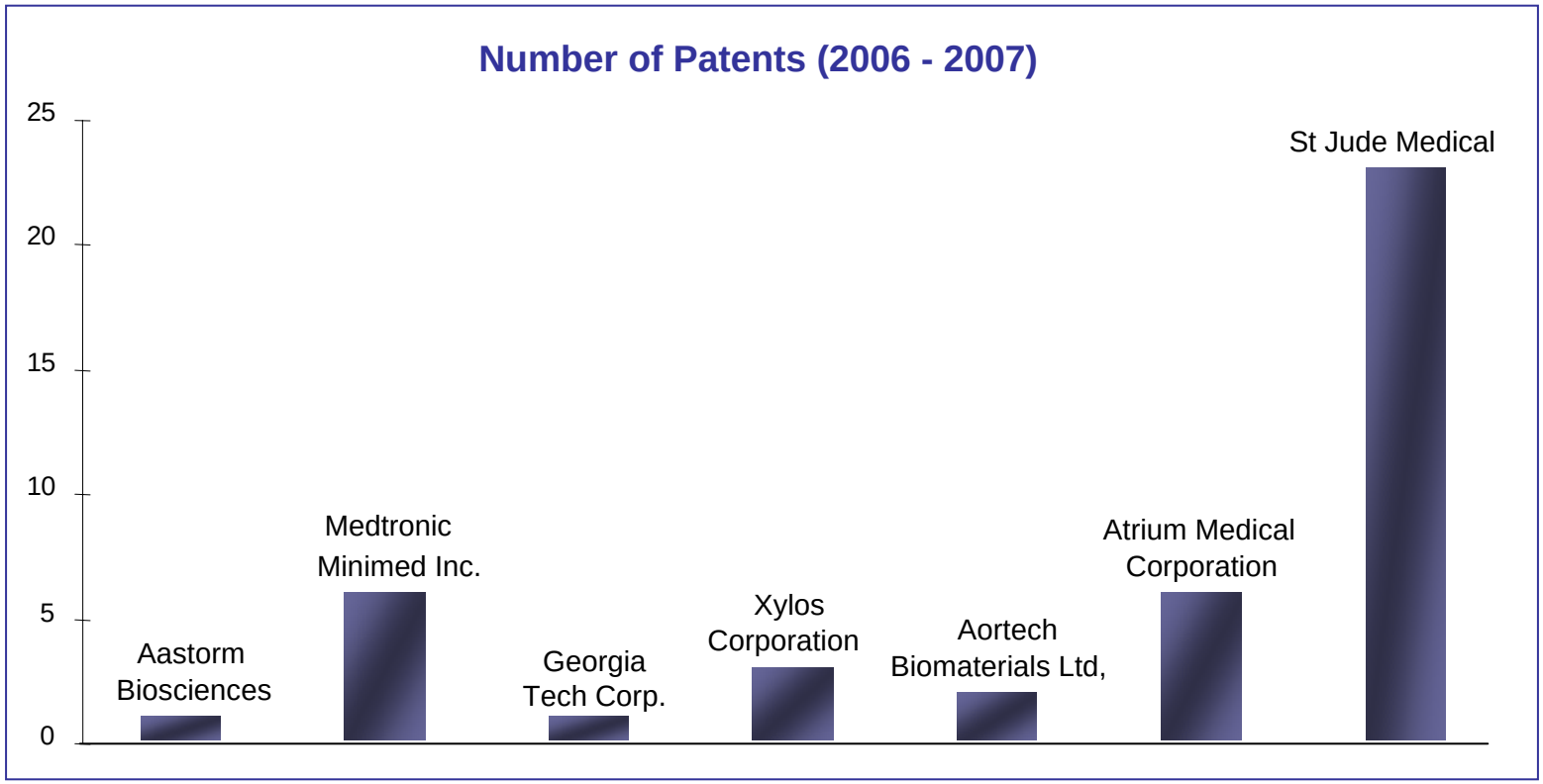
Higher cost of metal and membrane technologies

Processing biomaterials is a difficult task

High entry barrier restrains the growth of innovative materials

Strict regulatory requirements of new materials

Biomaterials IP Landscape

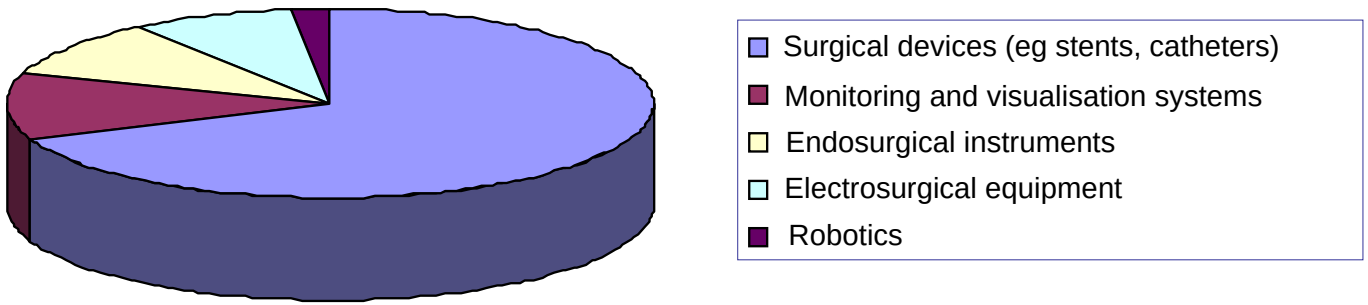


Minimally Invasive Surgery

Minimally Invasive Surgery

- Global market for minimally invasive surgery (MIS) devices and instruments was estimated to be worth $12B in 2005 and is predicted to reach $18.5B by 2011
- In 2005, US accounted for approximately 60% of the world market and is predicted to grow at an AAGR of 7.2%
- Technology offers significant benefits to both patients and healthcare providers: lowered costs; reduced trauma and pain; postoperative recuperation times; lowered infection rate; reduction in blood loss and cosmetic advantages.

MIS Market: Product Segmentation (2005)



- Principal applications are: gastrointestinal surgery; gynaecology; urology; non-cardiac vascular surgery; orthopaedic and cosmetic surgery.
- This e-scan will focus on market and innovation opportunities for minimally invasive technology within cosmetic surgery and orthopaedics.

Cosmetic Procedures

Cosmetic Surgery Market

MARKET SHARE

Europe

Total Revenue (2006) - $1.5 billion

CAGR (2007-2013) – 19.4 %

Projected Revenue (2013) - $5.3 billion

CHALLENGES

Reimbursement issues in certain regions of the world especially in EU

Lack of long-term clinical studies leading to product duplicity

Unregulated nature of cosmetic procedure industry and lack of professional expertise

DRIVERS

Consumer preference for less invasive cosmetic procedures

Social acceptance of cosmetic procedures

Increase in disposable income & relatively easy credit access

Ageing population and obesity epidemic

RESTRAINTS

Pricing pressures for new entrants

Fears and myths of long-term effects

Potential risk of infection

Market Segmentation

Cosmetic Procedures

Surgical

- Breast enhancement
- Liposuction
- Body contouring
- Eyelid surgery
- Nose jobs

Europe:

Market Revenues (2006):	$0.96B
Potential Revenues (2013):	$2.67B
CAGR (2006-2013):	15.8%

Non- Surgical

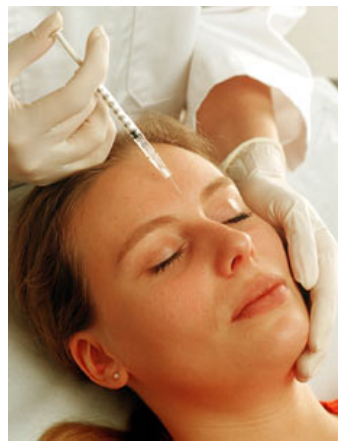
- Botox
- Facial Fillers
- Aesthetic Lasers
- Microdermabrasion
- Chemical Peeling

Europe:

Market Revenues (2006):	$0.57B
Potential Revenues (2013):	$2.62B
CAGR (2006-2013):	24.5%

Market

- There is a clear trend towards decreasing the invasiveness of cosmetic surgery procedures.
- According to the American Society for Aesthetic Plastic Surgery, minimally / non-invasive cosmetic procedures, such as energy-based aesthetics and microdermabraision, have risen dramatically with surgical or invasive cosmetic procedures accounting for only 17% of the total cosmetic procedures performed in 2006.
- In addition to predicted growth, this market is also attractive for a number of other reasons:
  - It is largely self-pay and so removes reimbursement risk for investors.
  - Product development cycle is shorter for less invasive, 'superficial' treatments as adverse events typically manifest themselves within 6 months.
  - Rapid adoption of new technologies by end-users as aesthetic practices strive to stay competitive in a consumer-driven market.
  - Repeat purchase boosts revenue stream.



Aesthetic Injectables

- There are an estimated 1 million users of facial injectables in the US. The major challenge lies in identifying a way to penetrate the 20-30 million strong US consumer base, who have the interest and financial capacity to participate in this market but chose not to. Decreasing the invasiveness of the procedures may encourage adoption.

Neurotoxins

- Botox is the most commonly used non-surgical procedure
- Sales reached $982M in 2006, a 24% increase in growth and up from the 18% recorded in the previous year. Owned by Allergan.
- Product marketed for both cosmetic and therapeutic indications.

Revance THERAPEUTICS

- Revance is developing a topical botulinum toxin to offer an alternative to the injectable form for both cosmetic and therapeutic (hyperhidrosis) applications. Potential benefits include improved product tolerability, pain-free, no loss of facial expressions and also, for hyperhidrosis, a reduction in side effects and removal of need for anaesthetic. Currently in phase 1 clinical trials.
- Recently raised $45M in series C financing.

Dermal Fillers

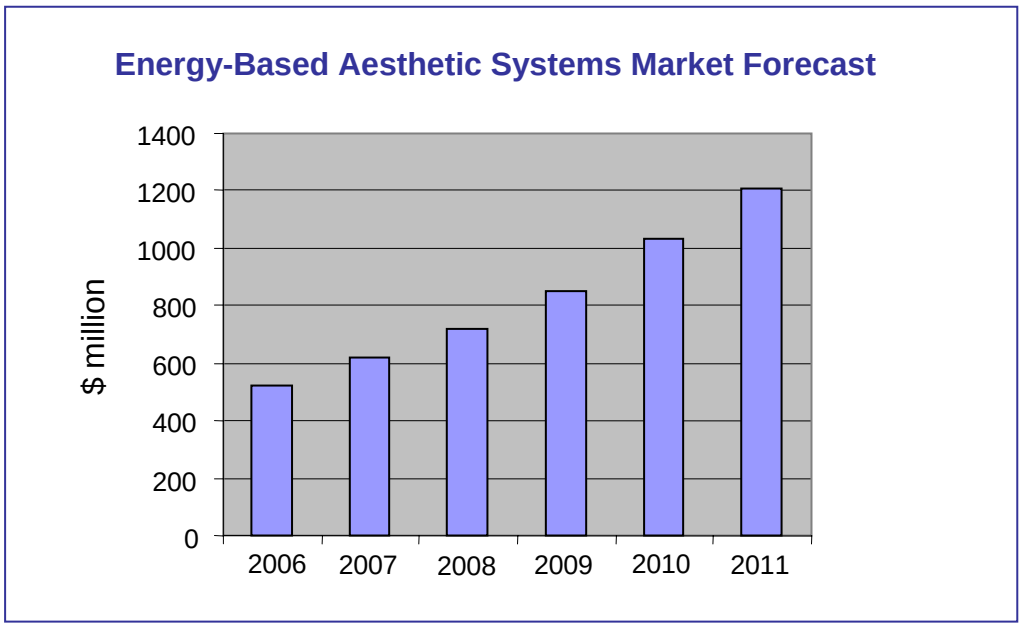
- In 2006, the global market was estimated to be $480M and growing at rate of 19%.
- 1.58 million procedures were conducted in US in 2005, 75% of which were hyaluronic acid based and 14% collagen based fillers.
- There is need for formulations, which are less invasive and have a prolonged duration of effect.

Juvéderm™ INJECTABLE GEL

- Juvederm is a hyaluronic acid gel that is designed to flow easier into skin and approved to last up to 1 year. Acquired by Allergan in 2007 for $216 million from Groupe Corneal Laboratories.
- Currently on the market. Primary indication for use is diminishing marionette lines & nasolabial folds compared to Botox, which primary indication is reduction of glabellar lines.

Energy Based Aesthetic Devices

- Energy based aesthetic devices utilise various forms of energy such as laser, radiofrequency, ultrasound and intense pulsed light to painlessly and non-invasively perform a variety of cosmetic procedures.
- The number of energy-based aesthetic procedures performed in the US is expected to grow from around 2.6 milllion in 2006 to more than 6 million in 2011, with corresponding aesthetic device CAGR estimated to be 18%.



Applications

- While laser hair removal is the leading energy-based aesthetic application in the US, new applications are appearing such as cellulite removal, skin resurfacing and skin tightening.

Selected Energy-Based Aesthetic Applications: Market Forecast 2006-2011 (in $M)

Year	Hair Removal ($M)	Skin Tightening ($M)	Cellulite Reduction & Non-Invasive Fat Removal ($M)
2006	296	76	13
2007	341	97	20
2008	375	122	40
2009	405	158	68
2010	437	210	125
2011	470	265	155
CAGR	**9.7%**	**28%**	**64%**

- However, the US device market is highly competitive, with more than 25 manufacturers of energy-based aesthetic equipment operating in this space in addition to smaller and emerging companies.

Fat & Cellulite Removal

- Non-invasive fat removal and / or cellulite treatment is viewed by many as the prime opportunity in the aesthetics device industry in the coming decade.
- The potential market size for cellulite treatment is huge with 85% of women reportedly have cellulite and prevalence cutting across all ages, fitness, economic and lifestyle boundaries.
- The potential market for non-invasive fat removal is also significant. According to American Society of Aesthetic Plastic Surgeons, 450,000 liposuction procedures and 170,000 abdominoplasties were performed in 2005 at an average per-procedure cost to patient of $2750 and $5500 respectively equating to a total expenditure of $2.2B. Decreasing the invasiveness of fat removal procedures should lead to market growth.
- Patient demand also appears strong despite the limited efficacy of current offerings.

ULTRASHAPE®

- Offers 2cm reduction in waist size
- Sold 170 systems last year (outside of US) at cost of $150K each
- Facilities owning the system are reportedly performing 30-35 treatments per month

CYNOSURE

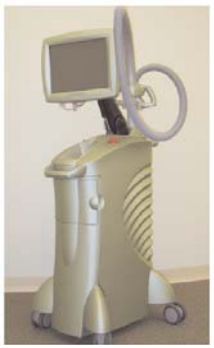
Syneron™

- Efficacy of both Cynosure and Syneron products ranged from 55-75%
- Typically 8-10 treatments at cost of $1.5-2.5K required with maintenance treatments needed approximately every 3 months.
- Syneron built sales up to $117 million in 2006; Cynosure had $78 million in sales in 2006.

- There is clear scope for technology innovation to improve outcomes. A new generation of devices is currently being developed using high frequency radiofrequency, ultrasound, heat or laser energy based technology to non-invasively remove fat and cellulite. As the market becomes more competitive, winners are likely to be those companies that discriminate themselves from the competition through demonstration of clinical efficacy.

Company Snapshot

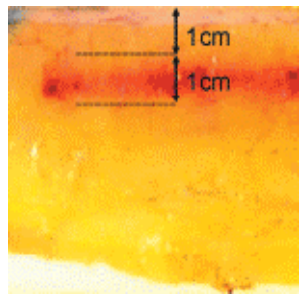
Improving the appearance of cellulite by reducing subcutaneous fat



- Non-invasive, dual wavelength laser that combines light energy, suction and mechanical massage to reduce cellulite
- Wavelength of 900nm is used to penetrate fat cells and liquefy the fat. A shorter wavelength of 650nm is used to increase cell permeability and facilitate fat clearance from the cell. These also help stimulate collagen production. Rollers help move the evacuated fat from interstitial space into the lymphatic system for drainage and a vacuum component helps laser diodes reach the right depth for tissue penetration. Consumers experience warm therapeutic massage.
- Efficacy demonstrated in a randomised, controlled trial with MRI taken pre and post treatment. 81% of the clinical study participants experienced “significant volumetric reduction in subcutaneous fat”.

Non-invasive body sculpting

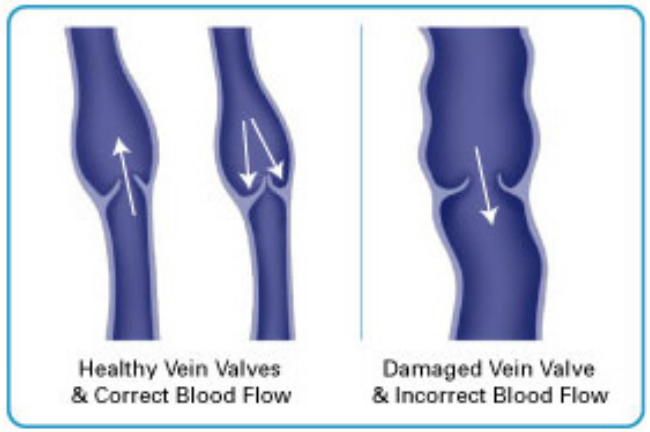
- An ultrasound transducer delivers energy across the skin surface at a relatively low intensity and brings this energy to a sharp focus in the subcutaneous fat. At the skin surface, the intensity of the ultrasound energy is low enough that no damage occurs. The focusing of the ultrasound beam at specific depths beneath the epidermis results in adipose tissue disruption. Macrophages are attracted to the area to engulf and transport the lipids and cell debris. This results in an overall reduction in local adipose tissue volume.



The LipoSonix transducer focuses to a precise subcutaneous depth to break down adipose tissue.

Hybrid clinical/cosmetic market

- Hybrid clinical & cosmetic markets also exist, such as varicose vein treatment.
- Varicose veins is a painful yet non-life threatening condition that is highly prevalent in Western populations, affecting up to 40% of Americans.
- Risk increases with age. More than half of US adults over the age of 60 suffer from the painful and unsightly venous disease.
- The demographic shift towards an ageing population together with the Baby Boomers need to 'look good and feel good' are two key factors driving innovation in this market.

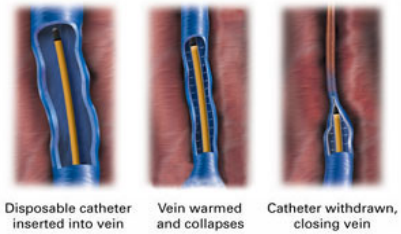


Source: www.vnus.com

- According to Millennium Research Group, the US market for varicose vein treatment devices was valued at nearly $105 million in 2006 with the European market valued at over $72 million in 2007.
- Surgical stripping is the gold standard treatment. However, it is an invasive, hospital based procedure conducted under general anaesthesia with long recovery times, post-surgical pain, nerve damage and scarring common. It is, therefore, not surprising that this is a significantly under-treated condition. While there are an estimated 1 million annual procedures in the US, some estimate there may be as many as 50 million US adults, who should but don't seek treatment, which makes varicose veins a potentially untapped market.
- Smaller companies are leading innovation in this area with Smith & Nephew the only large company player.

Varicose Veins Company Snap-shot

VNUS® MEDICAL TECHNOLOGIES, INC.



Minimally invasive alternative to vein stripping surgery

A thin catheter is inserted into the vein through a small opening. The catheter delivers radiofrequency (RF) energy to the vein wall, causing it to heat, collapse, and seal shut. Blood flow is re-routed through healthy veins. 90% of the treated veins remain closed and free from reflux 2 years after treatment. Patients report feeling only minor discomfort during the procedure and can resume normal activities immediately. Minimal to no scarring, bruising, or swelling is experienced following the procedure.

ANGIODYNAMICS®

VenaCure Laser Treatment

AngioDynamics has developed VenaCure as its lead venous product in a wider portfolio. The device treats reflux of the greater saphenous vein with laser light emitted to the target area through a thin fibre inserted into the vein, causing the vein to occlude while the body routes the blood to other veins. Offers immediate recovery, is pain-free and requires only local anaesthesia. Named one of Businessweek's Top 100 Hot Growth Companies for 2006.

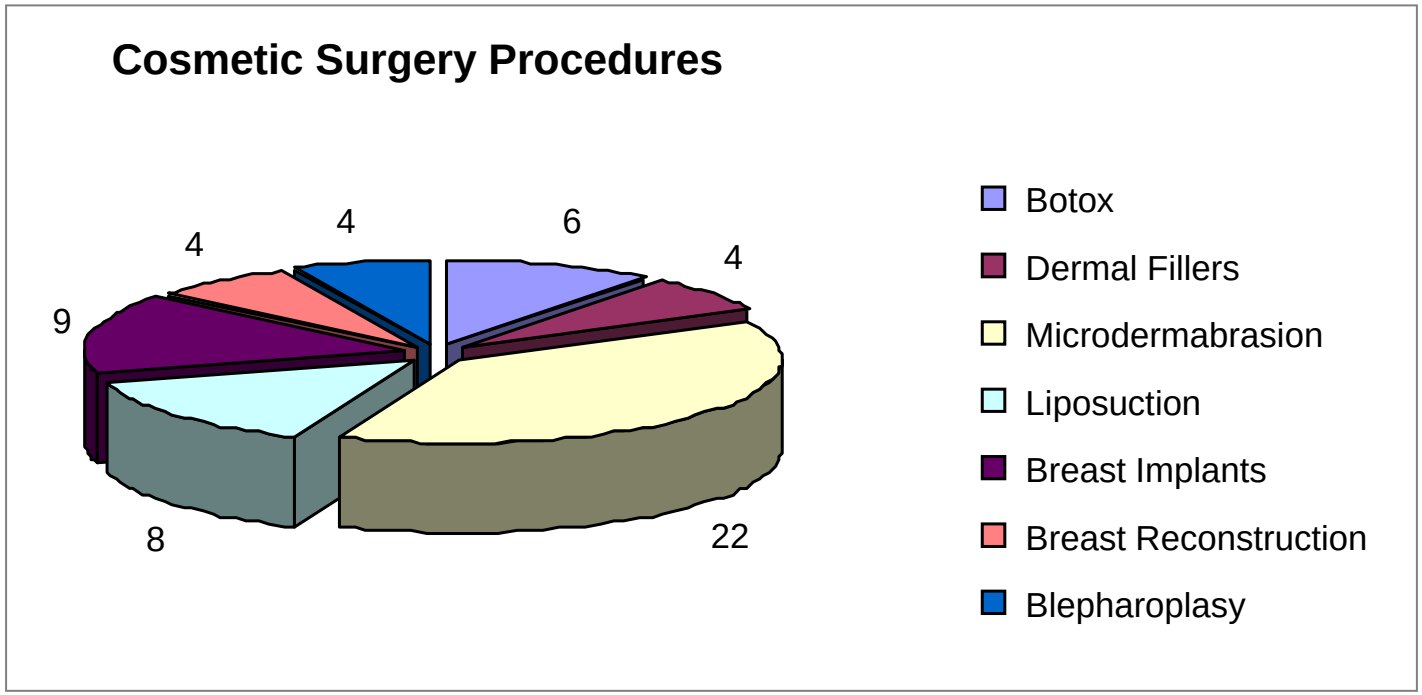
VASCULAR INSIGHTS

Mechanically enhanced endovenous chemical ablation

Founded in 2006 as a spin-out from Yale, Vascular Insights has developed a a minimally invasive, soft, flexible infusion catheter that enables varicose vein disease correction by mechanically enhanced endovenous chemical ablation (MEECA).

Reportedly requires no anaesthesia or hospitalisation and is pain-free. Unlike VNUS and AngioDynamics, the technology can be applied to greater (GSV) and lesser (LSV) saphenous veins and other varicosities.

IP Landscape



- The pie chart shows the patents filed for different cosmetic surgery procedures worldwide.
- Patents filed for a non-surgical procedures such as microdermabrasion are high, though botox remains the most commonly performed non-surgical cosmetic procedure.

Orthopaedics

Orthopaedics Market

MARKET SHARE

Global

Current market size (2006) - $29billion

CAGR (2005) – 8.8%

DRIVERS

Ageing population and rise in obesity

Uptake of orthopaedic surgery at earlier age

Development of better and longer-lasting implants & materials

Development of minimally invasive procedures

- The fastest growing segments are orthobiologics, spinal and trauma, whilst the more established markets for reconstruction implants and arthroscopy equipment are exhibiting more modest growth rates.
- The spinal market became the largest segment during 2006, surpassing the knee implant market for the first time.
- This e-scan will focus on opportunities in two segments: spinal and orthobiologics.

Minimally Invasive Spinal Surgery

- Minimally Invasive Spinal Surgery (MISS) is a relatively nascent but continually evolving area of focus for minimally invasive technologies.
- It can be defined as the performance of spinal surgery through small incision(s), usually with the aid of endoscopic visualisation.
- It enables surgeons to effectively treat disorders of the spinal discs with minimal muscle related injury with significant advantages to the patient.

The Benefits of Minimally Invasive Spinal Surgery

- In 1990s the state-of-the-art procedure for fusion of the lumbosacral spine was instrumented posterolateral fusion, which required removal of back muscles from their spinal attachments.
- However, dissecting the muscles results in significant perioperative pain, requiring significant pain medication and delaying return to full activity. Various layers of the individual muscle scar to one another resulting in a loss of their independent function. Wasting away due to loss of innervation is also noted and a permanent weakness of the back muscles results, which may limit patient's ability to perform physical work and is termed fusion disease.
- The minimally invasive spinal surgery techniques that have been developed offer significant advantages. These include reduced length of hospital stay, reduced requirement for postoperative pain medication, quicker recovery times, and avoidance of fusion disease.

- With the innovations in optics and video equipment, retractor and instrumentation systems, image-guided systems and new biological agents most of the traditional 'open' spine procedures can now be performed in a minimally invasive way. It is anticipated that further applications of minimally invasive approaches to spinal surgery will be observed in the near future with resultant reductions in morbidity.

Minimally Invasive Spinal Surgery

MARKET SHARE

US

Current market size (2006) - $2billion

CAGR (2006–2013) – 9.0%

Potential market size (2013) - $3.7 billion

CHALLENGES

Lack of differentiable products (spinal fusion & fixation) restricts the choice by surgeons

Domination by large medical device manufacturers restricts the growth of emerging companies

Mandatory physician training and evaluation delays market penetration for emerging technologies

DRIVERS

Increasing number of patients suffering from back pain

Better acceptance of minimally invasive techniques

Favorable increase in reimbursement rates for spinal surgery spurs a number of procedures expanding market opportunity

FDA approval of new devices reinforces growth

RESTRAINTS

Lack of clinical data dampens confidence and hinders reimbursement

Clinical complications associated with spinal procedures retard acceptance

Not every spine problem is treated this way, nor is minimally invasive spinal surgery the best choice for all patients

Spinal Implant Market

MARKET SHARE

Global

Current market size (2006) - $5.3billion

CAGR (2005) – 17%

DRIVERS

Move from fusion technologies to motion-preserving devices

Ageing population, rise in obesity and high prevalence of degenerative disc disease (DDD); DDD afflicts nearly half the US population between 40 and 60 years of age and approximately 90% of Americans over 60

Treatments for younger patients and uptake of orthopaedic surgery at earlier age

Development of better and longer-lasting implants, materials & minimally invasive procedures

Strong patient demand

CHALLENGES

Market slowed in 2006 due to difficult market environment

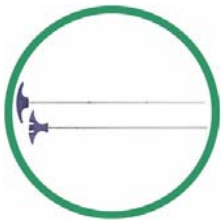
Clinical requirements of both the FDA (for product approval) and payers (for reimbursement) are leading to increased investment of time and money in order to gain product acceptance

Spinal Implants

- The spinal implants market has long been considered the 'sweet-spot' in the musculoskeletal industry.
- One of the industry's success stories is Kyphon, whose products are used in balloon kyphoplasty for treatment of spinal fractures caused by osteoporosis, cancer or trauma, and in stand-alone interspinous decompression for the treatment of lumbar spinal stenosis. Kyphon was founded in 1994, going public in 2002 and has since established itself as one of the fastest growing spine companies in recent years. It's portfolio includes:

The APERIUS™ PercLID™ System is the first Percutaneous stand-alone Lumbar Interspinous Decompression System.

KyphX® Exact™ Inflatable Bone Tamp: The KyphX® Exact™ IBT is a single plane inflation balloon designed for focused fracture reduction.



The Bone Filler Device is a stylet delivery system that provides mechanical advantage for introducing highly-viscous bone cement under low pressure in a controlled manner

KyphOs FS is the first cancellous bone substitute approved specifically for balloon kyphoplasty in stable traumatic vertebral body fractures.

- One of the device industry's biggest deals in 2006 was Kyphon's acquisition of St Francis Medical for $725M. St Francis's spinal motion preservation technology, the X STOP implant, was the first FDA-approved interspinous process device designed to treat lumbar spinal stenosis. Consolidation continued in 2007 with Medtronic acquiring Kyphon in Nov for $4.2B.
- There is believed to be significant scope for innovation in this sector, particularly in relation to motion preservation.

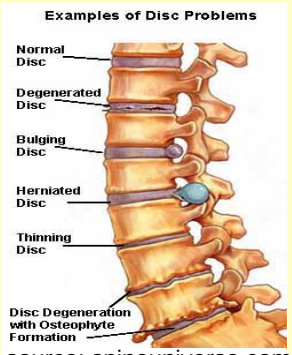
Motion Preservation

- While there are a number of factors driving growth in spinal orthopaedics, none is believed to be more important than the fundamental shift from the current leading spine fusion treatments to motion preservation approaches such as artificial discs and prosthetic disc nuclei devices. These devices aim to preserve the integrity of the spine while restoring normal physiological motion.

Spinal Fusion to Motion Preservation

The standard treatment for degenerative disc disease (DDD) is a surgical technique known as fusion, where the spine is strengthened and stabilised by fusing vertebrae together using bone graft or a graft substitute. Rods or screws are often used to facilitate fusion. However, patients lose a certain amount of mobility and flexibility in their spines as a result.

Artificial intervertebral discs are an alternative to spinal fusion in the treatment of DDD. Unlike spinal fusion which achieves pain relief through immobilisation, artificial discs maintain motion at the operative level once the damaged disc has been removed. By preserving normal physiological motion, it is thought this may also reduce or prevent the development of adjacent segment degeneration. In addition to circumventing the need for bone graft and the pain associated with bone graft extraction, motion preservation techniques promise a faster recovery and return to normal activity.



source: spineuniverse.com

- Motion preservation is forecast to achieve 16% growth per year till 2011 when it is estimated that motion preservation technologies will achieve revenues of US$5.1 billion and account for 50% of the market.
- There are numerous start-ups and more established players addressing this market opportunity. DePuy Spine, for example, gained FDA approval for its Charite artificial disc, a technology acquired upon the purchase of Link Spine group in 2003. Synthes-Stratec have since gained approval for ProDisc-L in 2006 and Medtronic approval for its Prestige Cervical Disc in July 2007. Medtronic are presently awaiting approval for a second cervical disc (Bryan) and a lumbar disc (Maverick), which it expects to receive in 2008.
- Others, such as Cytonics Corp, are developing technology to improve current diagnostic techniques. OrthoMEMS is developing a chip that can be inserted non-surgically into the intradiscal space where it can track load, motion and therefore spine function.
- Many VCs are now beginning to view this market as over-heated given the rash of investments that followed the first generation deals. However, it is clear that an appetite for this sector still remains.

Implant Industry News

- While the industry may be viewed as healthy given the innovation potential and market dynamics, it looks like it may be entering an unsettled phase due to recent reimbursement and regulatory issues.

- FDA approval is no longer enough to ensure adoption of a new technology and the outcome data required to satisfy payers and gain coverage is reportedly a moving target. The disappointing sales of the DePuy Spine's Charite can be directly linked to the difficulty in obtaining reimbursement. CMS initially issued a non-coverage decision although others such as Kaiser Permanente have since elected to cover DDD.

- The US Department of Justice has been examining the physician-industry relationships of 5 of the major orthopaedic manufacturers: Biomet; Depuy Spine; Smith & Nephew; Stryker Orthopaedics; Zimmer Spine.

  The companies have all reached a settlement with DOJ in Sept 2007 to avoid criminal prosecution relating to physician kickbacks. Zimmer, Depuy, Biomet and Smith & Nephew entered into deferred prosecution agreements and agreed to industry reforms in addition to paying a combined total of $311 million. Only Stryker avoided monetary penalties but will still enter a non-prosecution pact and agree to industry reforms and undergo corporate monitoring for 18 months.

  Each company must now conduct a needs assessment to determine the reasonable needs for consulting services and disclose consultants' names and payments on the company website. Physicians must also disclose their financial relationships to their patients.

- The Transparency in Medical Device Pricing Act was also proposed towards the end of last year. If passed, this will require companies to submit quarterly reports on average and median prices of implantable medical devices to the US government from Jan 2009, which is viewed by some as the first step towards government control of implant pricing.

Orthobiologics

MARKET SHARE

Global

Current market size (2006) - $2.3 billion

CAGR (2006–2011) – 18.3%

Potential market size (2011) - $5.3 billion

CHALLENGES

Insufficient supply of tissue limits market growth

Lack of clinical data restricts widespread acceptance of the products such as platelet concentrate systems

DRIVERS

Shift from reconstruction to bone induction

Aging baby boomer generation and their active lifestyle sparks the demand to exceed the number of procedures in the market

Half of all bone grafts are spinal fracture repairs and the increasing success rate of spinal fusion has increased procedure acceptance

Emergence of synthetic alternatives

RESTRAINTS

Disease transmission cases lead to scepticism regarding product safety

Public scrutiny of the tissue donation industry restricts acceptance of tissue-based products

Technology

Minimally Invasive Bone Grafting

Bone Marrow	Effective graft material in animal studies and increasing amount of human clinical research. Presence of immature bone forming cells and other cells are responsible for the effectiveness as a graft.
Bone Matrix Gel	Grafts of highly purified gel made from osteoconductive human bone are approved for clinical use and are available. The matrix can also be combined with bone marrow to provide an osteoconductive scaffold.
Setting Calcium Phosphate Cements	Injectable pastes of calcium and phosphate form a hard mass of calcium phosphate ceramic similar to hydroxyapatite mineral found in bone.

- Significant growth has been noted in orthobiologics as the orthopaedic market begins to shift focus from reconstruction to bone induction.
- Used increasingly in spinal, total joint, trauma and soft tissue surgeries, synthetic bone graft substitutes and resorbables are beginning to replace traditional autografts and allografts (bone bank grafts), which account for more than 75% of today's bone graft procedures.
- Bone graft substitutes and processed allograft products have significant future potential within orthopaedics.
- Bone growth factors are viewed as the hottest orthobiologic segment area and are already being used to accelerate fracture healing and decrease risk of spinal fusion failure. Despite being relatively new to the market, bone growth factors were responsible for $920M in EU sales in 2005. Indeed, according to Medtech Insight, with total European sales of $341M in 2005, the bone morphogenetic protein market is only 7% penetrated.

Company Snapshot

Medtronic — INFUSE Bone Graft

Medtronic INFUSE Bone Graft contains recombinant human bone morphogenetic protein (rhBMP-2), the genetically engineered version of a naturally occurring protein that is capable of initiating bone growth in specific, targeted areas of the spine. The product is approved for lumbar fusion with specific devices and for acute open fractures to the tibial shaft. Sales of Infuse are expected to increase until 2012, when it is estimated that it will be employed in about half of all spine procedures, generating a market of almost 225,000 procedures and $1.3 billion in sales.

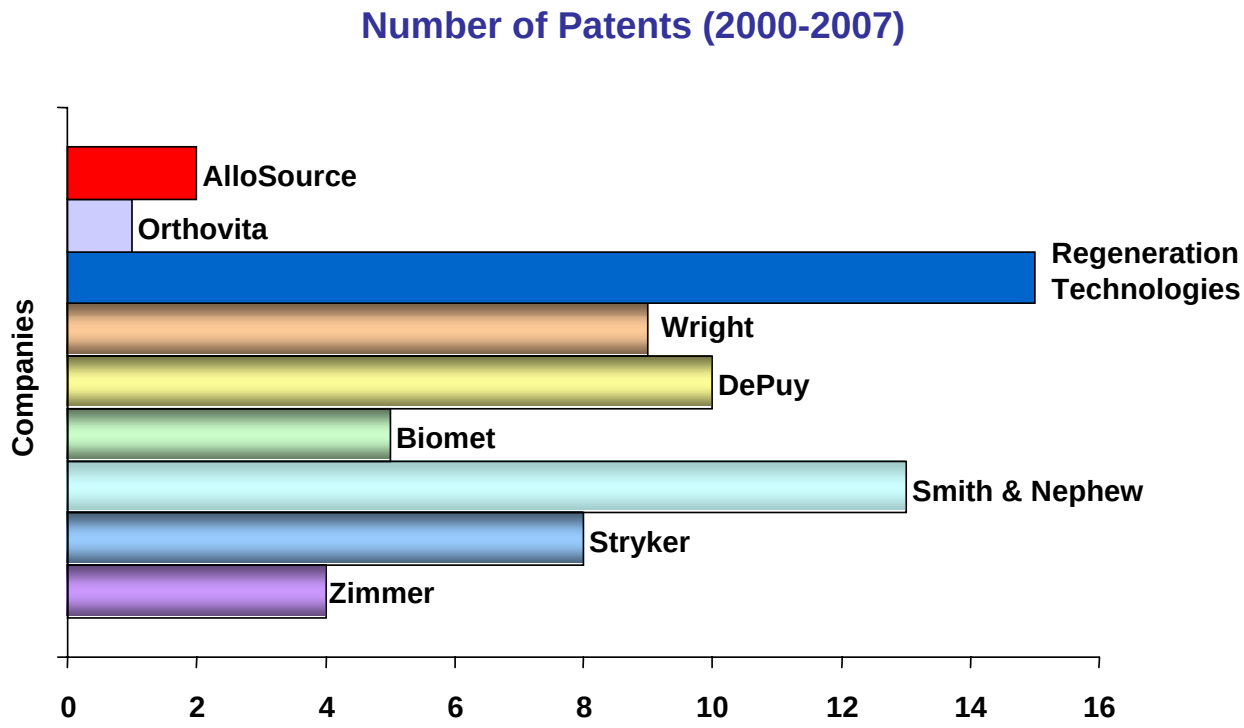
BIOMIMETIC THERAPEUTICS — Drug-device combination products for the repair of orthopaedic injuries

BioMimetic combines existing medical devices and a biologically active growth factor called rhPDGF-BB (recombinant human Platelet-Derived Growth Factor), which is one of the principal wound healing stimulators in the body. The rhPDGF-BB is reportedly well suited for various therapeutic applications due to its stimulation of a broad spectrum of cellular events critical for the initiation and progression of healing of periodontal and orthopaedic tissues. Its first drug device product GEM 21S combined rhPDGF-BB with a synthetic bone matrix, beta-tricalcium phosphate for periodontal bone defects and gum tissue recession.
The company sold its dental business to Luitpold in Jan 2008 for $44M and will now focus on developing its pipeline of product candidates targeting fracture healing. BioMimetic Therapeutics went public in May 2006, raising $31M and is based in Tennessee, USA.

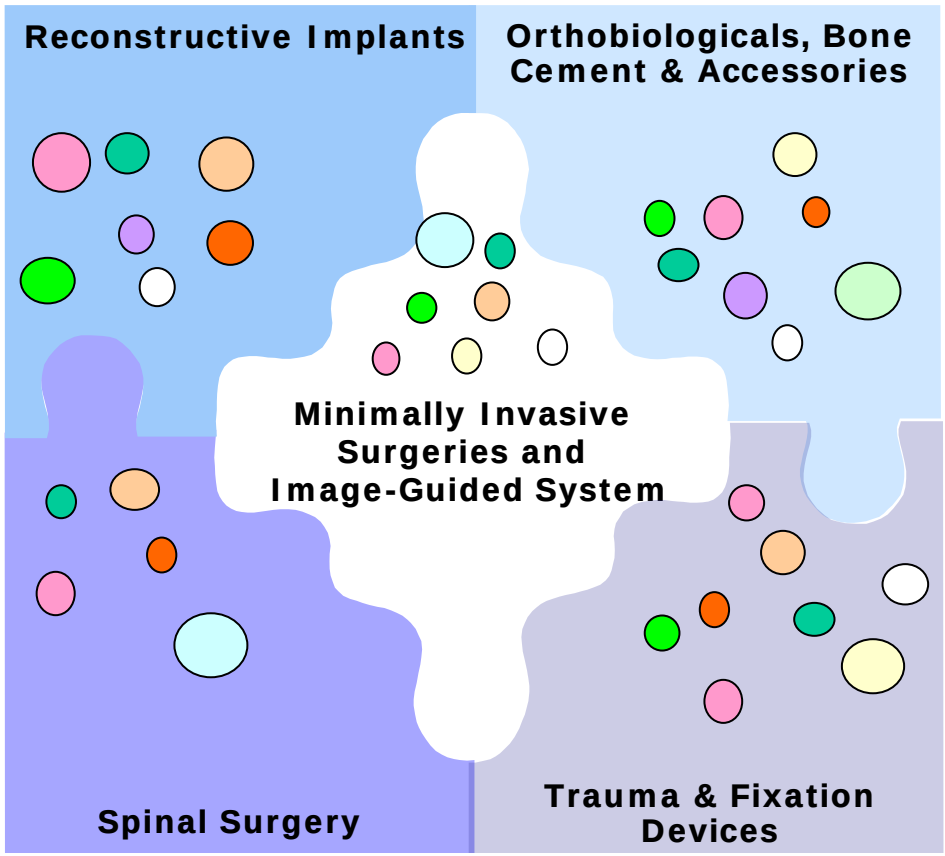
Apatech — Specialises in bone graft substitutes and synthetic bone graft technologies

Apatech have developed (i) Actifuse, a new class of bone graft material that combines osteoconductive and osteo-stimulatory activities, in a wide range of orthopaedic and spinal applications and (ii) AnaPore a synthetic and porous hydroxyapatite. Based in Elstree, England the company has raised $23M since 2001.

Orthobiologics IP Landscape



Key Players in Orthopaedics



- DePuy
- Stryker
- Zimmer
- Biomet
- Centerpulse
- Smith & Nephew
- Medtronic
- Wright Medical
- Osteotech
- Synthes-Stratec

Enabling Technology: Endoscopes

Endoscopy

- Endoscopy is the direct visual examination of any part of the inside of the body using an endoscope, which consists of (i) a tubular probe fitted with a tiny camera and bright light and (ii) a viewing screen that magnifies the transmitted images of the body's internal structures.
- It is routinely used in minimally invasive surgery to enable the surgeon to view the problem area without having to make a large incision.
- In addition to surgical incisions, it may also be inserted through a bodily orifice.

KEY PLAYERS (GLOBAL)

Given Imaging

Olympus

Karl Storz

Ethicon Endo

Medigus

KEY TRENDS

- Move toward application in diagnostics; GI Endoscopy is on the rise
- Increase in robotic-assisted surgery
- Investment in 3D image-guided surgery
- Natural Orifice Translumenal Endoscopic Surgery
- Capsule Endoscopy

Natural Orifice Transluminal Endoscopic Surgery (NOTES)

- NOTES is a new method of performing minimally invasive surgery through the mouth, anus, or vagina, which is being hailed as a revolution in minimally invasive surgery.
- Techniques include endolumenal procedures that (i) can be performed within an organ that can be directly reached via a natural orifice and (ii) those in which surgical devices are advanced through the natural orifice, which is then breached to gain access to the internal structure of interest.
- The first human incision-less operation was carried out using a flexible endoscope for transvaginal cholecystectomy in a 30-year-old woman with symptomatic gallstones at the University Hospital of Strasbourg in April 2007. It was performed without incision, save for a 2mm needle allowing for insufflation and control of intra-abdominal pressure. This was quickly followed by the first transgastric cholecystectomy procedure in Portland in June 2007.
- It represents a billion dollar industry not yet dominated by laproscopy market leaders. Olympus was one of the first investors in this emerging field and recently acquired Gyrus Group for $1.9B, which positions it to become a leader in NOTES.
- NOTES offers the advantage of reduced post-operative pain resulting in shorter recovery times and decreased requirement for pain medication. It may also offer a reduction in post-operative wound infections and avoids scarring. Post-operative leakage may, however, prove problematic; technology and procedures must be developed to ensure all entry points can be reliably closed.
- Companies such as Apollo Endosurgery, USGI Medical and Minos Medical are beginning to develop the tools and devices required to progress this field.

Technology

Capsule Endoscopy

- Can be defined as endoscopic visualisation enabled by a tiny camera, which can be swallowed by the patient.
- The small capsule contains a colour camera, battery, light source and transmitter. Once swallowed the camera moves naturally through the digestive tract while patients carry out their normal activities. The camera takes two pictures every second for eight hours, transmitting images to a data recorder that patients wear around the waist.
- Technique assists in diagnosing gastrointestinal conditions such as obscure gastrointestinal bleeding, malabsorption, chronic abdominal pain, and chronic diarrhoea.

Wireless bioDevices

SensaPill

Lab-on-a-Pill: capsule technology to detect bleeding

- A University of Glasgow spin-out, Wireless bioDevices, is aiming to develop a lab-on-a-pill – an extension of current camera-on-a-pill technology. While capsule endoscopy seeks to create a visual image of the remote area being sensed, the SensaPill aims to develop a remote chemical image.
- Once swallowed, the capsule detects bleeding inside the GI tract as it travels through, transmitting the real time measurements to a small external module attached to the body, before being excreted and discarded.
- SensaPill is able to distinguish between a variety of GI conditions and detect the early signs of bowel cancer. It overcomes two of the major problems with testing for bowel cancer as it (i) does not require sample collection so is easy to use, making it more acceptable to patients and (ii) is highly sensitive as it detects any bleeding at source.

Endoscopes Market

MARKET SHARE

Global

Total Revenue (2006) - $378 million

CAGR (2007-2013) - 5 %

Projected Revenue (2013) - $532 million

CHALLENGES

Inadequate training of surgeons affects market expansion

Reduction in healthcare budgets inhibits revenue growth of the markets – use beyond shelf-life common

Use of reusable or resposable instruments affects disposable device manufacturers

Established medical device manufacturers pose strong competition to new entrants

Low cost equipment manufacturers cannibalise market share despite poor quality

Endoscopes Market

DRIVERS

- Technology advancements and increasing interest in MIS
- Increase in number of surgery procedures encouraging market expansion: 80% of surgical procedures are minimally invasive
- Acceptance of MIS by private hospital authorities accelerates revenue growth
- Long-term cost efficiency encourages healthcare authorities to overlook the initial high investment
- Product bundling and customised products increase surgeon acceptance
- Lifestyle modification diseases indirectly encourage the growth of the market
- Gaining popularity of endosuites encourages market

RESTRAINTS

- Mature market retards revenue growth
- Cost containment hinders revenue growth and inadequate clinical evidence prevents market expansion
- Inadequate clinical evidence hinders market expansion

Conclusions & Next Steps

Conclusions

- This environmental scan has highlighted a number of technology applications, which are of interest given their innovation and market potential.

- Motion preservation and bone induction are seen as two of the hottest areas within orthopaedics. A marked shift from current spinal fusion treatments to **spinal implants** for motion preservation (eg artificial discs) is predicted which, given the prevalence of degenerative disc disease, makes an attractive market opportunity.

  Significant growth has been noted in **orthobiologics** as the orthopaedic market shifts focus from bone reconstruction to bone induction. Bone growth factors have already achieved nearly $1B in EU sales despite being relatively new to the marketplace. Orthobiologics are viewed as having significant market and innovation potential.

- The cosmetic procedures market is viewed as an area of opportunity given its non-reliance on reimbursement and the potential reduction in time to market. Non-invasive fat removal and cellulite treatment is viewed as the prime opportunity in the **aesthetics device** industry with significant market growth predicted. There is clear scope for technology innovation to improve the efficacy of current devices. Indeed, clinical efficacy is likely to be the leading product differentiator in the future.

Conclusions continued

- Opportunities now exist to develop **drug eluting stents** with improved safety profiles. While currently dominated by large cardiovascular players, recent questions over DES safety may serve to open up the market to new entrants. However, the cost of bringing new DES to the market may dampen interest in this area with current estimates predicting a new DES start-up to require more than $100M in financing and 5-7 years of product development time before achieving FDA clearance.

- **Neuromodulation** is an emerging field tipped to be a major growth area. It could potentially be used to treat a number of indications such as stroke, pain management and obesity. Neurostimulators suffer from relatively limited market penetration largely due to the lack of convincing clinical data supporting safety and efficacy. Industry is now seen to be adopting a more evidence-based approach to address this.

- **Implantable sensors** offer a number of benefits over conventional sensor technology. However, life-span is often limited either due to implant rejection or battery exhaustion and so technology challenges remain. A lengthy lag-time between academic research and commercialisation is noted and so this technology is likely to face competition from other emerging technologies such as non-invasive sensors and POC tests.

Next Steps

ITI Technology and Markets team will progress one the areas highlighted in this scan, orthobiologics, to a full foresighting analysis in order to gain further insight into the market opportunities around bone healing.

If you would like to discuss the scan findings and related opportunities with us further, please contact ITI Life Sciences at:

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