Medical Device Innovation: Challenges and Adaptation

Innovation in Healthcare
Weill Cornell Medical College
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Medical Device Innovation: The Hard Questions

• Is there headroom to continue developing new medical technology breakthroughs to make meaningful impact on global healthcare?
• Is the maturation of medical device therapies causing unnecessary product iterations to stay competitive?
• Is the relentless drive for marketable breakthrough technologies for competitive advantage… whether the patient needs it or not… causing the medical device industry to contribute to the problem of unaffordable healthcare, and not the solution to better health?
Medical Device Innovation:  
*The Current Assumptions (1)*

• There remains a large US and global burden of disease that new medical technological breakthroughs can help.

• Many medical devices have reached maturation where technological iterations have, and will have, diminishing returns

• The US and global medical market demands are shifting from employing the best possible technology, to attaining economic value and good clinical outcomes, agnostic to technology
Medical Device Innovation: The Current Assumptions (2)

• Medical device innovation has extended beyond premium market technology-specific objectives aimed at the physician, to providing a broader continuum of care, service and economic value solution, that serves an expanded stakeholder base and addresses healthcare systems needs.

• The throughput of current medical device evaluation is not keeping pace with the current broad innovation offerings, and mitigating clinical evaluation solutions are evolving.
Medical Device Innovation

• Healthcare challenges that motivate innovation
• Innovation activities
  • Technology
  • Manufacturing and “cost-down”
  • Generating economic value
• Challenges to innovation
• Policy and knowledge generation solutions
• Conclusions
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UNSUSTAINABLE ENTITLEMENT GROWTH WILL REQUIRE MAJOR REFORMS IN THE NEAR FUTURE

Projected Tax Revenue

Health Care Costs are the Primary Driver of Long-Term Budget Problems

“America cannot be great if we go broke. Our businesses will not be able to grow and create jobs, and our workers will not be able to compete successfully for the jobs of the future without a plan to get this crushing debt burden off our backs.”

- President’s National Commission On Fiscal Responsibility & Reform, 2010
Disease Burden—
29 disease spaces that have US gross prevalence > 2 million

Projected US Gross Prevalence, Year 2010 and 2020

Additional work in progress: Collaboration with Epidemiologists and Decision Science experts to characterize disease burden in terms of prevalence and healthcare costs (University of Minnesota, expected completion September 2009)
The ‘usual suspects’ are important in all parts of the world

Strategic Factors Critical to the Assessment

- Disease Burden
- Epidemiology
- Healthcare Economics
- Unmet Medical Needs

“...alleviate pain, restore health, and extend life.”

R&D Strengths
- Technology
- Synergies

R&D Strengths
Market Potential
Business Challenges
Competition

“Business Case”

Medtronic Competences

“To direct our growth in areas of biomedical engineering where we can display maximum strength and ability.”

“To make a fair profit...”
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History of modern biomedical technology innovation

- **1930s**
  - *Foley Catheter*
  - *Artificial Kidney*

- **1940s**
  - *Dental Implants*
  - *Heart-Lung Bypass*

- **1950s**
  - *Starr-Edwards Valve*

- **1960s**
  - *PTCA*

- **1970s**
  - *Percutaneous Valves*

- **1980s**
  - *Aortic Endograft*

- **1990s**
  - *Deep Brain Stimulation*

- **2000**
  - *Implantable Pacemaker*
  - *ICD*
  - *Total Hip*
  - *“Iron Lung”*
  - *Intraocular Lens*
  - *External Pacemaker*
  - *Total Disc*
  - *Palmaz Stent*
  - *Dental Implants*
  - *Heart-Lung Bypass*
  - *Starr-Edwards Valve*
• World Headquarters ——— Minneapolis
• European Headquarters —— Lausanne
• Asia/Pacific Headquarters —— Singapore
• 45,000 Employees/120 Countries
• $40-60 Billion Market Capitalization
• >6 million patients/year
• Revenue $16 Billion/2011
• Engineers/Scientists: >8,000
• R&D $1.6 billion/ 2011

Mission: Alleviate Pain, Restore Health, Extend Life
Transformational Drivers

Medical Device Therapies

Diagnostics & Monitoring

Device Technology, Miniaturization

Communications, Information Technology

Physiology, Biologics, Genetics
Medical Device Therapies

- Parkinson’s Disease
- Essential Tremor
- Dystonia
- Chronic Pain
- Gastroparesis
- Bowel Disorders
- Urinary Incontinence
- Obsessive Compulsive Disorder*
- Depression*
- Epilepsy*
- Bradycardia
- Heart Failure
- Tachycardia
- Obesity*
- Interstitial Cystitis
Medtronic CoreValve Technology

- 18FR catheter delivery system designed for ease of delivery and minimized need for surgical cut-downs
- Self-expanding multi-level frame allows for controlled release and partial repositionability
- Porcine pericardial tissue valve has supra-annular valve function
- Over 13,000 implants to date
Percutaneous Leadless Micro Pacemaker

Key Potential Benefits:

Less-invasive, easier to use, more cost effective

- Less implanted hardware ("invisible")
- Faster, simpler procedure (totally percutaneous, no surgery)
- Fewer complications (no lead or device pocket)
- Shorter hospital stay
- Easier follow-up
- MRI safe

Premier\Capsule-Tines_Pacing_v03.wmv
High Burden of Hypertension

- **1.2 billion patients** today, 1.5 billion prevalence by 2025
  - Co-morbidities include obesity and diabetes
- Currently **$500B annual global direct cost** of uncontrolled hypertension
- **50-70% uncontrolled** despite the availability of excellent medical therapy
- **#1 risk factor for stroke**
- A leading risk factor for **MI, heart failure, kidney failure and blindness**
Renal Sympathetic Afferent Nerve

Schlaich, Sobotka, Krum et al. Hypertension 2009

↑ Hypertrophy
↑ Arrhythmia
↑ Oxygen consumption
↑ Systolic HF
↑ HFPEF

↑ Renin Release → RAAS activation
↑ Sodium Retention
↓ Renal Blood Flow

Vasoconstriction

Insulin Resistance

Renal Afferent Nerves

↑ Renin Release
↓ Renal Blood Flow
Renal Nerves
- Arise from T10-L2
- Follow the renal artery to the kidney
- Primarily lie within the adventitia
- The only location that renal efferent & afferent nerves travel together

Renal Anatomy Allows a Catheter-Based Approach
Simplicity Catheter System

- 6F Compatible
- Propriety RF Generator
  - Automated
  - Low Power
  - Built in Safety Algorithms
- Articulating tip with RF electrode
- 4-6 focal 2-minute RF treatments along artery
- Median procedure time 38 minutes
39% of patients achieved blood pressure control (<140 mm Hg)
Hypertension May Just Be The Beginning…

Chronic activation of the sympathetic nervous system common in:

- Kidney Failure
- Sleep Apnea
- Heart Failure
- Diabetes
- Arrhythmia
Injectable Diagnostics & Monitors
Integrated Diagnostics

Device

Sensor Data
- Pressure
- Impedance
- Activity
- Heart Rate
- HRV
- AT / VT
- %pacing
- Vc
- Ischemia
- Perfusion
- Respiration
- Temperature
- S3
- TWA/HRT
- Glucose

Peripherals

Clinical data
- Weight
- BP
- BNP
- Medications

Demographic data
- Age
- Gender
- History

CareLink

Risk
- Heart Failure
- VT
- AMI
- Stroke
- Mortality

Unique Interface

EMR

EP

Card

NP

MD

Patient

Logic
> 800,000 patients on CareLink, > 4 million transmissions
Wafer Scale Device Assembly
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Design for Reliability and Manufacturability: Product Development Innovation

DRM Practices

- Voice of Customer
- Concept Engineering
- Requirement Flow-Down
- Use Condition
- Control
- Capability
- DFR
- DFMA
- Robust Design

Design for Reliability and Manufacturability: Product Development Innovation
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COST AND ACCESS QUICKLY BECOMING FUNDAMENTAL MARKET NEEDS

THE GLOBAL HEALTHCARE MARKET IS CHANGING

**Underlying Demand Drivers**
- Increasing burden of chronic disease
- Demographic shifts / aging of population

**Cost**
- Rising cost burdens on governments
- Payment reforms
- Pressure on provider economics

**Stakeholders**
- Broadening of stakeholder base
- Increasing alignment of clinical & economic buyers

**Emerging Markets**
- Rise in wealth
- Healthcare as government priority
- Local competition
ADAPTING TO THE NEW HEALTHCARE ENVIRONMENT

OUR TWO STRATEGIES TO IMPROVE GROWTH

UNIVERSAL HEALTHCARE NEEDS

- Improve Clinical Outcomes
- Expand Access
- Optimize Cost & Efficiency

Economic Value

Globalization
Building on our focus on the physician

Serving a broader set of stakeholders

Building on:

**Outcomes**
- Clinical evidence quality
- Treatment guidelines

**Access**
- Physician reimbursement
- Ease of use

**Efficiencies**
- Procedure efficiency
- Device price

**Physician**

**Administrator**
- Clinical evidence quality
- Quality measures
- Readmissions

**Payer**
- Clinical evidence quality (HTA)
- Reduced complications

**Patient**
- Quality of life
- Mortality benefit
- Patient satisfaction
- Physician support
- Invasiveness
- Cost effectiveness
- Budget impact
- Affordability / Liquidity

Medtronic
KEEPING MEDTRONIC THERAPIES CORE TO THE SOLUTION

EXPANDING ACROSS THE CARE CONTINUUM

CVG
Syncope
Management

RTG
Diabetes
Management

Diagnostics

Medtronic
Therapy

Monitoring

Medtronic
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Health Continues to Drive Major R&D

R&D Distribution by Industry: 2005

- Health: $87.3 B (22%)
- Technology: $26.3 B (6.5%)
- Chemicals and Energy: $28.4 B (7.0%)
- Software/Internet: $20.0 B (4.9%)
- Aerospace and Defense: $16.1 B (4.0%)
- Industrials: $23.2 B (5.7%)
- Telecom: $5.4 B (1.3%)
- Other: $10.0 B (2.5%)
- Consumer: $15.4 B (3.8%)

Total R&D = $407 B

Reported 2005 R&D as % of Reported 2005 Sales by Industry with change from 2004

- Software/Internet: 11.2%
- Computing and Electronics: 3.9%
- Aerospace and Defense: 7.5%
- Technology: 4.0%
- Auto: 4.0%
- Industrials: 2.2%
- Consumer: 2.0%
- Telecom: 1.5%
- Other: 1.5%
- Chemicals and Energy: 1.1%

2005 Total: 3.84%
Medical Technology Bets are Getting Larger

510(k)/PMAs
1-3 Years
$1-10M

Pre Market Approval (PMA)
5-7 Years (clinical trials)
$30-300M

PMA, Drug / Device Combos
7-10 Years (clinical trials)
$100-300M

New Drug Application (NDA)
12-15 Years (clinical trials)
~$300-400M
Future Considerations

Tailwinds

• More technology leverage
• Focus on HC Innovation

Headwinds

• Regulatory Requirements
• Increasing Device Complexity
• Rising Global Evidence Demands
• Local Content Requirements
• More post-approval trials
• Increases in Taxes/Fees
MEDICAL DEVICE EXCISE TAX

• January 2013
• 10-year Period
• Finance PPACA

2.3% Excise Tax

Industry Implications

• $20 Billion
• Reduced R&D
• Limits Innovation

Provider Implications

• Fewer Advances in Care
• Limited Patient Access

PARTNERSHIP for HEALTH POLICY
BROAD IMPLICATIONS OF HEALTH CARE REFORM FROM A DEVICE PERSPECTIVE

**Coverage Expansions**
Insurance mix will determine access and utilization

**Comparative Effectiveness**
Industry will have to raise its game in proving the effectiveness and value of medical technologies

**Payment/Delivery System Reform**
Focus on efficiency, quality and aligned incentives

**Independent Payment Advisory Board (IPAB)**
Significant wildcard that could limit patient access and reduce payments

Poorly executed CER, device tax, arbitrary payment/pricing cuts and inappropriate limits on utilization could jeopardize incentives that spur med-tech innovation
Comparative Effectiveness Research

• Emerging critical tool for informed decision making
  – Potentially more relevant comparisons than placebo
  – Offers multiple comparisons, CEA
  – Real world outcomes in practice settings, less restricted entry for better generalizability
  – Patient-centered in terms of comparative groups and endpoints that reflect patients values and preferences

• In early stages of development and application
  – Methods are flexible to accommodate new comparisons in a non-perturbed research setting
  – Variable levels of validity across the CER research space spectrum: EHRs/Registries/RCTs
  – Conclusions and inferences for many CER studies may be less valid than placebo-controlled RCTs
  – May penalize early stage technology
Cost/day of ICD therapy has decreased:
1. Reduced procedure time (12 to 2 days)
2. Increased battery life (1 to 9 years)
3. Improved device therapy (4x therapies)
4. Better medical outcomes (multi. studies)

TAVR: Innovative new technology

Significant clinical benefit in a patient population not previously treatable

Adds new costs to the health care system (because no previous intervention)

Will incentives under shared savings/accountable care programs discourage utilization?

Medtronic CoreValve® System*

- Replaces dysfunctional native aortic valve
- Porcine pericardial tissue valve sutured into a self-expanding nitinol frame
- Supra-annular valve position preserves circularity at level of valve function
- 18Fr catheter delivery system

*Caution. Investigational device. Limited by United States law to investigational use.
LONG-TERM PRESSURES WILL HEIGHTEN ALIGNMENT ON CLINICAL AND EFFICIENCY MEASURES TO IMPROVE CARE

Manufacturers
Clinical & Economic Outcomes

Providers
Quality & Efficiency of Care

Improved Patient Access & Health
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Current Demands for Clinical Evidence (1)

- Interest in effectiveness over efficacy
  - Healthcare value
- Keeping pace with technology compels more than head-to-head and time-to-time focus
  - Need for timely and dynamic evidence in practice
  - Real-time data analysis
  - Real time learning
- More continuity between fragmented studies
  - Better coordination, efficiency, longitudinal follow-up

Adapted from “Learning What Works,” IOM, 2011
Current Demands for Clinical Evidence (2)

- Comparison of two or more practical alternatives rather than placebo alone
  - Comparative effectiveness research (CER)
- Focus on the unique patient rather than the average population effect
  - Patient-centered outcomes research (PCOR)
- Expanded analysis
  - Systematic reviews
  - Innovative research strategies
  - Clinical registries
  - Coverage with Evidence Development

Adapted from “Learning What Works,” IOM, 2011
Evaluating the Total Product Life Cycle (TPLC)

• **Pre-market: Efficacy determination by pivotal RCT**
  – Hypothesized effect and indication
  – Proof of device principle, mechanism of action, additional data fields beyond clinical practice
  – Semi-experimental, “unreal” conditions

• **Market release dynamics**
  – Broad uptake by various users: maverick, conservative, alternative providers
  – Broadened application beyond labeled patients indications, new uses
  – Average providers/users, variable health care systems
  – Discovery of new favorable and unfavorable properties

• **Post-market evaluation**
  – Extension of the pivotal RCT cohort to long-term follow-up
  – Initiation of a new, larger cohort study to evaluate performance and discover/measure adverse events against expectations (OPC/comparators)
  – Develop risk detection, device/machine clinical surrogates
  – Device design and quality feedback loop
Medical Device Lifecycle

Outcomes of Interest

Device Safety & Durability, Manufacturing Reliability

Safety and Efficacy for pre-defined discrete indication

Device Performance: Durability and Product Safety

Patient Outcomes: Rare Events, Efficacy for Broader Patient & Operator Population

Ideas, Design, Bench & Mfg Validation

Pre-Market Pilot & Pivotal Evaluation

FDA/Panel Analysis and Approval

Post-Market Studies & Surveillance

Next Gen Improvements & Obsolescence

Device Performance:

Device Safety & Durability, Manufacturing Reliability

Safety and Efficacy for pre-defined discrete indication

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Next Gen Improvements & Obsolescence
Medical Device Lifecycle
Pathophysiology-Treatment Variables

- Spec $\delta$
- Narrow Patient Factors
- Clinical, Device Stress
- Broad Patient, Operator Factors
- Unknown Disease, Device Factors

Device Design → Bench Measurement → Pilot Pivotal Outcomes → Device performance → Real World Outcomes → Rare AE Long-term Effects

Medical Device Lifecycle (Class III)

Traditional Evaluation Methods

- Pre-Market Pilot & Pivotal Evaluation
- FDA/Panel Analysis and Approval
- Post-Market Studies & Surveillance
- Next Gen Improvements & Obsolescence

- Ideas, Design, Bench & Mfg Validation
- Bench Stress & Lifetime Testing
- Prospective Single Arm & RCTs
- Required Post-market studies, Marketing studies, Physician-sponsored studies, MDRs, Maude

RCT
Problems with RCTs

• High validity, narrow application
  – Powered for specific hypothesis test
  – Inference based on average sample effect

• Poor generalizability
  – Minority of target population passes screen
    • Eligibility includes parameters for trial participation which limits general inference to the target population

• Large and expensive
  – Minimal economies of scale
  – Increased demand for evidence will not be satisfied by RCTs alone
Observational Methodology

• Better generalizability, broader application
• Less valid than RCT for efficacy
• Great improvements in confounding control
  – Propensity scoring, tiered analysis
  – Instrumental variables
  – Better attention to completeness of ascertainment
• Offers more scalable, and reusable and cost-efficient research platforms
• Offers live data analysis for quicker application of the results
• Incorporation with clinical management systems
• Allows broader comparisons
Drug-Eluting or Bare-Metal Stents for Acute Myocardial Infarction


From Brigham and Women’s Hospital (L.M., P.G., M.R.V., Z.Z.), the Harvard Clinical Research Institute (L.M.), Harvard Medical School (L.M., T.S.S., R.E.W., K.Z., A.L., S.-L.T.N.), and the Harvard School of Public Health (S.-L.T.N.) — all in Boston. Address reprint requests to Dr. Mauri at Brigham and Women’s Hospital, 75 Francis St., Boston, MA 02115, or at lmauri1@partners.org.


- Mass DPH PCI Database
- 7217 patients: AMI, 4/03 – 9/04
- DES-4016, BMS-3201
- Propensity score matching
- 2-year mortality, repeat revascularization, recurrent MI

Figure 1 (facing page). Clinical Outcomes after Stenting for Myocardial Infarction.

The graphs show the cumulative 2-year incidence of death (Panel A), myocardial infarction (Panel B), and repeat target-vessel revascularization (Panel C) in the matched sample of patients receiving bare-metal or drug-eluting stents. Error bars are 95% confidence intervals. P values were calculated by the paired t test.
Medical Device Lifecycle (TPLC)

Leverage Observational Methods With RCTs

Observational/Surveillance Tools

- Spec δ
- Narrow Patient Factors
- Clinical, Device Stress
- Broad Patient, Operator Factors
- Unknown Disease, Device Factors

Device Design → Bench Measurement

Device performance → Real World Outcomes


- Real World Outcomes
- Unknown Disease, Device Factors
- Broad Patient, Operator Factors
- Clinical, Device Stress
- Narrow Patient Factors
- Spec δ

Device performance
Clinical Research and the Broader “Stakeholdership”

• Moving from paternal healthcare model to a more equitable one

• Stakeholder decision makers
  – Patient
  – Caregiver
  – Physician, Nurse, Chiropractor
  – Hospital
  – Health Plan
  – Payer
  – Government Agencies
  – Academia, Medical Societies/Guidelines

• Dissemination and Uptake in a language each stakeholder can understand
Patients Want More Access to More In-depth and Personal Data
The Patient-Centered Outcomes Research Institute (PCORI) helps people make informed health care decisions, and improves health care delivery and outcomes, by producing and promoting high integrity, evidence-based information that comes from research guided by patients, caregivers and the broader health care community.
PCORI’s Board of Governors Represents the Entire Health Care Community

PCORI Board of Governors, March 2012 in Baltimore, MD
Unlocking the potential of NHS Patient Data in Research + other

Observational & Interventional

3.667  3.587  3.576
3.707  3.510  3.455
3.482  3.476  3.558
3.523  3.509  3.540
3.602  3.623  3.612
3.765  3.771  3.763
3.800  3.797  3.744

Quality • NHS Clinical • Linkage • Real world • Randomised • PROs • Population 52M+
TOTAL NUMBER OF JOINTS REGISTERED IN NJR MARCH 2012 approximately 1.35 Million
The Sentinel Initiative

- FDA effort to create a national integrated (linked) electronic surveillance system that to monitor product safety continuously, pro-actively, and in real-time as a complement to existing systems.

- Will gather clinical and administrative data held by existing health-information holders
  - EHR Systems
  - Administrative and Insurance Claims Databases
  - Registries

- Data will be managed by its owners
  - Health data kept behind existing privacy firewalls
  - Queries would be sent to the participating data holders
  - Data holders would send summary results to FDA

- Clinical outcomes oriented
  - Focused on following exposure cohorts for outcomes of interest
  - Not focused on events such as out of box, design issues or mechanical failures

- Currently largely drug-focused.
  - Incorporation of UDIs into health-related data sources will expand Sentinel capabilities to conduct active device surveillance
FDA Medical Device Epidemiology Network (MDEpiNet) Initiative
Preparing raw clinical data for publication: guidance for journal editors, authors, and peer reviewers

Iain Hrynaszkiewicz¹*, Melissa L Norton¹, Andrew J Vickers², Douglas G Altman³

Abstract

In recognition of the benefits of transparent reporting, many peer-reviewed journals require that their authors be prepared to share their raw, unprocessed data with other scientists and/or state the availability of raw data in published articles. But little information on how data should be prepared for publication - or sharing - has emerged. In clinical research patient privacy and consent for use of personal health information are key considerations, but agreed-upon definitions of what constitutes anonymised patient information do not appear to have been established. We aim to address this issue by providing practical guidance for those involved in the publication process, by proposing a minimum standard for de-identifying datasets for the purposes of publication in a peer-reviewed biomedical journal, or sharing with other researchers. Basic advice on file preparation is provided along with procedural guidance on prospective and retrospective publication of raw data, with an emphasis on randomised controlled trials.

In order to encourage its wide dissemination this article is freely accessible on the BMJ and Trials journal web sites.
Medtronic Post Approval Network
May 2012
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Conclusions

• Medical Device Technology will continue to innovate for technological breakthroughs to reduce the US and global burden of disease

• Device maturation is occurring, and technology innovation is shifting to economic value designs, more reliability, and health systems solutions

• There are policy and evaluation headwinds that may be mitigated by
  • leveraging network systems registries and EHRs,
  • knowledge generation through better transparency
  • novel dissemination methods to better inform broad stakeholder base and their medical decisions
  • deliver innovations faster via research policy changes