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U.S. Medical Device and Diagnostics Industry Updates

Global Corporate Advisory Americas

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〈Summary〉

○ The U.S. medical device industry is going through substantial changes as a number of powerful forces reshape the industry. Obamacare has a profound impact on the U.S. healthcare system (please refer to our report published in October 2014). It is expediting the transition of U.S. healthcare system from a fee-for-service model to a value based model. It encourages efficiency achieved through a larger scale. As a result, providers (hospitals) and payors (managed care companies) have been pursuing scale through mergers.

○ Not wanting to lose bargaining position vs. their customers, medtech companies are joining the merger wave. Three mega deals took place in Medtech last year. We believe there are sound rationales for medtech mergers and expect more to come. For companies not participating in M&A, we believe their competitive position will deteriorate in the highly consolidated segments.

○ The insurance expansion beginning in 2014 has boosted hospital admission rate. Benefiting from Obamacare and the recovering economy, medtech industry revenues have improved. Industry is expected to grow at low-mid single digit rate for the next five years. The improving revenue trend enhanced medtech executives' confidence in their businesses. They in turn have been actively repositioning their businesses through M&A.

○ In this report, we review the recent trends of medtech industry with the primary focus on cardiovascular devices, orthopaedics, and diagnostics. We examine the dynamics in these three medtech sectors and try to identify attractive areas for investment.

○ In CV device area, there are exciting new technologies in AF, TAVR, CGM, DCB, neuromodulation, etc. We believe for market entry, peripheral vascular market and neurovascular market are the most attractive. For the orthopedics market, orthobiologics, sports medicine and extremities are the most attractive areas. In diagnostics, key growth areas are NGS, CDx, and POC. Innovations in these areas should attract investment.

Industry Research Division, Mizuho Bank

Executive Summary

- U.S. Medtech industry has turned the corner. Since the later part of 2013, we have witnessed an improving revenue trend. The roll-out of Obamacare since January 2014 has spurred growth of hospital admission and other forms of healthcare utilization. The improved employment picture also provides a favorable backdrop for healthcare utilization. As a result, medtech industry is expected to grow at low-mid single digit in the next several years.
- Across healthcare, there is a greater emphasis on delivering value. Obamacare has accelerated this transition with the creation of ACOs and other outcome-based incentives. The old model of fee-for-service is being supplanted by alternative payment models. Medtech industry needs to develop more clinical as well as economic evidence to support its products.
- Industry participants believe a larger scale could help them better meet the challenges brought on by Obamacare and the shifting healthcare landscape. Therefore, consolidation is occurring throughout the chain of healthcare. Providers are consolidating, which helped prompt consolidation among managed care companies. To retain the bargaining power vs. the providers and payers, medtech industry followed suit. In 2014, three mega deals took place in medtech (Medtronic/Covidien, Zimmer/Biomet, and Becton Dickinson/CareFusion), which substantially realigned the industry ranks. We believe there are very sound rationales for medtech mergers and expect more to come.
- This report provides an overview of medtech industry trend and examines the three key categories in medtech – cardiovascular, orthopedics and in vitro diagnostics. We note there are many other product categories in medtech, but due to the limit of space, they are out of scope of this report. For small-mid companies considering entering into the U.S. market, we believe peripheral vascular and neurovascular markets are attractive on the vascular side and orthobiologics is attractive on the musculoskeletal side.
- In the cardiovascular device market, traditional stalwarts such as CRM and interventional cardiology have anemic growth. Device makers are shifting investments to high-growth areas such as atrial fibrillation, peripheral vascular disease, TAVR, DCB, BVS, congenital heart defects, etc. A core theme is "intervention" devices that can directly treat and improve patients' outcome. The emphasis on evidence-based innovation will be beneficial to the device companies not only on the competitive front (differentiate against competitors) but also on the pricing front (better pricing from payers).
- The orthopedic market is expected to grow at 3% over the next five years. TJR and spine are slower growers while extremities, sports medicine and orthobiologics are fast-growing segments. Following two big mergers, DePuy and Zimmer have emerged as two giants in the industry. We believe this has created pressure on remaining players as big players can bundle their broad product portfolios and also offer ancillary services. Some companies (e.g., Wright Medical) have adopted a niche-focus strategy.
- On the financing side, though still lagged far behind biopharma IPOs, medtech IPOs have ramped up over the last two years. In 2014, by our count, 12 medtech companies went public in the U.S., raising a total $750mn. However, excluding a few big winners, post-IPO performance has been unimpressive. The lackluster performance of medtech IPO suggests IPO may not be a great exit option for medtech venture investors. On the acquisition side, large medtech companies have become quite selective in terms of what to acquire. Private medtech companies need to clearly demonstrate the clinical and economic value of their products and a sales trajectory before a buyer can make a decision. Overall, it is not so easy for medtech venture investors to achieve exit. As a result, they have reduced venture investment in medtech. This may be a concern for large medtech companies as there will be fewer innovative targets to pick in the future.
- Diagnostic industry is expected to grow at 4-5% per annum. Key issues in the IVD industry include pending FDA regulation of LDTs, reimbursement pressure, high-growth potential for NGS, increasing trend of test decentralization to point of care (POC), broadening use of companion diagnostics (CDx), etc. Recent M&A activities have focused on NGS, POC and CDx. There have also been two mega M&A deals in the IVD and life science industry – Danaher's acquisition of Pall and Merck KGaA's acquisition of Sigma Aldrich. We noticed acquisition premium has increased from a few years ago.

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Glossary and Abbreviations

Abbreviation	Explanation
510(k)	Also called Premarket Notifications (PMNs). A device is eligible for the 510K process if FDA deems it to be "substantially equivalent" to a product already on the market. A 510K application generally doesn't require clinical studies.
AAA	Abdominal Aortic Aneurysm
ACA	Accountable Care Act, also known as **Obamacare**, is the legislation passed in 2010 to expand insurance coverage.
ACO	Accountable Care Organization
AF or A-Fib	Atrial Fibrillation
BVS	Bioresorbable vascular scaffold
CE mark	Market authorization in EU countries
CGM	Continuous glucose monitoring
CHF	Congested Heart Failures
CLIA	US Congress passed the Clinical Laboratory Improvement Amendments for CMS to regulate and standardize diagnostic testing done in different laboratories. There are three classes of tests under CLIA: waived test, test of moderate complexity, and test with high complexity. Clinical labs must be certified to conduct certain tests.
CMS	Centers for Medicare and Medicaid Services
CRM	Cardiac Rhythm Management
CRT	Cardiac Resynchronization Therapy
CDRH	FDA's Center for Devices and Radiological Health
CV	Cardiovascular
DBS	Deep brain stimulation
DCB/DEB	Drug coated balloon/Drug eluting balloon
DES	Drug Eluting Stent
Device classes	Medical devices are classified into three classes in the U.S. - Class III device as one that supports or sustains human life and posses the highest level of risk (e.g., ICDs, Stents); Class II devices pose a moderate potential for harm and the risk can be mitigated by specific controls and performance standards (e.g., wheelchairs and infusion pumps), and Class I devices posses minimal potential for harm and general control is enough to assure safety (e.g., bandages).
Device recalls	FDA asks the manufacturers to recall a defective device either for correction or removal from the market. There are three classes of recalls – Class I (high risk), Class II (less risk), and III (low risk).
DOJ	U.S. Department of Justice
DRG	Diagnosis-related Group
EP	Electrophysiology
GPOs	Group Purchasing Organizations
HDE	humanitarian device exemption; Similar to PMA, but less requirement for showing effectiveness
HHS	The U.S. Secretary of Health and Human Services
HUD	Humanitarian use device is for conditions afflicting less than 4000 individuals in the U.S.
IC	Interventional Cardiology
ICD	Implantable Cardioverter Defibrillators
IDE	Investigational Device Exemptions. It allows the investigational device to be tested in clinical trials.
IVD	In Vitro Diagnostics
IVUS	Intravascular ultracound
IHC	Immunohistochemistry
MHBK/IRD	Industry Research Division of Mizuho Bank
LDT	Lab developed test
MDx	Molecular Diagnostics (Dx stands for Diagnostics)
MIS	Minimally Invasive Surgery
MRI	Magnetic resonance imaging
NGS	Next-generation sequencing
OCT	Optical Coherence Tomography
PCI	Percutaneous Coronary Intervention
PMA	Pre-market Authorization is the full FDA application process for Class III medical devices.
POC	Point of Care
PVD/PAD	Peripheral vascular disease/Peripheral artery disease
SCS	Spinal cord stimulation
TAVR	Transcatheter aortic valve replacement
TMVR	Transcatheter mitral valve replacement
THV	Transcatheter heart valve
TJR	Total joint replacement
Company	BSC (Boston Scientific), MDT (Medtronic), STJ (St. Jude Medical), J&J (Johnson & Johnson), S&N (Smith & Nephew)

Source: Compiled by MHBK/IRD based on public company reports

I. Recent Trends of Medical Device Industry

A. M&A Deals Have Realigned Industry Landscape

With several major medtech M&A deals in 2014, the rank of leading Medtech companies has been reshuffled (see Table 1). Many leading medtech companies in the world have made large-scale acquisitions in 2014 and 2015. Medtronic's $43bn acquisition of Covidien created a behemoth in the industry. Tying J&J for $27bn sales, Medtronic carries unparalleled heft in the industry and raised the pressure on competitors which so far have been on the sidelines of sector consolidation. Similarly, Zimmer's acquisition of Biomet transformed the orthopedic market landscape. Bigger is indeed better in medtech industry. Today's environment is characterized by payer/provider consolidation, increasing influence of government in healthcare, greater emphasis on delivering value, and corporate activism partly spurred by shareholder activism, all of which favors big companies. These deals fulfilled a number of strategic objectives for the acquirers (see Table 2). In our view, the wave of consolidation that has been sweeping through healthcare in general and medtech industry in particular hasn't finished yet. Mega deal like the Medtronic/Covidien deal has pushed for other CV devices companies to get bigger. For example, recently St. Jude acquired Thoratec, and Sorin merged with Cyberonics. In both deals, there is limited synergy between the merging businesses. Besides bulking up in scale, Medtech companies are also jettisoning non-medtech businesses to focus solely on medtech. Danaher announced its intention to split into two companies – a medtech company and an industrial company. Baxter has already split up into a medtech company and a new biopharma company named Baxalta.

Table 1 Top Medical Technology Companies in the World

Rank	Company	Total 2014 Med Tech Sales ($bn)	Total Company 2014 Sales ($bn)	% of Total Company Sales	Country	Strategic Action since 2014
1	J&J	27.5	74.3	37%	U.S.	Divested Cordis
2	Medtronic	27.4	27.4	100%	Ireland	Acquired Covidien; redomiciled to Ireland. Many small acquisitions.
3	GE	18.3	148.6	12%	U.S.	
4	Siemens	16.6	103.4	16%	Germany	Divested several medical businesses, including hearing aid, microbiology.
5	Beckton, Dickinson (+Carefusion)	12.3	12.3	100%	U.S.	Acquired CareFusion
6	Philips	12.0	27.8	43%	Netherlands	Acquired Volcano
7	Cardinal Health	10.6	101.1	10%	U.S.	Acquired Cordis from J&J
8	Abbott	10.1	20.2	50%	U.S.	Spun off pharma business; Entered into EP through two acquisitions
9	Baxter	10.0	10.0	100%	U.S.	Split into two public companies - Baxter (medtech) and Baxalta (biopharma)
10	Stryker	9.7	9.7	100%	U.S.	Acquired robotic company MAKO
11	Danaher	9.0	19.9	45%	U.S.	Acquired Pall, Nobel Biocare, Siemens Microbiology. Will split up into two public companies - one focused on healthcare and the other on industrial
12	Zimmer (+Biomet)	7.8	7.8	100%	U.S.	Acquired Biomet
13	Boston Scientific	7.6	7.6	100%	U.S.	Acquired multiple businesses
14	B. Braun	7.1	7.1	100%	U.S.	
15	Fresenius	6.7	30.2	22%	Germany	
16	St. Jude	5.6	5.6	100%	U.S.	Acquired Thoratec. Small acquisitions.
17	3M	5.6	31.8	18%	U.S.	
18	Smith & Nephew	4.6	4.6	100%	UK	Acquired sports medicine ArthroCare
19	Olympus	4.3	10.2	42%	Japan	
20	Terumo	4.0	4.0	100%	Japan	
21	Getinge AB	3.4	3.4	100%	Sweden	
22	C.R.Bard	3.3	3.3	100%	U.S.	
23	Varian Medical	3.0	3.0	100%	U.S.	
24	Dentsply	2.9	2.9	100%	U.S.	
25	Hologic	2.5	2.5	100%	U.S.	
26	Edwards Lifesciences	2.3	2.3	100%	U.S.	
	Total ($bn)	$234.1	$681.1	34%		

Source: Compiled by MHBK/IRD based on public company reports

Table 2 Benefits of Recent Medtech Mergers

Deals	Announce Date	Achieve Greater Scale/ Diversification	Entry Into New Attractive Areas	Enhance Global, EM Reach	Cost Synergy	Tax Inversion	EPS Accretion	Use of Overseas Cash
Medtronic/Covidien	16-Jun-2014	√	√	√	√	√	2016	√
Zimmer/Biomet	24-Apr-2014	√		√	√		2016	√
Becton Dickinson/CareFusion	06-Oct-2014	√	√	√	√		2016	
Cyberonics/Sorin	26-Feb-2015	√	√	√	√	√	2016	
Wright Medical/Tornier	27-Oct-2014	√	√	√	√	√	Second full year	

Source: Compiled by MHBK/IRD based on public company reports and Capital IQ. EM: emerging market.

In terms of corporate footprint, the traditional division of cardiovascular, musculoskeletal, hospital supply remains (Table 3). But firms in each segment are getting bigger. This list could get shorter as more companies within a segment decide to join forces. Although there is a good economic case for more mergers, we believe one impediment is management, as mergers will lead to redundancy at the top.

Table 3 Competitive Footprint of Major Medtech Companies

Company	CRM	EP	IC	DES	THV	Vascular Imaging	PV	Neuro - vascular	AAA	Vascular closure	Neuro-modulation	Diabetes (pump/CBGM)	Orthopedic Joint Recon	Trauma	Spine	Sports Medicine	Endoscopy	Wound closure
Market Size ($bn)	$10.0	$3.4	$9.0	$4.0	$1.5	$0.8	$3.5	$1.8	$1.4	$1.0	$2.2	$1.9 / $0.5	$15.4	$7.1	$9.0	$4.6	$5.0	$4.1
Growth Rate	0%	11%	2%	-1%	15%	5%	7%	10%	6%	5%	8%	5% / 25%	3%	5%	2%	6%	5%	2%
J&J		√	Exit	Exit				√	√			√	√	√	√	√	√	
Medtronic	√	√	√	√	√		√	√	√		√	√			√			
Abbott		√	√	√			√			√		√						√
Boston Scientific	√	√	√	√	√	√	√				√						√	
St. Jude Medical	√	√			√	√				√	√							
Terumo			√	√		√	√	√	√	√								
Cook			√	√			√		√								√	
W.L. Gore			√				√		√									
Edwards					√					√								
Cardinal			√				√			√			√					
Philips (Volcano)						√	√											
C.R.Bard							√			√								
Getinge AB			√							√								
Sorin +Cyberonics	√				√						√							
B. Braun							√											√
Stryker								√					√	√	√	√	√	
Zimmer (+Biomet)													√	√	√	√		
Smith & Nephew													√	√	√	√		√
Olympus																	√	

Source: Compiled by MHBK/IRD based on public company reports. Note: we only included some notable therapeutic device categories in the table. We excluded general hospital supplies and general surgery products. CRM (cardiac rhythm management), EP (electrophysiology), IC (interventional cardiology), DES (drug eluting stent), THV (transcatheter heart valve), PV (peripheral vascular), AAA (Abdominal aortic aneurysm), CBGM (continuous blood glucose monitoring).

B. Major Trends Facing the Medtech Industry

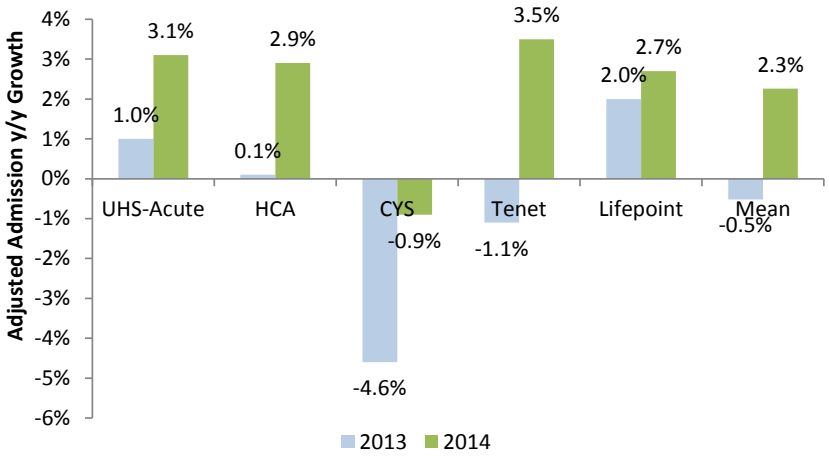
1. U.S. Healthcare Reform and the Potential Repeal of Device Excise Tax

Coverage expansion under ACA/Obamacare started on January 1, 2014. For a detailed discussion of ACA, please refer to Mizuho Industry Focus report, titled "Updates and Implications from Obamacare" published on October 7, 2014. Basically we believe the roll-out has been a success as judged by the enrollment number. Device tax implemented from January 1, 2013 has hit large-cap medtech company earnings by 3-4% and small-mid cap device makers much worse than that (even to double-digit). So repeal of the tax will be a very favorable development for the medtech industry. With Republican controlling both the Senate and the House, the political support for a repeal grows stronger. But after the April passage of the massive $200bn "doc fix" bill to address physician payment for treating Medicare patients, there is perhaps less fiscal room for repealing medtech excise tax.

2. Medtech Revenues Have Been Improving

For several years following financial crisis, medtech industry faced severe revenue pressure. The downturn has ended. Since the later part of 2013, we have witnessed a stable to improving revenue picture. Since January 2014, the implementation of Obamacare provided a boost to medical utilization. As of September 2015 an estimated 17.6 million are enrolled in ObamaCare, including 15.3 million in the Marketplace and Medicaid and 2.3 million young adults in their parents' plans. Under the ACA the uninsured rate has fallen form a high of 18% to below 11.4%. This is over a 35% reduction in total uninsured. Benefiting from ACA roll-out, U.S. for-profit hospitals reported much improved admission growth in 2014 compared to 2013 (see Figure 1). As the U.S. employment picture brightens, commercial volume has been firm. Healthcare utilization provides a favorable backdrop for medtech companies. Correspondingly, we have seen stabilization and improvement across many major medtech categories such as CRM, DES, joint reconstruction, etc. Hospitals are still under pressure for budget cuts. Pricing pressure for medical devices still exists but is not getting worse. So overall, medtech industry has a favorable operating environment. Currently major medtech companies are growing at 4-5% per annum and small-mid cap companies are growing faster than that.

Figure 1 U.S. For-Profit Hospital Adjusted Admission Annual Growth



Source: Compiled by MHBK/IRD based on public company reports

3. Consolidation Accelerates

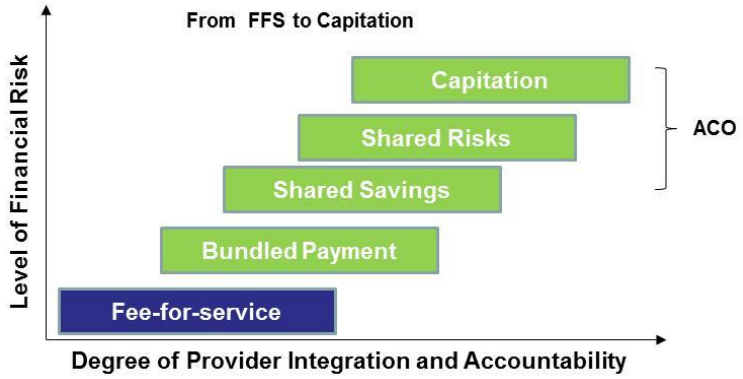
Facing severe reimbursement cuts and incentive changes under Obamacare, hospitals have accelerated consolidation. Across the nation, more hospitals are joining forces with each other and also sometimes with physician groups to create big health systems. In 2014, there were close to

100 hospital mergers. Hospital mergers make very good economic sense. Hospitals mergers can lead to a dominant provider in a particular location, making it hard for managed care companies to bargain with the provider. Partly prompted by provider consolidation, managed care companies have also increasingly resorted to mergers to enhance scale. Anthem's proposed acquisition of Cigna and Aetna's proposed acquisition of Humana would reduce the number of U.S. national managed care company from 5 to 3. As payers and providers consolidate, as a supplier, medtech industry also needs to grow in scale. Hence, we have seen several mega deals in 2014. We believe Medtronic's acquisition of Covidien is a watershed moment in the cardiovascular device industry. It sets up a high bar for scale and may pressure mid-sized companies such as St. Jude, Edwards Lifesciences to get bigger. Recently Sorin and Cyberonics announced merger to create a bigger player. St. Jude acquired Thoratec.

4. Delivering and Demonstrating "Value" Is A Core Theme in Medtech

Across healthcare, there is a greater emphasis on delivering value. ACA has accelerated this transition with the creation of accountable care organizations (ACO) and other outcome-based models. The old model of fee-for-service is being supplanted by alternative models (see Figure 2).

Figure 2 Transition of U.S. Healthcare Payment Model



Source: HealthSouth

For the first time in history, HHS set up goals for value-based payment models. In an article published in a March issue of New England Journal of Medicine, HHS secretary Sylvia Burwell outlined specific goals for linking Medicare payment to value.

- HHS set a goal of tying 85 percent of all traditional Medicare payments to quality or value by 2016 and 90 percent by 2018 through programs such as the Hospital Value-Based Purchasing and the Hospital Readmissions Reduction Programs.
- To have 30% of Medicare payments tied to quality or value through alternative payment models by the end of 2016, and 50% of payments by 2018. Alternative payment models include ACOs and bundled payment arrangement.

Under this environment, Medtech companies are constantly under pressure from payers and providers to demonstrate the value of their products. In addition to clinical benefits, to satisfy payers and providers, medtech companies need to show the economic benefits of their innovation vs. existing products. We believe pricing pressure is more prevalent in the lower-technology device categories where substitution can be easily found. In the high-technology areas, if manufacturers can demonstrate the value of their products, they can still get premium pricing. One example is TAVR, which has received favorable reimbursement coverage from CMS.

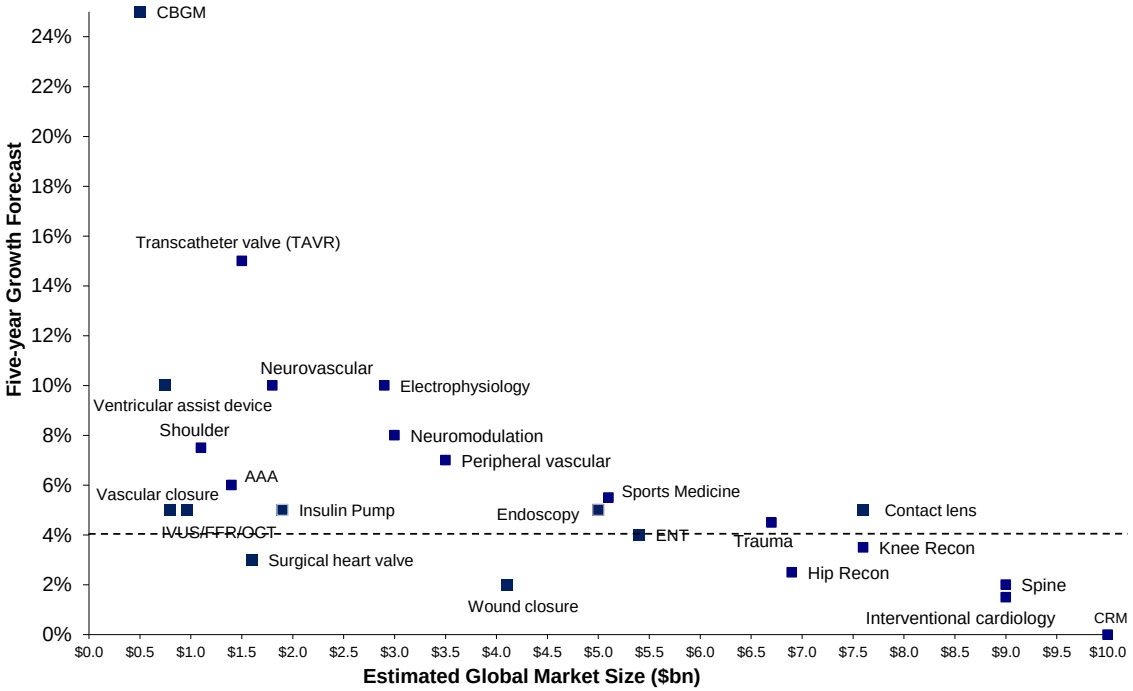
5. Strong Currency Headwind

The strengthening dollar vs. the world's major currencies has created substantial revenue headwinds for the medtech industry. Adverse currency translation is expected to result in 4-5% revenue hit in 2015.

II. Growth Trends of Key Medtech Companies/Segments

Figure 3 lists the current market sizes and expected growth rates for a number of medtech segments. The dotted line of 4% represents average medtech industry growth rate. Seeking higher growth, medtech players are attracted to segments above the 4% line.

Figure 3 Market Sizes and Mid-Term Growth Rates of Key Medtech Segments



Source: Compiled by MHBK/IRD based on Public Company Reports Note: Some larger markets are not graphed, including dental market ($15bn, 3% growth), IVD ($55bn, 5%), hearing aid ($8.5bn, 3-4%), etc.

In addition to continuously improving upon existing products, medtech industry has invented new product categories that are expected to drive industry sales growth (see Table 4). For example, after a long process, Boston Scientific (BSC) finally received FDA approval in this March for the Watchman device, which is indicated for left atrial appendage (LAA) closure to reduce Atrial Fibrillation. BSC believes the Watchman device represents a market opportunity of $500mn by 2019. Another high-potential product is drug coated balloon (DCB) for peripheral vascular diseases. The DCB market is expected to exceed $1bn in 2020. Some new device innovations (such as S-ICD and BVS) are likely to take market share in the existing markets. Therefore their net impact on overall industry growth may be more muted. However, overall these new device innovations are expected to boost growth in the medtech industry.

Table 4 New Medical Device Categories

New Device Category	Potential Market Size
Subcutaneous ICD	$750mn
Left Atrial Appendage Closure	$500mn market by 2019.
Drug Eluting Balloon	$1-1.45bn by 2020
Heart Failure Monitoring (e.g., CardioMEMs)	?
Renal Denervation	?
Transcatheter Mitra Valve	?
Bioresorbable vascular scaffold (BVS)	?

Source: Compiled by MHBK/IRD based on public company reports

As we stated earlier, large medtech companies are looking at 4-5% top-line growth over the next several years on a constant currency basis. This is a balance of growth rates of their large portfolios, which have high-growth segments weighed down by low-growth segments. Small-mid cap medtech companies are expecting higher growth rates as their businesses are often in high-growth segments (see Table 5).

Table 5 Medtech Industry Revenue Growth Trend

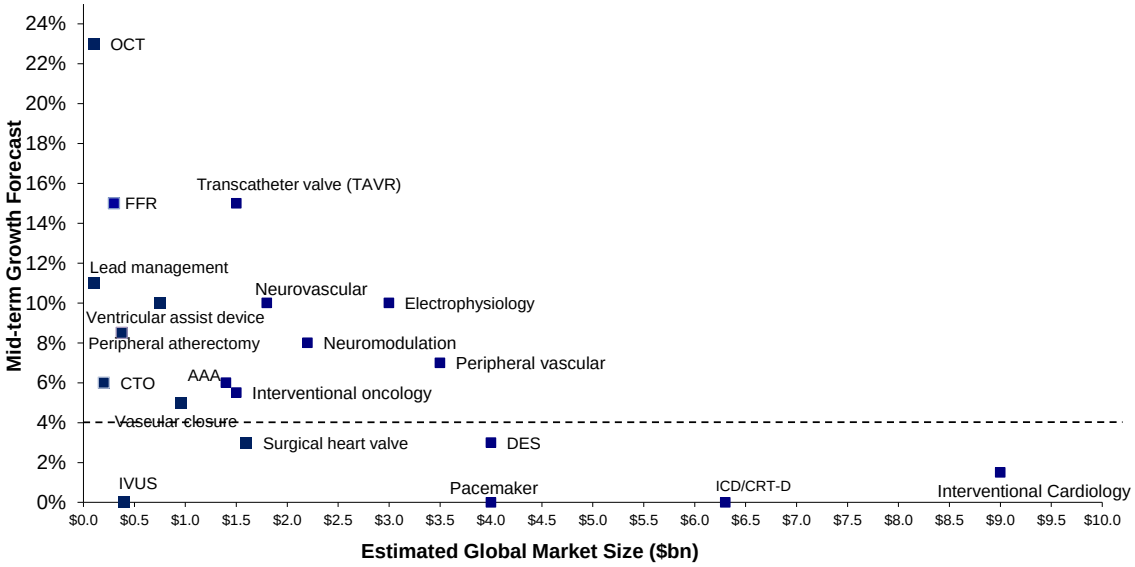
Ticker	Company Name	2013	2014	2015E	2016E	FY13	FY14	FY15E	FY16E
	Large Cap (>$5bn)								
ABT	Abbott	$19.7	$20.2	$20.6	$21.6	3.2%	3.0%	1.6%	5.1%
BAX	Baxter	$15.0	$16.7	$9.9	$10.1	7.4%	11.4%	-40.6%	1.6%
BDX	Becton, Dickinson	$8.1	$8.4	$10.3	$12.7	4.5%	4.7%	22.0%	23.8%
BSX	Boston Scientific	$7.1	$7.3	$7.5	$8.1	-2.5%	3.4%	2.6%	7.5%
BCR	C. R. Bard	$3.0	$3.3	$3.4	$3.6	3.1%	9.0%	2.8%	4.7%
EW	Edwards Lifesciences	$2.0	$2.3	$2.5	$2.7	7.7%	13.6%	6.8%	8.8%
HOLX	Hologic	$2.5	$2.5	$2.7	$2.8	23.7%	1.3%	7.4%	5.5%
ISRG	Intuitive Surgical	$2.2	$2.1	$2.4	$2.6	3.0%	-5.7%	11.3%	10.2%
JNJ	J&J	$71.3	$74.3	$70.2	$72.4	6.1%	4.2%	-5.5%	3.1%
MDT	Medtronic	$16.6	$16.9	$20.6	$28.9	2.4%	2.0%	22.1%	40.3%
LSE:SN.	Smith & Nephew	$4.4	$4.6	$4.7	$4.9	5.2%	6.1%	0.8%	5.6%
STJ	St. Jude	$5.5	$5.6	$5.6	$6.2	0.0%	2.2%	-0.9%	11.1%
SYK	Stryker	$9.0	$9.7	$9.9	$10.5	4.2%	7.2%	2.8%	5.4%
VAR	Varian	$2.9	$3.0	$3.1	$3.2	4.8%	3.6%	1.8%	3.6%
ZBH	Zimmer	$4.6	$4.7	$6.2	$7.7	3.4%	1.1%	32.9%	23.5%
	SMid Cap (<$5bn)								
DXCM	Dexcom	$160.0	$259.2	$381.8	$528.2	60.2%	62.0%	47.3%	38.3%
ELGX	Endologix	$132.3	$147.6	$154.6	$175.0	24.8%	11.6%	4.7%	13.2%
HTWR	Heartware	$205.5	$278.4	$283.1	$305.4	85.3%	35.5%	1.7%	7.9%
INGN	Inogen	$75.4	$112.5	$149.8	$173.7	55.3%	49.2%	33.1%	15.9%
PODD	Insulet	$247.1	$288.7	$309.0	$361.1	16.9%	16.9%	7.0%	16.9%
IART	Integra Lifesciences	$836.2	$928.3	$880.1	$967.7	0.6%	11.0%	-5.2%	10.0%
XENT	Intersect ENT	$17.6	$37.9	$65.3	$95.3		114.9%	72.4%	45.8%
NUVA	NuVasive	$685.2	$762.4	$811.1	$872.0	10.5%	11.3%	6.4%	7.5%
SPNC	Spectranetics	$156.7	$202.1	$244.6	$265.4	11.7%	29.0%	21.0%	8.5%
THOR	Thoratec	$502.8	$477.6	$495.6	$529.8	2.3%	-5.0%	3.8%	6.9%
TRNX	Tornier	$239.7	$294.5	$355.9	$499.2	12.0%	22.9%	20.8%	40.3%
TRIV	TriVascular	$19.5	$31.8	$37.5	$46.7	261.4%	63.0%	18.1%	24.5%
VASC	Vascular Solutions	$109.2	$124.7	$146.6	$164.0	11.0%	14.2%	17.6%	11.8%
WMGI	Wright Medical	$239.7	$294.5	$355.9	$499.2	12.0%	22.9%	20.8%	40.3%

Source: Compiled by MHBK/IRD based on data from Capital IQ

III. Cardiovascular Device Industry

The center of gravity has shifted in CV device industry. Although traditional major cardiovascular device segments (ICD, pacemaker, stent) are still generating big sales, they have anemic growth and are dominated by a few big players with small share shifts. So increasingly CV device companies are shifting investments to areas with above-average growth potential (see Figure 4). Table 6 highlights the focus areas for many CV medtech companies. In the rest of this section, we will discuss some of these high-growth areas.

Figure 4 Market Sizes and Mid-Term Growth Rates of CV Device Segments



Source: Compiled by MHBK/IRD based on public company reports

Table 6 High Growth Areas for CV Medtech Companies

Disease Areas	Current Market Size	Growth Rate	Key Recent Events
Electrophysiology (AF)	$3bn	11-14%	- Abbott entered into AF market through two acquisitions - Contact sensing ablation catheter was approved and launched
Peripheral vascular disease	$3.5bn	High single-digit	
- DCB	$80mn	$1-1.5bn in 2020	Both Medtronic and Bard received FDA approval. Bard entered into a marketing collaboration with BSC.
- Atherectomy	$375mn	High single-digit	
HF hemodynamic monitoring	$70mn in 2015		FDA approved STJ's CardioMEMS in May 2014.
LAA Closure	NA		BSC's Watchman device was approved
Neurovascular	$1.8bn	10%	
Neuromodulation	$2.2bn	8%	- DRG SCS stimulation is gaining traction. STJ acquired Spinal Modulation. - Cyberonics combined with Sorin.
TAVR	$1.5bn	15%	
Vascular Assist Device	$750mn	10%	
BVS	NA		

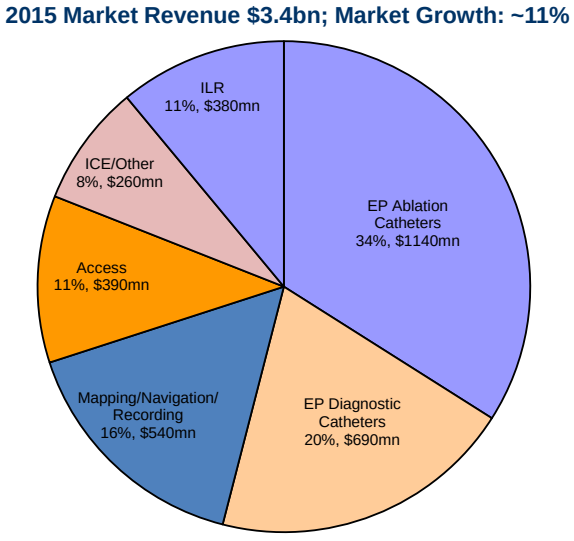
Source: Compiled by MHBK/IRD based on public company reports

A. Electrophysiology (AF) Market

Worldwide EP market is about $3.4bn in 2015 and is expected to grow at ~11% per annum for the next five years. The AF ablation market is only about 2% penetrated. With improving success rate enabled by new technology, AF market will grow at double-digit rate in the next five years. Given the high growth potential, AF ablation is considered a very attractive market for CV medtech players.

With $1.1bn in sales, EP ablation catheter is the largest segment (see Figure 5) and is growing at 13% worldwide and 15% in the U.S. Atrial Fibrillation (AF) ablation represents the majority of EP ablation cases and is the primary driver for the market growth. Most ablation catheters employ radiofrequency (RF) energy while some companies use cryo, laser/light or ultrasound energy (see Table 7). In recent years, manufacturers have made big improvement on primarily two technologies to improve the success rate of AF ablation. One is ablation catheter. For example, contact force sensing technology has contributed to higher procedure success rate. Contact force sensing catheter allows physicians to apply adequate force for the ablation procedure. The technology increased the 1-year single-procedure success rate of AF ablation from 50% to 70-80%. Biosense Webster received FDA approval for ThermoCool SmartTouch ablation catheter in February 2014. St. Jude Medical received FDA approval for TactiCath contact-sensing catheter in October 2014. The second technology is to use advanced mapping and navigation to help physicians identify the specific area of a person's heart where abnormal electrical impulses originate. The advance in mapping and navigation can also boost the 1-year success rate from 50% to 70-80%. Abbott acquired Topera in October 2014. Topera gained FDA approval for its 3D mapping system in January 2014.

Figure 5 2015 EP Market Segments



Source: St. Jude Medical February 2015 Investor Day

Table 7 Energy Sources for EP Ablation by Key Competitors

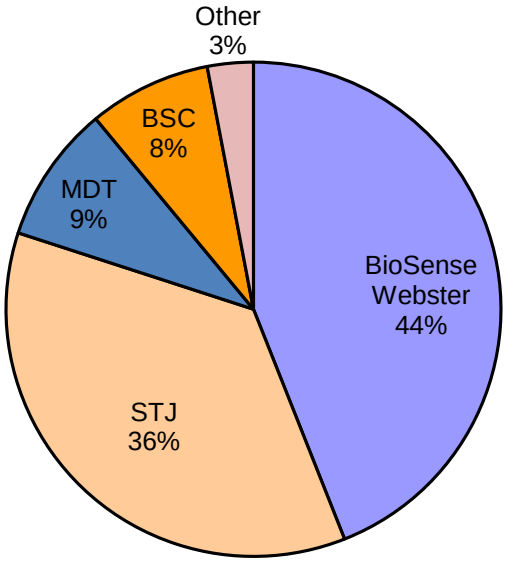
Energy Modality	Radiofrequency	Cryo	Laser/Light	Ultrasound
Medtronic	PVAC	Arctic Front		
St. Jude	Safire BLU Duo; Therapy Cool Path Duo			Epicor
Boston Scientific	Blazer; Chilli			
Biosense Webster	Thermocool			
CardioFocus			CardioLight	
nContact Inc.	EPi-Sense			
AtriCure	Synergy Ablation system			

Source: Compiled by MHBK/IRD based on public company report

A key competitive trend in EP ablation is major players often amass a complete suite of products that cover all the main segments as listed in Figure 5. This has obvious sales synergy for the EP labs and at the same time raises the barrier of entry for new-comers. It may not be enough for a company to just own ablation catheter. It also needs to have diagnostic catheters, access products, and mapping & navigation systems.

As shown in Figure 6, J&J's subsidiary Biosense Webster is the #1 player in the EP market, followed by St. Jude, Medtronic, and Boston Scientific. We estimate Biosense Webster and St. Jude combined have 80% market share. Biosense Webster is by far the biggest player by having close to half of the market. But its market share is eroding due to rapid growth of St. Jude Medical and Medtronic. St. Jude has launched a number of new products over the recent years. Medtronic's AF Solutions business has been growing 30% per annum, drive by global growth of the Arctic Front CryoAblation System and strong double-digit growth from the international launch of PVAC Gold phased RF systems. Boston Scientific acquired Bard EP business in 2013. It has launched its mapping system and ablation catheters in Europe. Recently, Abbott entered into the EP market through two acquisitions - Topera Medical and Advanced Cardiac Therapeutics.

Figure 6 EP Market Share



Source: Compiled by MHBK/IRD based on public company report

Table 8 lists the major products and strategic deals by the major EP players. Players in the EP market have made many acquisitions in the past to round off their portfolios (see Table 9 and Table 10). As a result, the number of remaining independent EP companies has been dwindling (see Table 11).

Table 8 Key Competitors in EP/ AF Ablation Market

	AF Ablation Catheter / System	Comments	FDA approval	Market position	2014 AF sales	Acquisitions in AF
J&J Biosense Webster	ThermoCool;	ThermoCool was the first catheter approved in the U.S. for AF. Single-procedure success rate is ~50%.	2009	#1	~estimated $1,300mn	Atrionix for $63mn in 2000
	ThermoCool SmartTouch	This contact-sensing catheter received FDA approval. It has success rate of ~70%.	Feb. 2014			
St. Jude	Therapy Cool Path catheter	Bi-directional Irrigated Ablation Catheter	Apr. 2011	#2	$1,044mn (+9%; 11% growth fixed FX)	- EndoCardial Solutions 2005 - MediGuide mapping system 2008 - EP Medsystems 2008 - Endosense in Aug. 2013
	Safire BLU Catheter	Bi-directional Irrigated Ablation Catheter	Apr. 2011			
	Safire BLU Duo		Jan. 2012			
	Therapy Cool Path Duo		Jan. 2012			
	MediGuide Enabled Ablation Catheters	Catheters to be used with 3-D magnetic tracking	Aug. 2013			
	FlexAbility catheter	Received CE Mark in July 2014	Jan. 2015			
	TactiCath	Contact-sensing catheter.	Oct. 2014			
Medtronic	Arctic Front cryoballoon AF ablation system	Arctic Front is approved both in the U.S. and EU. In the STOP AF trial, Actic Front showed 70% success rate at 1 year compared to 7% on drug therapy.	Dec. 2010	#3	$429mn for AF and other sales(+30% for AF)	- ATS Medical for $370mn in 2010 - CryoCath for $380mn in 2008 - Ablation Frontiers for $225mn in January 2009
	Pulmonary Vein Ablation Catheter® (PVAC GOLD)	Phase RF Catheter	2014			
Boston Scientific	Blazer, Chilli RF Abaltion product	CE mark in Europe; U.S. trial		#4	EP sales of $227 (47%)	- Acquired Bard EP business for $275mn in June 2013 - Rhythmia Medical (mapping and navigation) for $265mn in Oct. 2012 - CryoCor for $17.6mn in 2008
	Rhythmia mapping system	CE Mark in May 2013				
Abbott	RhythmView™ workstation and the FIRMap™ diagnostic catheter	Received 510k approval and CE Mark	2013	New entrant		- Entered into the EP in October 2014 by acquiring Topera Medical - Gained an option to acquire Advanced Cardiac Therapeutics
CardioFocus	HeartLight Endoscopic ablation system (EAS)	Received CE mark in July 2009; U.S. IDE trial ongoing.				

Source: Compiled by MHBK/IRD based on public company report

Table 9 Comments on Notable Recent Deals In EP

Aquirer	Target	Announce Date	Deal Value ($mm)	Revenue Trailing ($mm)	Price/Sales Trailing	Area
Atricure	nContact	05-Oct-2015	$99			Novel ablation technology
Medtronic	CardioInsight	19-Jun-2015	$93			Mapping for atrial fibrillation
Abbott	Topera	29-Oct-2014	$250			Diagnostic catheter and mapping system for AF
Abbott	Advanced Cardiac Therapeutics	29-Oct-2014				Ablation catheter for AF
St. Jude	Endosense	19-Aug-2013	$331			Contact force sensing for AF
Boston Scientific	CR Bard EP Business	28-Jun-2013	$275	$111	2.5	Electrophysiology
Boston Scientific	Rhythmia Medical	08-Oct-2012	$265			Mapping/navigation for AF.
Medtronic	ATS	29-Apr-2010	$370	$76	4.9	Heart valve and cryoablation technology
Medtronic	Ablation Frontiers	12-Jan-2009	$225			Radiofrequency AF ablation catheter
St. Jude	MediGuide	22-Dec-2008	$300			Mapping/navigation
Medtronic	CryoCath	25-Sep-2008	$360	$40	9.0	Cryoablation catheter
Boston Scientific	CryoCor	16-Apr-2008	$18			Cryoablation catheter
St. Jude	EP MedSystems	09-Apr-2008	$92	$19	3.5	EP mapping and navigation
St. Jude	EndoCardial	23-Sep-2004	$272			EP Mapping and navigation
J&J	Atrionix	27-Dec-2000	$63			Ablation catheter for AF

Source: Compiled by MHBK/IRD based on public company report

Table 10 Comments on Notable Recent Deals In EP

Deal	Date	Value ($mn)	Comments
Abbott - Topera	Oct-14	$250	Mapping/navigation could lead to industry-leading success rate (80% at year 1). Good entry via superior technology.
Abbott - Advanced Cardiac Therapeutics	Oct-14	NA	Option to acquire this ablation catheter company. Ablation catheter will go with the mapping system from Topera deal.
St. Jude Medical - Endosense	Aug-13	$331	Endosense is a pioneer in the ccontact force sensing catheter ablation field. This acquisition gives St. Jude a strong foothold in this emerging area.
Medtronic - ATS Medical	Apr-10	$370	ATS Medical helps boost Medtronic's business in the surgival ablation area.
Boston Scientific - Rhythmia Medical	Oct-12	$265	Rhythmia has attractive products for EP mapping and navigation. This deal helps complement BSX's catheter products in AF.
Boston Scientific - Bard electrophysiology	Jun-13	$275	Strengthen BSC's presence in the EP market and helps it compete with bigger players.

Source: Compiled by MHBK/IRD based on public company report

Table 11 Independent Companies in the EP Market

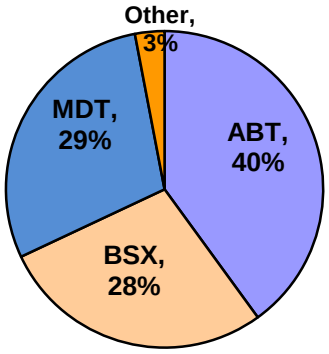
Company Name	Category	Subcategory	Year founded	Location	Stage of development	Main products	Market Cap if public ($mn)	Sales ($mn)
CardioFocus	Electrophysiology	Ablation catheter (image guided)	1990	MA	CE Mark, IDE trial	HeartLight		
AtriCure	Electrophysiology	Surgical ablation		OH	Market	Synergy; AtriClip	$606	$123
MRI Interventions	Electrophysiology	MRI-guided ablation	1998	TN	Development	ClearTrace	$44	$3
Acutus Medical	Electrophysiology	Dipole density mapping	2011	CA	CE Mark	Katheter		
Micromed SpA	Electrophysiology	Dx and monitoring	1982	Italy	Market	MyoQuick		
Securus Medical Group	Electrophysiology	Temperature mapping probe	2011	OH	Development			
Hansen Medical	Electrophysiology	Intravascular robotic navigation	2002	CA	Market	Sensei X	$68	$18
Stereotaxis	Electrophysiology	Intravascular robotic navigation	1990	MO	Market	Epoch	$21	$38

Source: Compiled by MHBK/IRD based on public company report

B. Drug Eluting Stents (DES)

Worldwide DES Market is about $4bn and is flat to slightly declining per year. The market share grab between the current DES platforms (Xience, Promus and Endeavor) is mostly over. Abbott is the market leader, followed by MDT and BSX (Figure 7).

Figure 7 Global DES Market Share



Source: Compiled by MHBK/IRD based on public company reports

Third-generation DES is emerging. DES with biodegradable polymer coatings has the benefit of optimal healing and the potential to reduce DAPT (dual anti-platelet therapy) and bleeding complications. BSC's SYNERGY and Biotronik's Orisiro Hybrid DES are being marketed in Europe. Last November, BSC reported results from the EVOLVE II trial for its SYNERGY DES. SYNERGY showed non-inferiority to Promus Element. The principal investigator of the trial commented SYNERGY is an easy stent to deploy, has good operating characteristics, and is designed to promote healing. At BSC's recent analyst day on May 5th, BSC commented SYNERGY has quickly captured the premium segment of the DES market. It now has over 50% market share in the ten focus EU countries. In early October, BSC received FDA approval for the SYNERGY stent. Based on the EU experience, it is likely to take substantial U.S. market share.

Another major advance in DES is bioresorbable vascular scaffold (BVS). BVS offers several potential advantages over DES, including less stent thrombosis, less DAPT, improving lumen modeling, etc. Abbott is the leader in BVS with its Absorb BVS. At the recent TCT conference, Abbott presented positive results from the ABSORB III trial, which showed Absorb BVS comparable to Xience DES on the primary endpoint of one-year target lesion failure rates (7.8% vs. 6.1%). Abbott filed PMA in July. Besides Abbott, a number of other companies are developing BVS (see Table 12). However, BSC believes the current BVS technology is not yet ready for prime time. BSC believes metallic stent will continue to be the main stay of DES.

Table 12 BVS under Development

Company	BVS Device	Trial Name	Eluted drug	Stent Material	Status	Polymer
Abbott	Absorb BVS	Absorb	Everolimus	PLLA	CE Mark in 1/2011. Filed PMA in July 2015.	PDLLA
Elixir Medical	DESolve	DESolve	Novolimus	PLLA	CE Mark in May 2013.	PLLA
REVA Medical	Fantom	FANTOM II	Sirolimus	Desaminotyrosine Derived Polycarbonate	CE Mark trial ongoing	Poly-tyrosine-derived polycarbonate polymer
Biotronik	DREAMS	BIOSOLVE II	Sirolimus	Metal-Mg alloy	Trial started in October 2013.	
Arterial Remodeling Technologies (ART)	ARTS BRS	ARTDIVA	No	PLDL	FIH trial started in July 2012	PLDL (Polylactic acid polymer that include both D- and L- isomers)
Amaranth Medical	Fortitude	MEND-II	No	PLLA	Started MEND-II trial in Sep. 2014.	PLLA

Source: Compiled by MHBK/IRD based on public company reports

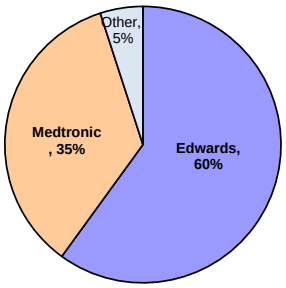
C. TAVR Market

Transcatheter aortic-valve Replacement (TAVR) is one of the hottest fields in interventional cardiology. The market has been growing at a torrid pace and is expected to continue to do so. For example, industry leader Edwards Lifesciences projects its TAVR worldwide underlying sales to grow at 15-25% in 2015. Edwards expects TAVR market to double from $1.5bn in 2014 to $3bn in 2019, which represents growth CAGR of 15%. Even with the expansion, the market is still far from saturated. The potential market size of TAVR exceeds $5bn.

The market remains a duopoly between Medtronic and Edwards Lifesciences (see Figure 8). Prior to 2014, Edwards was the only TAVR player in the U.S. Medtronic CoreValve received FDA approval for patients ineligible for surgery in January 2014 and approval for high-risk patients in June 2014. Currently CoreValve competes with SAPIEN XT in the U.S. In contrast to the U.S. dynamics, the European market has at least seven players (see Table 13).

Competitors have moved beyond first generation valves. For example, Edwards is phasing out the first-generation SAPIEN and is marketing second-generation SAPIEN XT in its place. Edwards further expects to receive FDA approval for third-generation SAPIEN 3 in 2016. The newer generation products seek to improve upon early-generation products on a number of areas including reduction of paravalvar leak, ease of delivery and implantation, multiple access routes, full-range of sizes to fit a patient's anatomy, etc. TAVR technology is certainly maturing to the greater benefits of patients. Reimbursement is also quite favorable for TAVR. For FY2015, CMS finalized two new DRGs for TAVR, which leads to a 15.7% increase over FY2014. Beyond TAVR, TMVR is the next major market. TMVR market size is expected to be 3-4x TAVR. However in TMVR, one device is unlikely to be suitable for all patients.

Figure 8 TAVR Market Share



Source: Edwards Lifesciences

Table 13 Competitive TAVI Platforms

Brand	SAPIEN THV	SAPIEN XT	SAPIEN 3	CoreValve	Engager	Lotus Valve	Portico	JenaValve	Accurate TA	Direct Flow
Company	Edwards Lifesciences	Edwards Lifesciences	Edwards Lifesciences	Medtronic	Medtronic	BSC	St. Jude Medical	Jena	Symetis	Direct Flow Medical
Product Picture										
Valve material	Bovine pericardial leaflets	Bovine pericardial leaflets	Bovine pericardial leaflets with sealing cuff	Porcine pericardial leaflets	Porcine pericardial leaflets	Bovine Pericardial leaflets	Bovine pericardial leaflets and porcine cuff	Porcine pericardial leaflets	Porcine pericardial leaflets	Bovine pericardial leaflets
Frame material	Stainless steel stent frame	Cobalt chromium stent frame	Cobalt chromium stent frame	Nitinol stent frame	Nitinol stent frame	Braided Nitinol	Nitinol stent frame	Nitinol stent frame	Nitinol stent frame	Polymer frame
Expanding method	Balloon expandable stent	Balloon expandable stent	Balloon expandable stent	Self-expanding stent	Self-expanding stent	Controlled mechanical expansion	Self-expanding stent	Self-expanding stent	Self-expanding stent	Inflatable double ring
Delivery	22 and 24 French TF; TA Delivery	18 French TF; TA Delivery	14 French TF; TA	18 French Delivery	29 French TA Delivery	18 French TF Delivery	18 French Delivery	TA	TA	TF Delivery
CE Mark	Sep-07	Mar-10	Jan-14	May-07	Feb-13	Oct-13	Nov-12	Sep-11	Oct-11	Jan-13
FDA approval	Nov-11	Jun-14	Expected in 2016	Jan-14		2017				
Plan	Phase out									

Source: Compiled by MHBK/IRD based on public company data

D. Peripheral Vascular Market

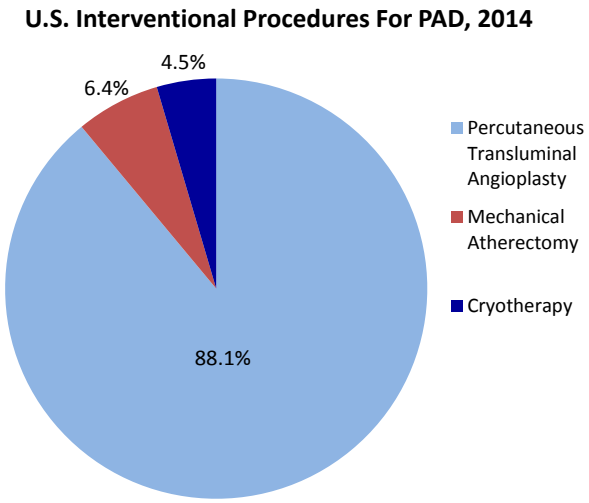
While coronary intervention is a mature market, peripheral vascular market is fast growing. The peripheral vascular disease market is worth $3-3.5bn and is expected to grow at high-single digit over the next four years. According to the American Heart Association, approximately 8.5 million Americans are affected by PAD. Another estimate pegs the U.S. PAD prevalence around 18 million patients. Worldwide, industry participants estimate in total 100-200 million people are affected by PAD. With aging population, rising prevalence of obesity and diabetes, PAD prevalence is increasing. PAD is caused by clogged arteries in the leg due to plaque formed by atherosclerosis. PAD in the leg arteries is the most often, but can also occur in other areas. The most common treatment is percutaneous transluminal angioplasty (PTA), with atherectomy and cryotherapy having a small slice of the market (see Figure 9). Within PTA, angioplasty catheter is the largest segment, with the rest spread around various access devices. Compared to the coronary market, peripheral vascular market is fragmented and has a range of players from large companies to small-medium companies (Table 14). Fast-growing segments include DCB, DES, atherectomy, and other new interventional products (Table 14). Vascular access products are slow growers.

Table 14 Competitive Landscape in Peripheral Vascular Market

Company	PTA Balloon	Guide Catheter	Guide Wire	CTO Crossing	Stent	DES	DCB	Atherectomy	Thrombectomy	VCF
Abbott	√	√	√		√ (SUPERA)	√ (Xience)				
BSC	√	√	√	√	√ (Epic, Express LD)	√ (Eluvia)	√ (Lutonix, Ranger)	√ (Jetstream, Rotablator)	√ (Angiojet)	√
Cook	√	√	√		√ (Zilver)	√ (Zilver PTX)	√ (Advance 18 PTX)			√
Cordis (Cardinal)	√	√	√	√	√ (FLEX)					√
CR Bard	√			√	√ (LifeStent)		√ (Lutonix)			√
Medtronic / Covidien	√	√	√	√	√ (EverFlex)		√ (IN.PACT)	√ (Turbohawk, Silverhawk)		
Terumo	√	√	√		√ (Misago)					
Spectranetics	√	√		√			√ (Stellarex)	√ (TurboElite, TurboTandom)		
Angiodynamics	√	√	√							
Volcano (Phillips)				√				√ (Phoenix)		√
Cardiovascular Systems								√ (Stealth 360, Diamondback 360)		
Biotronik							√ (Passeo-18 LUX)			
B. Braun	√									√

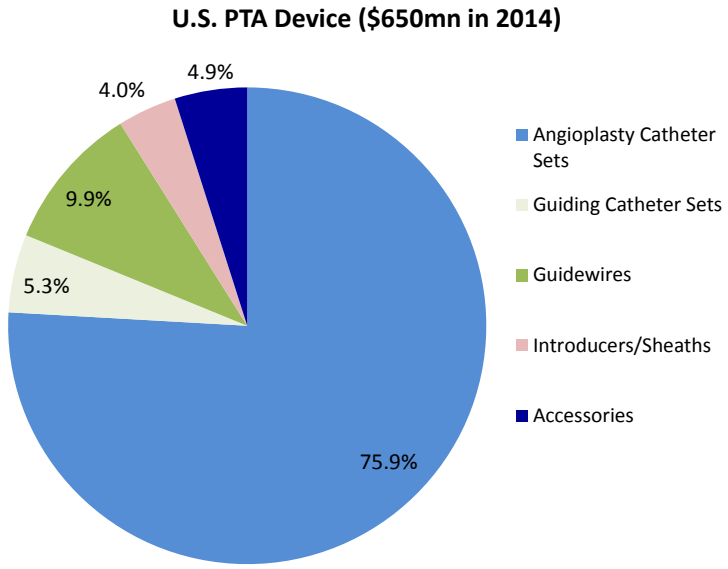
Source: Compiled by MHBK/IRD based on public company reports.

Figure 9 Composition of U.S. PAD Interventional Procedures



Source: Medtech Insight

Figure 10 U.S. PTA Devices Market, 2014



Source: Medtech Insight

Current PTA treatments include uncoated balloon angioplasty, (the so called POBA or "plain-old balloon angioplasty") and stents. However, they all have shortcomings. The main problem for POBA is low efficacy. Restenosis is a common problem. Stents, especially DES, have marked improvement in efficacy (see Table 15). But they have a number of disadvantages, including movement-related fracturing, foreign material in the vessel that could affect vessel wall, requiring dual antiplatelet therapy, etc. One major innovation is drug-coated balloon, which have greater clinical efficacy than POBA (see Table 15), and also avoid the disadvantages of stent.

DCB is balloon coated with drugs such as Paclitaxel to reduce restenosis. During PTA procedure, drug is quickly released to the vessel wall. As the balloon is withdrawn, there is no foreign material left in the vessel. This "nothing left behind" concept is very appealing to physicians. DCB is expected to become a big market from nothing. It is expected to grow from $80mn in this year to around $1bn near the end of this decade. There are two leading DCB platforms. CR Bard's Lutonix DCB received FDA approval in October 2014 and became the first DCB on the U.S. market. Quickly on the heel of Lutonix, FDA approved Medtronic's IN.PACT Admiral DCB in January 2015. Both approvals are for upper legs. For BTK (below the knee) PAD, DCB has not had good success. For example, Medtronic's BTK IN.PACT Amphirion DCB showed no clinical benefits over POBA. Besides Bard and Medtronic, there are a large number of companies developing DCBs, many of which have received approval in Europe (see Table 16). Given DCB's appealing attributes, many companies are developing them in coronary as well as peripheral applications.

Table 15 Comparison of Efficacy Results of Various PAD Treatment Technologies

Device	Patency Results
POBA	40-50%
BMS	70-80%
DES	80-90%
DCB	70-90%

Source: Compiled by MHBK/IRD based on public company reports

Table 16 Competitive DCBs Under Development

Company	Product	Eluting drug	Indication	Status
Bard	Lutonix	Paclitaxel	Peripheral	FDA approval; CE Mark
Medtronic-invatec	IN.PACT Admiral	Paclitaxel	Peripheral	FDA approval; CE Mark
Medtronic-invatec	IN.PACT Falcon	Paclitaxel	Coronary	CE Mark
Spectranetics	Stellarex	Paclitaxel	Peripheral	U.S. IDE trial; CE Mark
Boston Scientific	Ranger	Paclitaxel	Peripheral	CE Mark
Boston Scientific	Agent	Paclitaxel	Coronary	CE Mark
Medrad (Bayer)	Contavance	Paclitaxel	Peripheral	CE Mark
Biotronik	Passeo-18 Lux	Paclitaxel	Peripheral	CE Mark
Biotronik	Pantera LUX	Paclitaxel	Coronary	CE Mark
B. Braun	SeQuent Please	Paclitaxel	Coronary	CE Mark
EuroCor GMBH/Opto Circuits (India)	Freeway	Paclitaxel	Peripheral	CE Mark
EuroCor GMBH/Opto Circuits (India)	Dior II	Paclitaxel	Coronary	CE Mark
Aachen Resonance GMBH	Elutax SV	Paclitaxel	Coronary	CE Mark
Blue Medical Devices	Protégé, Pioneer	Paclitaxel	Coronary	CE Mark
Cook Medical	Advance 18 PTX	Paclitaxel	Peripheral	CE Mark
Cardionovum GMBH	LEGFLOW	Paclitaxel	Peripheral	CE Mark
Cardionovum GMBH	Restore	Paclitaxel	Coronary	CE Mark
Concept Medical	Magic Touch	Sirolimus		In development
Micell Technologies		Sirolimus		In development

Source: Compiled by MHBK/IRD based on public company reports

Another high-growth area is atherectomy. Atherectomy is used to debulk plaque before treatment with PTA or stent. With increasing prevalence of calcified and hard lesions and improving atherectomy technology, atherectomy market is expected to grow briskly. Atherectomy market for PAD is about $300mn and is growing at ~10% a year. Market potential for PAD atherectomy is projected to be over $1bn. Atherectomy for coronary procedures is estimated to be ~$100mn market, growing at low-mid single digit. The market potential for coronary is also estimated to be $1bn. Covidien and Cardiovascular Systems (CSII) are leaders in the market, each controlling estimated 40% share. With some technology advantage, Cardiovascular Systems has been taking market share. CSII has grown sales by over 25% year/year for the last three years. Other players include Spectranetics, BSC, Volcano (now part of Phillips). Notable emerging players are Avinger and Shockwave Medical (see Table 17).

Table 17 Comparison of Atherectomy Devices

Company	Product	Method	PAD	CAD
Covidien/Medtronic (FoxHollow)	Turbohawk	Directional	√	
	Silverhawk	Directional	√	
Cardiovascular Systems	Stealth 360	Orbital	√	
	Diamondback 360	Orbital	√	√
Spectranetics	TurboElite	Laser	√	
	ELCA	Laser		√
Boston Scientific	Rotablator	Rotational		√
Bayer (now BSX)	Jetstream XC/SC	Rotational	√	
Volcano (AtheroMed)	Phoenix	Rotational	√	
Avinger	Pantheris	Directional with OCT	√ (EU)	
Shockwave Medical	In development	Lithoplasty		

Source: Compiled by MHBK/IRD based on public company reports.

E. Update of the Neurovascular Market

Stroke is a debilitating medical condition and is poorly addressed by current therapies. According to the World Health Organization, an estimated 15 million people worldwide suffer a stroke each year. In the U.S., around 800,000 people have a stroke annually. Of these, 87% have an acute ischemic stroke (AIS), and 13% have a hemorrhagic stroke. Neurovascular devices are used by neurosurgeons and neuro-interventionalists to treat stroke. According to market leader Stryker, world neurovascular market is currently around $1.3bn and is projected to grow at high single-digit (this estimate excludes carotid artery stent system).

Neurvascular products are broadly divided along the lines of cerebral aneurysm, ischemic stroke, and general access/balloon (see Table 18). A cerebral aneurysm is a weak spot in the wall of a blood vessel within the brain, characterized by an abnormal "ballooning" or widening of the vessel. When a brain aneurysm ruptures, the result is hemorrhagic stroke and is often fatal. Although hemorrhagic stroke is only 13% of total stroke (vs. 87% for ischemic stroke), it represents the majority (estimated 70-80%) of total neurovascular market. Embolic coil has become the standard of care. Brain aneurysm treatment has been migrating from surgical clipping to endovascular coiling. According to the leader in the coil market, Terumo, in 2013, 61% brain aneurysm procedures in U.S. and Europe used coiling and 39% used clipping. By 2016, the ratio will change to 65% coiling and 35% clipping. Stent-assisted coiling or balloon-assisted coiling are used for difficult cases such as wide-neck intravascular aneurysms. Flow diverter such as Pipeline™ Embolization Device from Covidien, is a notable new option for cerebral aneurysms. Instead of placing embolic material inside the aneurysm sac, a stent-like device is placed in the parental blood vessel of the aneurysm sac to divert blood away from the aneurysm. After the implantation, blood flow to the aneurysm is decreased and the aneurysm will be closed after a period. Total aneurysm market is growing at close to mid-single digit, with coils growing slower than non-coils.

As shown in Table 18, established devices to treat acute ischemic stroke include PTA and intracranial stent for intracranial atherosclerotic diseases, and thrombectomy devices to remove clot in large vessel occlusion. Of the various segments, cerebral thrombectomy is projected to have the most robust growth, driven by highly unmet medical need, strong clinical data and device innovation (see Table 19).

Table 18 Major Neurovascular Products

Device Categories	Devices
Access/Balloon	Guidewire, Micro catheter / Guiding catheter, balloons
Treatment for cerebral aneurysms (hemorrhagic stroke)	
Established devices	Clippings, coils (bare metal, coated), Stent-assisted coiling; balloon-assisted coil
New devices	Stent-based Flow diverters, intravascular occlusion devices, liquid embolization systems
Treatment for acute ischemic stroke (AIS)	
Established devices	PTA, intracranial stent, carotid stent, thrombectomy devices
New devices	Stent retrievers

Source: Compiled by MHBK/IRD based on public company reports

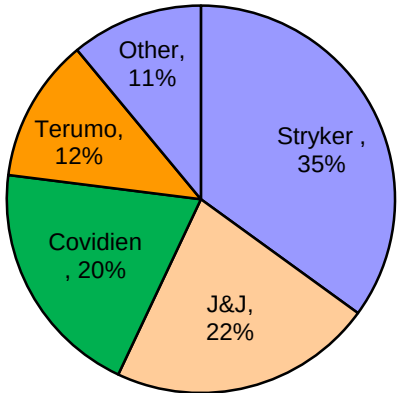
Table 19 U.S. Neurointerventional Systems, Market Forecast, 2013-2018 ($mn)

Market Segment	2013	2014E	2015E	2016E	2017E	2018E	CAGR
Cerebral Aneurysm and AVM Endovascular Embolization Systems	$318.1	$330.9	$343.9	$357.1	$370.6	$384.6	3.9%
Wide-Neck Cerebral Aneurysm Embolization Enabling Stent Systems	$36.2	$37.2	$38.6	$39.4	$40.6	$42.4	3.2%
Distally Protected Carotid Artery Stent Systems*	$181.3	$201.6	$226.8	$245.0	$269.5	$299.0	10.5%
Intracranial Stent Systems	$8.1	$6.3	$6.3	$6.8	$7.2	$6.7	-3.7%
Cerebral Thrombectomy Systems	$73.4	$78.3	$85.5	$89.1	$96.0	$113.5	9.1%
Total Neurointerventional System Sales	$617.1	$654.3	$701.1	$737.4	$783.9	$846.2	6.5%

Source: Medtech Insight.

Stryker is the market leader, followed by J&J, Covidien and Terumo (see Figure 11). A key trend for the neurovascular market is for players to move beyond basic access device and coils to high-growth areas such as stents, flow diverters, thrombectomy devices (clot retrievers), liquid embolic, etc. As shown in Table 20, major neurovascular companies have been trying to flesh out their product offerings to have a total solution for stroke.

Figure 11 Global Neurovascular Market Share



Source: Compiled by MHBK/IRD based on public company reports

Table 20 Competitive Landscape of Major Neurovascular Companies

Company	Stryker	Covidien/ Medtronic	J&J (Codman Neuro)	Terumo (Microvention)	Penumbra	Other Players
Embolic Coil	√	√	√	√	√	
Access Devices	√	√	√	√	√	
Remodeling Balloons	TransForm Occlusion Balloon	HyperForm, HyperGlide	Ascent	Scepter occlusion balloon		
Coil Assist Stent	Neuroform EZ			LVIS		
Stent-based Flow Diverter	Surpass NeuroEndoGraft Flow Diverter;	Pipeline (U.S. approved)	ENTERPRISE Vascular Reconstruction Device	FRED		Balt Extrusion
Liquid Embolic Systems		Onyx	TRUFILL			
Mechanical Thrombectomy for ischemic stroke (FDA approved)	Trevo Provue Stent Retriever	Solitaire FR stent retriever			Penumbra System; ACE	Balt Extrusion, Neuravi, phenox
Carotid Artery Stent		√	√			Abbott, BSC

Source: Compiled by MHBK/IRD based on public company reports

Below we review several high-potential segments of neurovascular market.

1. Cerebral Thrombectomy Devices

Cerebral thrombectomy is a fast growing segment. First-generation device Merci Retriever from Concentric Medical (Stryker) received approval in 2004, but it has mediocre efficacy. Second-generation devices are far more superior (see Table 21). Especially notable are the so-called Stent retriever devices such as Solitaire from Covidien and Trevo from Stryker. Both stent retrievers soundly beat Merci in various efficacy measures in robust clinical trials (see Table 21).

In December 2014, results from the 500-patient "MR CLEAN" trial were published in The New England Journal of Medicine, which for the first time clearly demonstrated the benefits of thrombectomy device over medical treatment (IV iPA). The results of the 500-patient trial demonstrated an absolute difference of 13.5% in the rate of functional independence in favor of intra-arterial intervention with no significant difference in

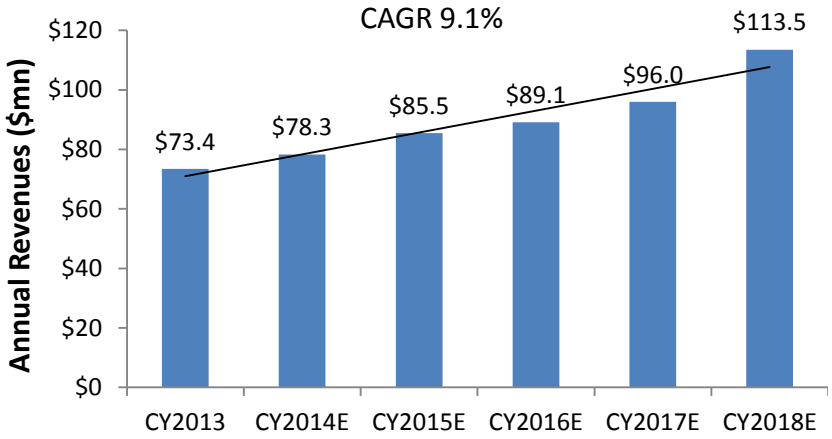
mortality or symptomatic intracerebral hemorrhage. This trial is expected to boost sales of thrombectomy devices, which is projected to grow at 9% CAGR over the next five years (see Figure 12). Covidien has 56% market share (see Figure 12), followed by Stryker (35%) and Penumbra (9%).

Table 21 New Generation Cerebral Thrombectomy Devices

Company	Device	Approval	Clinical Data
Covidien	Solitaire FR stent retriever	Mar-12	SWIFT trial was stopped early and it showed overwhelming superiority over Stryker's 1st generation Merci Retriever (recanalization 68.5% vs. 24.1%; good neurological outcome at 90 days 58.2% vs. 33.3%; lower use of rescue therapy 20.7% vs. 43.6%, lower 90-day mortality 1.7% vs. 38.2%, and device-related SAE 8.6% vs. 16.4%).
Stryker	Trevo XP ProVue stent retriever	2/2014	TREVO2 trial showed higher revascularization (86.4% vs. 60%) and better functional independence (Rankin Scale≤2, 40% vs. 21.8%) than Merci Retriever.
Penumbra	Penumbra Systems	Dec-07	Penumbra Stroke Trial showed 81.6% revascularization and low SAE of 3.2%

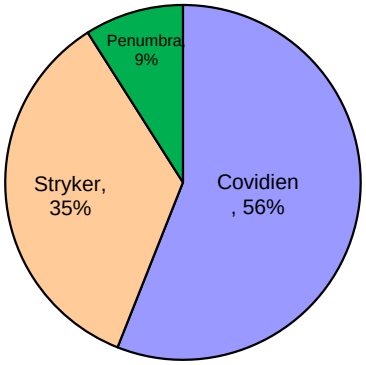
Source: Compiled by MHBK/IRD based on public company reports

Figure 12 Projected Sales Growth of U.S. Thrombectomy Devices



Source: Compiled by MHBK/IRD based on data from Medtech Insight

Figure 13 Market Share of U.S. Cerebral Thrombectomy Devices



Source: Compiled by MHBK/IRD based on data from Medtech Insight

2. Flow Diverter for aneurysm

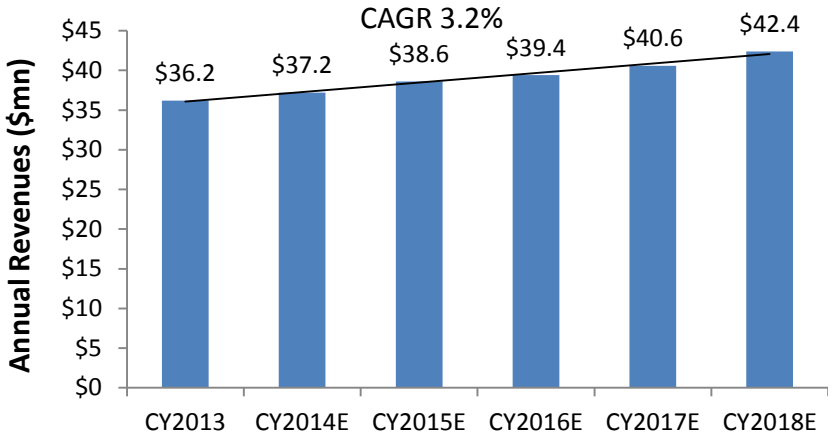
Stand-alone coils are not suitable for wide-neck cerebral aneurysms, which account for 20%-25% of all invasively treated cases. Stents are often used for this purpose. Flow diversion is a technique used to treat large or giant wide-necked brain aneurysms in which the device is placed in the parent blood vessel rather than in the aneurysm sac. Covidien's Pipeline Embolization Device (PED) is the only FDA approved flow diversion device. In clinical trials, it has shown 1-year occlusion rate above 85%. However, a product recall in 2014 was a setback. In February 2015, Covidien further received FDA approval for Pipeline FLEX. Pipeline FLEX gives physicians more control over the implantation of the device. Stryker and J&J have CE Mark for their flow diverter devices (see Table 22). As these products gain U.S. approval, sales could ramp up over time. Currently, modest growth was forecasted for this category (see Figure 14).

Table 22 Flow Diverter Devices

Company	Device	Approval Status	Comments
Covidien	Pipeline Embolization Device (PED)	April 2011 FDA approval	For the treatment of large or giant wide-necked intracranial aneurysms of the internal carotid artery
Covidien	Pipeline Flex	European launch in June 2014. FDA approval in February 2015.	Allows doctors to recapture, reposition and redeploy.
Stryker	Surpass NeuroEndoGraft Flow Diverter	CE Mark	Acquired from Surpass Medical
J&J	ENETERPRISE Vascular Reconstruction Device	CE Mark	

Source: Compiled by MHBK/IRD based on public company reports

Figure 14 Projected Sales Growth of U.S. Flow Diverter Devices



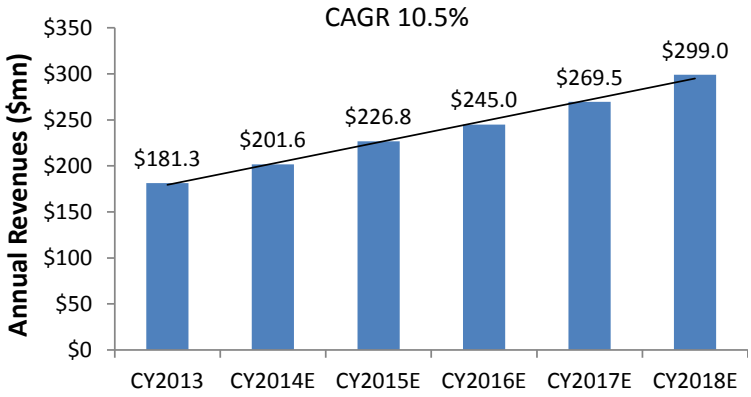
Source: Compiled by MHBK/IRD based on data from Medtech Insight

3. Carotid Artery Stenting (CAS) System

CAS has several advantages over the gold standard carotid endarterectomy (CEA). First of all, CEA is an open surgery procedure. Some patients either are not candidates for open procedure or are unwilling to go through with the procedure. In contrast CAS is minimally invasive procedure. CAS also has the advantage of treating inaccessible lesions and possible revisions. However initial experience with CAS suggested perhaps lower efficacy vs. CEA. The perception changed in 2010 when the results from the Carotid Revascularization Endarterectomy versus Stent Trial (CREST) demonstrated non-inferiority of CAS vs. CEA. In May 2011, the FDA approved CAS for "standard surgical risk" carotid stenosis indications traditionally managed with CEA. CAS market is projected to grow at10.5% per annum (see Figure 12), driven by the non-inferiority clinical data, improving technology, approval to standard-risk patients, and patients preference for less invasive procedures.

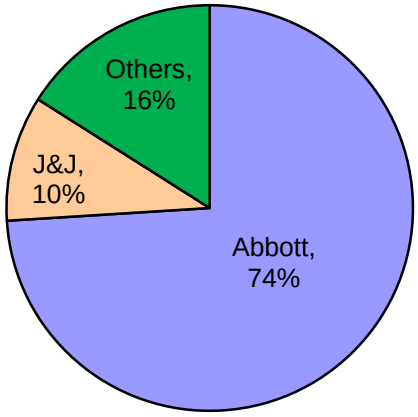
Five companies – Abbott, BSC, J&J, Covidien and Metronic – have secured FDA approval for distally protected CAS devices for high surgical risk patients. In May 2011, Abbott received FDA approval for standard surgical risk patients based on the data of the CREST trial (for which Abbott Vascular's CAS system was used). Other companies are expected to also receive similar approval. In 2013, high-risk carotid stenosis was 63.3% of the market ($114.7mn), while standard-risk was 36.7% ($66.6mn). This label expansion to standard-risk patients will help drive growth of the market.

Figure 15 Projected Sales Growth of U.S. CAS Devices



Source: Compiled by MHBK/IRD based on data from Medtech Insight

Figure 16 Market Share of CAS Devices



Source: Compiled by MHBK/IRD based on data from Medtech Insight

4. M&A Deals in Neurovascular Market

Neurovascular market is a specialized market with focused call points. The size of target physicians is estimated 3,000 globally, which is much smaller than the 50,000 physicians for coronary intervention. Therefore a small company is viable in neurovascular market. M&A has always been the primary route for large device companies to enter into the neurovascular market (see Table 23).

- Stryker entered into Neurovascular filed in 2011 by acquiring the neurovascular business of Boston Scientific.
- Terumo entered into the neurovascular business in 2006 by acquiring MicroVention.
- Covidien entered the market by acquiring ev3 in 2010.
- Medtronic entered the market by acquiring Covidien in 2014.

In addition, large companies have used acquisitions to get into attractive areas such as flow diverters, stent retrievers and other cerebral thrombectomy devices (see Table 23). We expect M&A will continue to be a key lever for companies to grow in the neurovascular intervention market.

Table 23 Historical M&A Deals in Neurovascular Intervention

Aquirer	Target	Announce Date	Deal Value ($mn)	Revenue Prior Yr ($mm)	Price/Sales	EV / EBITDA	Therapeutic Area
Medtronic	Covidien	16-Jun-2014	$42,900	$10,329	4.2	15.4	Broad
Covidien	Nfocus	19-Feb-2013	$72				stent diverter for brain aneurysms
Stryker	Surpass Medical	16-Oct-2012	$100				Brain aneurysm
Covidien	MindFrame	02-Jul-2012	$75				Stroke clot retriver
Stryker	Concentric Medical	31-Aug-2011	$135				Acute ischemic stroke intervention
Stryker	BSX Neurovascular	28-Oct-2010	$1,500	$348	4.3		Neurovascular
Johnson & Johnson	Micrus Endovascular	12-Jul-2010	$388	$91	4.3	23.2	Neurovascular
Covidien	Ev3	01-Jun-2010	$2,547	$473	5.4	30.4	Peripheral and neuro vascular
ev3, Inc.	Chestnut	03-Jun-2009	$150				Flow diverter (Pipeline)
Terumo	MicroVention	28-Feb-2006					Neurovascular

Source: Compiled by MHBK/IRD based on data from Medtech Insight

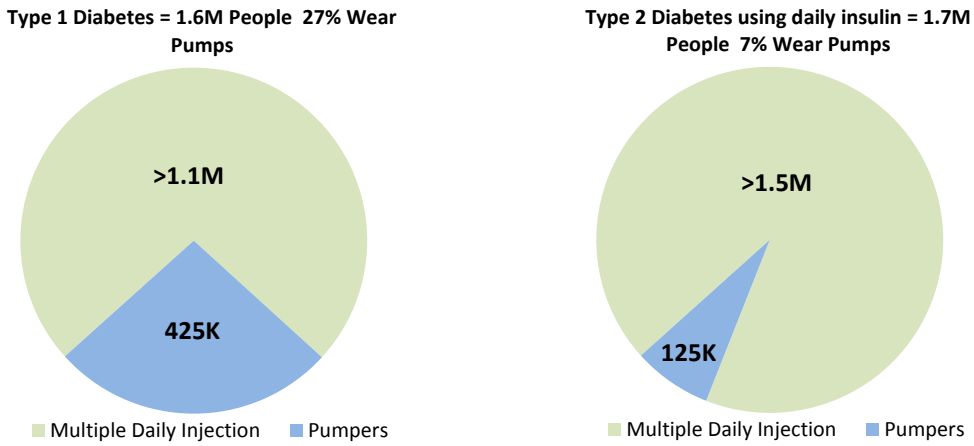
F. Update of the Diabetes Device Market

As a number of large CV medtech companies are also leading players in the diabetes device market, we discuss the insulin pump and continuous glucose monitoring (CGM) markets in this section. Insulin pump market is currently worth $2bn and is projected to grow at 5% per annum. CGM market is $500-600mn and is growing at over 25% per year. The long-term goal is to achieve a closed-loop system or artificial pancreas (AP), whereby CGM and insulin pump are integrated with an algorithm to deliver insulin according to real-time changes in blood glucose levels. CGM and insulin pumps are highly complementary. Broader market adoption of CGM spurs adoption of insulin pumps as patients can more readily customize their bolus insulin injection. All major insulin pump manufacturers outside of Medtronic have entered into joint development collaboration with CGM leader DexCom. Medtronic is the only company that has chosen to use its own proprietary systems (i.e., integrate in-house insulin pumps with in-house CGM). While in the long-term an open system may be the preferred option, in the near-term Medtronic has a huge start in terms of integrating pumps with CGM. Its insulin pump 530G is the only pump on the market that has a low threshold suspend feature.

1. Insulin Pumps

Insulin pump market is currently worth $2bn and is projected to grow at mid-single digit per annum. Insulin pump has several advantages over Multiple Daily Injections (MDI) of insulin. As insulin pump delivers insulin continuously, it has better glycemic control and no need of multiple daily self-injections compared to MDI. Currently, insulin pump penetrates about 27% Type 1 diabetic patients and 7% Type 2 insulin-using diabetic patients (see Figure 17). The argument for insulin pump in T1DM is especially strong. The penetration is expected to exceed 50% in the future.

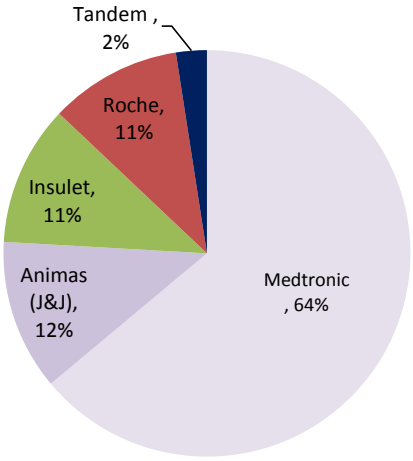
Figure 17 Market Penetration of Insulin Pumps



Source: Compiled by MHBK/IRD based on public company reports

Medtronic is the leader in insulin pumps by having around 64% market share (see Figure 18). It entered into the market in 2001 with the acquisition of Minimed and MRG for $3.7bn. J&J entered into the pump market through its February 2006 acquisition of Animas for $518mn. It currently has approximately 12% share. Roche entered into the market by acquiring Disetronic in 2003. Most of Roche's pump sales are outside of the U.S. and it has around 11% global share. Insulet and Tandem Diabetes are two independent insulin pump companies noted for their innovative products.

Figure 18 Worldwide Insulin Pump Market Share



Source: Compiled by MHBK/IRD based on public company reports

There is generally not much differentiation among different brands of insulin pumps with a few exceptions:

- Insulet's OmniPod is the only insulin pump without tubing (infusion sets).
- Tandem Diabetes offers the only touch-screen insulin pump.
- Several pumps have been integrated with CGM. At the simple level, CGM data is displayed on the pump receiver, but the CGM data doesn't automatically affect pump behavior. Examples include Vibe from Animas and T:slim G4 from Tandem. Both pumps are linked to DecCom's G4 CGM sensor. However this integration may become less meaningful in the future as blood glucose data may be displayed on smartphones. At a more advanced level, CGM directly influence pump action. Medtronic's 530G is the only pump with such as feature. It suspends insulin delivery at low blood glucose level to avoid hypoglycemia.

Table 24 lists the insulin pumps from major supplies. Most of the pumps are for T1DM although some are for T2DM. T2DM pump market is estimated to be $300-400mn, which is one fifth of the T1DM pump market. However, several small players such as Valeritas and CeQur have developed pumps for T2DM.

Table 24 Insulin Pumps from Major Competitors

Company	Products	Diabetes	Stage	Description
Medtronic	530G	Type 1	Launched	Only pump with low threshold suspend feature
	640G	Type 1	U.S. trial ongoing	Integrate with Enlite 3 CGM. Improved algorithms.
	670G	Type 1	U.S. trial ongoing	Able to respond to both high and low glucose with continuation or suspension of insulin delivery.
	Paradigm Veo	Type 2	Launched	CGM integration
Insulet	OmniPod	Type 1	Launched	Tubeless pump
	Next Gen PDM	Type 1	510k filing in late 2015	Integrate with DexCom G5 sensor. Touch screen.
	Pump partnered with Eli Lilly	Type 2	U.S. trial ongoing	Pod delivers Eli Lilly's U-500 insulin
Tandem	t:slim	Type 1	Launched	Touch screen
	t:slim G4	Type 1	Launch in 2015	Integrated with DexCom G4 sensor.
	t:flex	Type 2	Launched in 2015	
Animas (J&J)	Animas VIBE	Type 1	Launched	Integrated with DexCom G4 sensor.
	Finesse	Type 2	U.S. trial ongoing	

Source: Compiled by MHBK/IRD based on public company reports

2. CGM

DexCom, Medtronic and Abbott are the major competitors in CGM. DexCom is the technology leader. Accuracy is a key differentiating feature among CGM products. Prior to the October 2012 launch of DexCom's G4 sensor, CGM's accuracy was lacking. G4 sensor increased accuracy as measured by MARD (mean absolute relative difference) from ~16% to ~9% for the current G4 Platinum sensor. With this improved accuracy, CGM penetration into the T1DM market increased from 6% to the current 15%. Over time, CGM should become the stand of care for T1DM. In addition to boosting CGM adoption, the launch of G4 shifted market share to DexCom's favor at the expense of Medtronic and Abbott. As a result, DexCom grew its sales year/year by about 60% in both 2013 and 2014. In 2015, DexCom projects sales to increase 35-40%.

Medtronic and Abbott are trying to catch up. Medtronic is developing Enlite 3 sensor, which may have MARD in the 10-11% range. Although this represents an improvement over Enlite 2, it is still not substantiated by data and may not be enough to match DexCom's performance. Abbott is launching Libre sensor in Europe and is running clinical trials in the U.S. Libre doesn't have the traditional alarm/alert system of traditional CGM, but it has accurate sensor. One advantage of Libre is its "factory calibration," which means it doesn't require patient calibrate with finger sticks.

Table 25 Major CGM Competitors

Company	Products	Stage	Description
DexCom	G4 Platinum	Launched	
	G4 Platinum AP	Launched in U.S. in late 2014	MARD ~9%. Best in class efficacy
	G4 SHARE Receiver	Launched in U.S. in early 2015	Allow CGM data to be sent to smartphones or cloud
	G5	U.S. approval in late 2015	Bypassing the need for a receiver, CGM sends data directly to smartphone or cloud.
Medtronic	Enlite 2	Launched	
	Enlite 3	U.S. trial ongoing	MARD could be 10-11%, smaller size
Abbott	Freestyle Libre	U.S. trial ongoing	Factory calibration. On-demand reading.

Source: Compiled by MHBK/IRD based on public company reports

G. Update of the Neuromodulation Market

Neuromodulation market rivals atrial fibrillation and diabetes market in size and high growth rates and thus is very attractive to device makers. Worldwide neuromodulation market is currently worth ~$3bn in 2014 and is projected to grow high-single digit over the next five years. Neuromodulation is vastly underpenetrated. As medtech companies show robust data for highly refractory patients, neuromodulation will overcome the resistance of adoption and achieve broader use. The largest market of neuromod is the $1.5bn spinal cord stimulation (SCS) for pain, followed by $500mn deep brain stimulation (DBS) for movement disorders (see Table 26). Neuromodulation market has been growing at high-single digit rate per annum. However, U.S. growth flattened in 2014 for the large SCS segment due to a new physician reimbursement system for trialing SCS in the office setting. CMS implemented this policy on January 1, 2014 and has had a major negative impact on trialing SCS in physician offices. However this negative market development is temporary and most observers expect the market to resume growth in high-single digit in 2015.

Table 26 Key Market of Neuromodulation

Neuromodulation Category (Indications)	2014 Revenues	Share	Mid-term Growth rate
Spinal cord stimulation (Pain)	$1,500	50%	5-7%
Deep brain stimulation (Parkinson's Disease, Dystonia, Essential Tremor, OCD)	$500	17%	10-15%
Vagus nerve stimulation (Epilepsy, Depression)	$280	9%	High-single digit
Sacral nerve stimulation (Urinary Incontinence, Fecal Incontinence)	$475	16%	
Other - Gastric stimulation (obesity); - Percutaneous Tibial Nerve Stimulation, other (Urinary Incontinence)	$250	8%	
Total	$3,000		High-single digit

Source: Compiled by MHBK/IRD based on public company reports

Neuromodulation market is dominated by the top three companies (see Table 27). Medtronic is the largest player and has ~61% market share. This is followed by Boston Scientific (15% share) and St. Jude Medical (14% share). In the large SCS segment, Medtronic has a leading 41% market share, followed by Boston Scientific (30% share), St. Jude Medical (26%) and Nevro (2%).

Medtronic is the pioneer in neuromodulation and introduced the first SCS in 1984. Medtronic has a complete product line-up, leading in SCS, DBS, Sacral nerve stimulation and gastric stimulation. Medtronic's neuromodulation business has grown steadily in recent years. In its FY2014, neuromodulation sales grew 5% from $1.8bn to $1.9bn. Growth is led by InterStim sales (sacral nerve stimulation) and DBS. In the SCS market, *RestoreSensor SureScan* MRI system has helped Medtronic defend its market share in SCS. Other SCS products include *RestoreULTRA*, *RestoreADVANCED*, and *PrimeADVANCED* systems. Medtronic has been working on MRI-compatible products. It is also working on products that offer personalized pain relief. For example, this includes *High Density Stimulation*, which gives higher amount of energy and can be used to optimize pain management.

Boston Scientific entered into the pain market in 2004 through the acquisition of Advanced Bionics in 2004. It launched the Precision SCS system in 2004. In August 2013, BSC launched its next-generation Precision Spectra SCS in the U.S. The system allows better targeting of pain and ease of programming. It is the first 32-contact and uses a new neuro-targeting computer algorithm

called Illumina 3D. In 2014, BSC's sales of neuromodulation business were $437mn, a 3% increase from 2013. Main driver was the Precision Spectra System, which helped BSC gain 5% U.S. SCS market share. In addition to SCS products, BSC markets DBS system Vercise in Europe. In September 2012, Vercise received CE Mark for the treatment of certain movement disorders including Parkinson's disease, tremor, and dystonia. BSC is conducting U.S. IDE trial for Vercise.

St. Jude Medical is the third largest player worldwide (14% share), but the second-largest player outside of the U.S. (30% market share). St. Jude's U.S. modulation business has been severely hampered by a long-standing FDA warning letter issued in July 2009. Because of this warning letter, St. Jude couldn't introduce any new products in the U.S. between 2009 and 2014 and its U.S. business suffered. This dichotomy of performance was also reflected in St. Jude's 2014 financial results, which showed revenue growth of 25% internationally, versus a 5% decline in the U.S. In August 2014, St. Jude finally resolved this warning letter and is on the path to have a complete revamp of its neuromodulation product line. The company launched Protégé in the U.S. and Prodigy SCS in international market. In the second half of 2015, St. Jude plans to launch *Proclaim*, a new primary cell platform for chronic pain, and *Infinity*, for movement disorders. Both products will be MRI compatible. St. Jude has also developed an Invisible Trial System, which will launch in both the U.S. and EU in 2015. This device allows patients to conceal the system during the trial phase of the implantation and is therefore considered patient friendly. The company developed a next-generation burst SCS system called Prodigy. Burst stimulation could offer similar or better pain relief with less paresthesia compared to traditional tonic stimulation. In April 2015, St. Jude exercised its option to acquire Spinal Modulation, which developed the next-generation Axium SCS system targeting DRG (dorsal root ganglion). DRG stimulation allows physicians to precisely targeting pain in specific anatomical areas. In DBS, St. Jude has only less than 10% market share in international market. However, St. Jude plans to launch *Infinity DBS* in second half of 2015 for Parkinson's and Essential Tremor. *Infinity* has a number of advantages over traditional DBS such as precise stimulation and decreased power usage.

Another notable player is Cyberonics. It is uniquely position in vagus nerve stimulation (VNS) for Epilepsy. Recently, the company merged with Sorin to become LovaNova. The potential synergy between VNS for heart failure with Sorin's CRM business was cited as one of the reasons for the merger.

A notable new comer in neuromodulation is Nevro. The company's Senza SCS system delivers high-frequency stimulation to spinal cord. This has advantage of offering pain relief without the side effects of paresthesia (the tingling sensation associated with traditional SCS). In a randomized, controlled trial (RCT), Senza showed better pain relief and no reports of uncomfortable stimulation (0% compared to 44%) compared to traditional SCS. On May 8th, Senza received FDA approval. It is expected to be launched soon and capture a notable share of the SCS market.

Table 27 Key Players in Neuromodulation

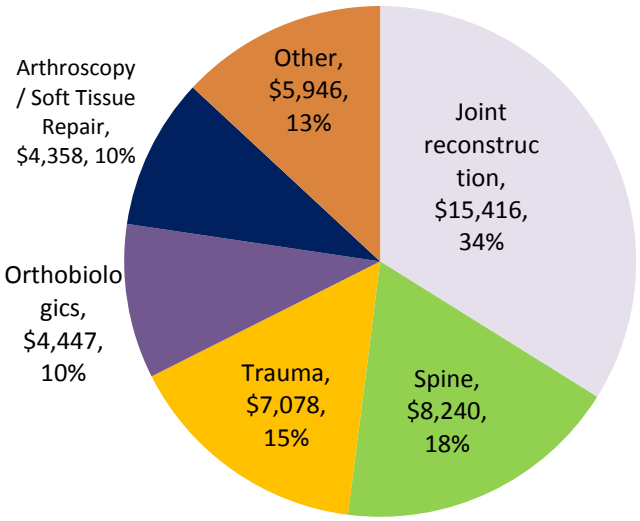
Company	Major Brands	FY2013 Sales ($mn)	FY2014 Sales ($mn)	FY2014 Sales growth	Market share	Acquisitions
Medtronic	PrimeAdvanced; RestoreSensor, RestoreAdvanced; RestoreUltra; Activa PC, RC; Soletra; Kinetra; InterStim	$1,812	$1,898	5%	61%	
St. Jude	Eon, Protégé, Prodigy, Proclaim, Axium, Libra DBS system, Brio DBS system,	$426	$437	3%	14%	- $1.2bn acquisition of Advanced Neuromodulation Systems in 2005; - Acquired NeuroTherm (RF ablation) in 7/2014 - Acquired Spinal Modulation, a specialist in DRG stimulation in May 2015.
Boston Scientific	Precision Spectra, Precison Plus, Precison Novi, Vercise DBS	$453	$472	4%	15%	- acquired Advanced Bionics for in 2004.
Cyberonics	VNS therapy	$254	$282	11%	9%	- Merged with Sorin in 2015
Nevro	Senza (HF10)	$23	32.6	39%	1%	

Source: Compiled by MHBK/IRD based on public company reports. Excludes cochlear implants

IV. Orthopedics Industry

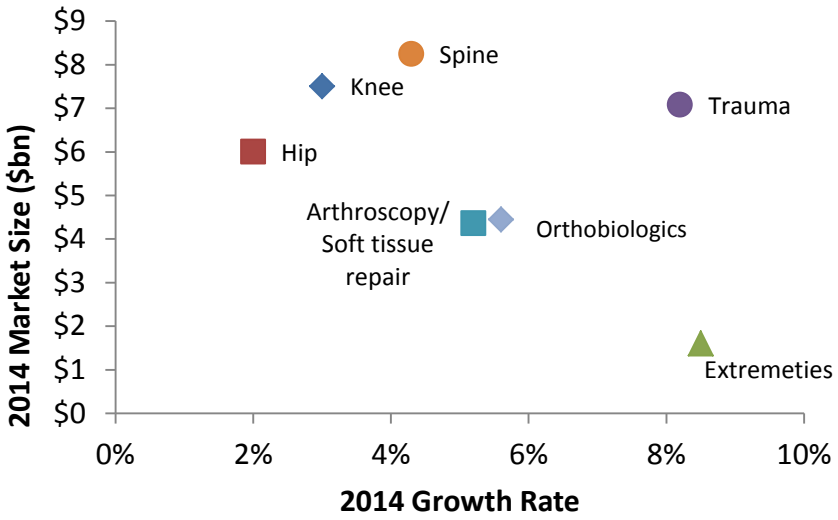
Worldwide sales of orthopedic products are estimated to be about $45.5bn in 2014, which represents growth of 3% from 2013. Major segments include joint reconstruction (hip, knee and extremities), spine, trauma, orthobiologics, arthroscopy/soft tissue repair, and others (see Figure 19). As shown in Figure 20, Extremities, Trauma, Orthobiologics and Arthroscopy led the growth in 2014, but stalwarts such as Hip, Knee and Spine also registered healthy growth.

Figure 19 Orthopedic Product Sales by Market Segment



Source: Compiled by MHBK/IRD based on data from ORTHOWORLD

Figure 20 Orthopedics 2014 Market Size and Growth Rates



Source: Compiled by MHBK/IRD based on data from ORTHOWORLD

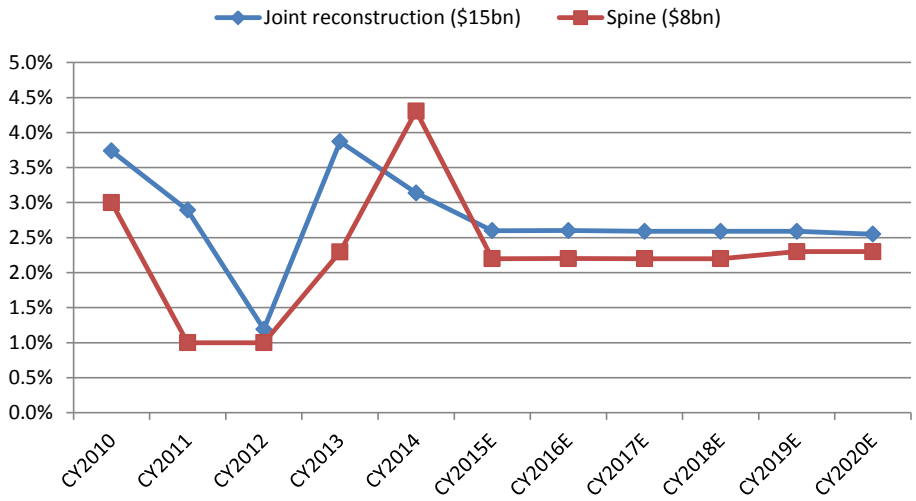
Most segments are projected to grow at low-mid single digit for the next five years (see Table 28). Of the major device categories, notably joint reconstruction and spine have turned the corner from previous low level of growth (see Figure 21).

Table 28 Projected Sales Growth of Major Orthopedic Segments

Sales ($mn)	2004	2015E	2020E	2015 Growth	2015-2020 CAGR
Joint reconstruction	$15,416	$15,817	$17,968	2.6%	2.6%
Spine	$8,240	$8,422	$9,408	2.2%	2.2%
Trauma	$7,078	$7,545	$9,983	6.6%	5.8%
Orthobiologics	$4,447	$4,545	$5,093	2.2%	2.3%
Arthroscopy / Soft Tissue Repair	$4,358	$4,562	$5,702	4.7%	4.6%
Other	$5,946	$6,095	$6,474	2.5%	1.2%
Total	$45,485	$46,986	$54,628	3.3%	3.1%

Source: Compiled by MHBK/IRD based on data from ORTHOWORLD

Figure 21 Growth Trend of Joint Reconstruction and Spine



Source: Compiled by MHBK/IRD based on data from ORTHOWORLD

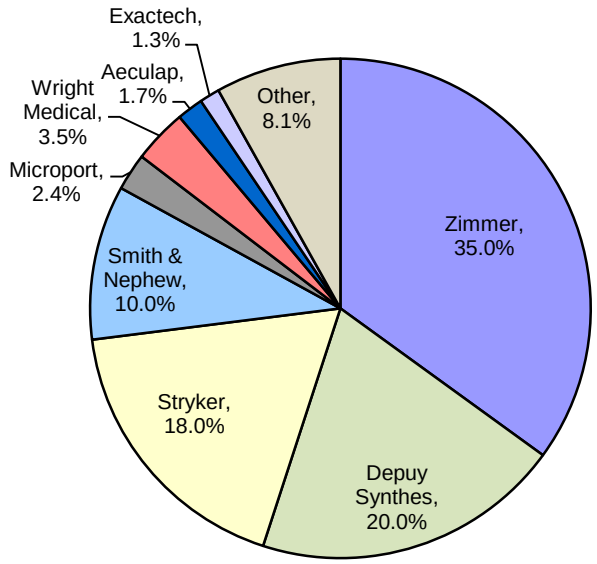
A. Joint Reconstruction

The joint reconstruction market has recovered from anemic growth in 2011/2012 to steady, low-single digit growth. Procedure growth has been steady in the low-single digit range. Pricing pressure hasn't worsened. Hip ($6bn) and Knee ($7.5bn) are growing at 2-3% per annum. Although extremities ($1.6bn) are growing at 8-9% per annum, its low weight in overall joint reconstruction cannot bring up the sector average growth rate.

Two major transactions announced in 2014 will significantly change the competitive landscape. Zimmer's 2014 acquisition of Biomet for $13.35bn has substantially changed the market share structure. Before the merger, Zimmer and Biomet had 23% and 12% market share respectively. The combined company has 35% share, far out-stripping next-tier competitors (see Figure 22). The $3.3bn merger between Wright Medical and Tornier will create a top player in extremities, the fastest growing segment of joint reconstruction. Over the last year, there has been periodical media speculation of a Stryker – Smith & Nephew tie-up, but Smith & Nephew has shunned this idea. Another notable development was Microport's acquisition OrthoRecon business of Wright Medical in 2013 for $290mn. The deal ushered in a Chinese player in the joint reconstruction market. But so far it hasn't been a disruptor that causes significant market share shift.

Among hot topics in joint reconstruction, robotic-guided surgery appears to gain more popularity. Stryker leads in robotic orthopedic surgery through its acquisition of MAKO Surgical in September 2013. In August, FDA approved MAKO's RIO system for total knee reconstruction. This is in addition to RIO's existing approved indications for partial knee and total hip. In October, Smith & Nephew acquired the orthopedic robotic company Blue Belt Technologies for $275mn. Another hot topic is more emphasis on the value and outcomes of ortho reconstruction procedures.

Figure 22 Global Joint Reconstruction Market Share

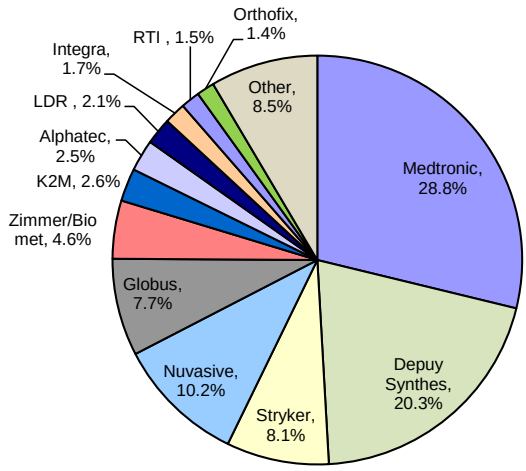


Source: Compiled by MHBK/IRD based on ORTHOWORLD and public company reports

B. Spine

The spine market has recovered from the no-growth period of 2010-2011 to low-single digit growth. Spine market experienced several headwinds in 2010-2011, including weak procedure volume due to weak economy and concern over value (spine fusion for back pain) and safety (e.g., INFUSE) of spine procedure, growing prevalence of Physician Owned Distributorships (PODs), and price declines. Since then, growth of PODs has stalled and scrutiny over spine procedures' economics and safety has subsided. As a result, procedure volume has been stable to increasing. Going forward, most observers expect the spine market to grow at low-single digit rate. Leading the growth in spine market are mid-sized pure-play spine companies such as Nuvasive, Globus Medical, LDR Holding, and K2M Holdings. They have taken shares from large medtech players. Big spine players have been preoccupied by mergers. Medtronic is in the process of a $42.9bn acquisition of Covidien. The 2011 acquisition of Synthes by DePuy has led to integration issues. Merger of Zimmer and Biomet led to the consolidation of their respective spine businesses. Integra LifeSciences Holdings Corp. announced it would divest its spine and biologics business into a separately traded company named SeaSpine by the end of this year. Going forward, M&A deals in the spine market are likely be small tuck-in deals aimed at bolstering product portfolios. Top players already have big market shares.

Figure 23 U.S. Spine Market Share



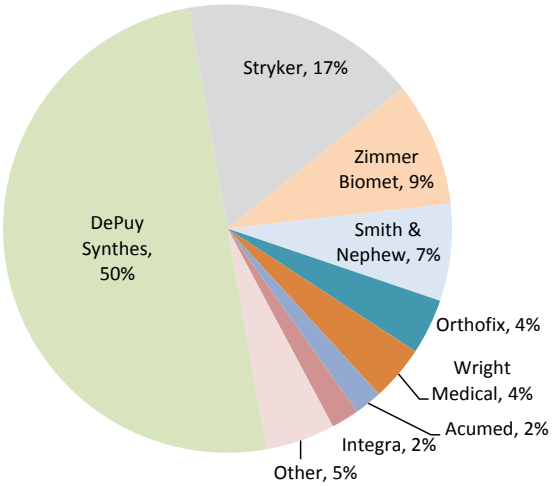
Source: Compiled by MHBK/IRD based on data from Medtech Insight (data through Q3 2014)

C. Trauma

The $7bn trauma market has generated surprisingly strong growth over the recent years. In the past, trauma was regarded as a stable but low-growth market. Trauma is primarily driven by the rate of accidents (car, fall, or other conditions that could lead to a fractured bone). Devices to treat trauma are used to restore the fractured bone to the proper position and alignment. The rate of car accident around the world has not grown much. But as people get more active and as they age, there are increasing rate of other accidents. Trauma market is expected to grow at mid-single digit for the next five years.

M&A has also transformed the trauma market. J&J/DePuy acquired Synthes, which was the undisputed leader in trauma. Zimmer-Biomet and Wright Medical-Tornier deals also added the level of consolidation in the trauma market. The post-merger integration of DuPuy and Synthes has not gone very smoothly. Therefore, other players in trauma have gained some market share at the expense of DuPuy/Synthes.

Figure 24 Worldwide Trauma Market Share

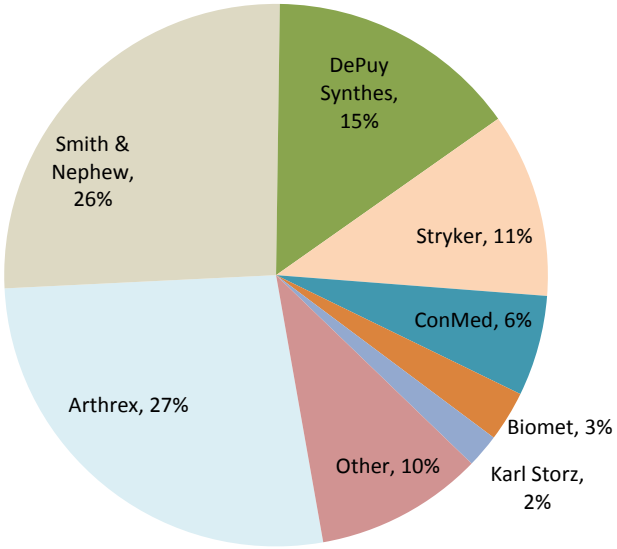


Source: Compiled by MHBK/IRD based on data from ORTHOWORLD

D. Arthroscopy/Soft Tissue Repair

The arthroscopy and soft tissue repair procedures are used to treat injuries resulting from sports, work, and other physical stressors. Sports medicine is a robust market. Compared to other major orthopedic segments, there are a lot of new innovations in this category. One notable innovation for soft tissue repair is knotless suture. Another hot development area is anterior cruciate ligament (ACL) reconstruction. The $4bn market is expected to grow at mid-single digit over the next five years. There are seven players in this market with sales above $90mn, led by the pure play Arthrex. Reportedly Arthrex will have revenues close to $2bn by the end of this year. Thanks to the $1.7bn purchase of ArthroCare in 2014, Smith & Nephew now has the second largest share in this attractive market. DePuy Mitek is the third player. Stryker acquired hip arthroscopy company Pivot Medical in 2014 and is the fourth-ranked player.

Figure 25 Worldwide Market Share for Arthroscopy and Soft Tissue Repair

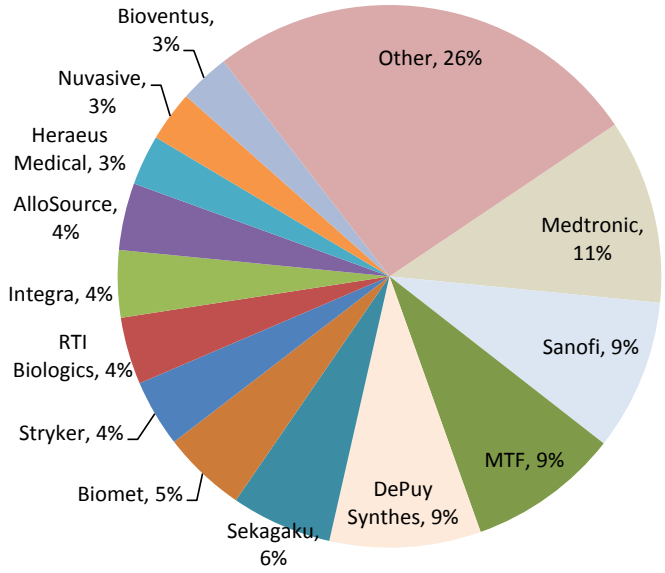


Source: Compiled by MHBK/IRD based on data from ORTHOWORLD

E. Orthobiologics

Orthobiologics include a wide variety of biologic materials such as autograft, allograft, synthetic biomaterials, stem cells, protein growth factors (such as BMP), platelet rich plasma, Hyaluronic acid, etc. They are used across various orthopedic procedures to support tissue healing and restoration through their regenerative potential. As this approach involves naturally occurring material and is tied to regenerative medicine, it is viewed very favorably by the industry and patients. Thus, the orthobiologic market (especially the stem cell segment) is considered a high-growth market. In 2014, the market grew 5.6%. However, one criticism for orthobiologics is that the industry hasn't generated clinical data to back up the claimed benefits. Due to this concern, ORTHOWORLD forecast orthobiologic growth to decelerate to 2.3% over the next five years. However, this forecast seems pessimistic. We believe this market could still see healthy growth in the mid-single digit range. Competition is mostly based on innovation, rather than market access. We could see more innovation on biomaterials and stem-cell based orthobiologics. The orthobiologic market is highly fragmented. It is not one holistic market. Rather, it is made of distinctive, often mutually exclusive segment. For example, the $900mn Hyaluronic acid market is a market of its own with its unique player mix and product dynamics.

Figure 26 Worldwide Market Share of Orthobiologics



Source: Compiled by MHBK/IRD based on data from ORTHOWORLD

F. Notable M&A Deals in the Orthopedic Industry

As shown in Table 29, many M&A transactions have occurred in the orthopedic industry. The choice of acquisition targets often reflects the perceived attractiveness of the products at the time of acquisition. A number of years ago, spine was a hot area. But as spine market cooled, the number of deals in spine has sharply declined. Recently, there have been more deals in extremities, sports medicine (ArthroCare), orthopedic robotics (MAKO Surgical and Blue Belt Technologies), biomaterial, and emerging market (Trauson and Kanghui). As discussed earlier, the Zimmer-Biomet merger in 2014 is poised to transform the industry. The combined company will have a dominant share in the joint reconstruction market. We believe in the device industry, bigger is indeed better. Having a bigger scale helps device makers sell their products to hospitals in bundles, thus gaining volumes at the expense of some price concession. A full product line can also better leverage an organization's sales force. In addition, a big company can wrap some service component around their product offering, therefore getting closer to the customers (sometimes may be able to exclude competitors). Similar to what CV behemoth Medtronic is doing in the cath labs, Zimmer is also trying to offer services and total solution to optimize operating rooms for hospitals. Zimmer's Hospital Services and Solutions concept is a tool to help hospitals standardize care delivery using evidenced based procedure and reduce cost. The concept is seen by Zimmer as "economic selling, not product selling."

Table 29 M&A Transactions in Orthopedics

Aquirer	Target	Announce Date	Deal Value ($mn)	Premium 1-Day	Premium 30-Day	LTM Sales ($mn)	Price / Sales	EV / EBITDA	Therapeutic Area
Smith & Nephew	Blue Belt Technology	29-Oct-2015	$275			$19	14.5		Orthopedic robotics
Wright Medical	Tornier	27-Oct-2014	$1,500	28%		$311	4.8		Extremity implants
Zimmer	ETEX	01-Oct-2014							Bone fillers
Stryker	Small Bone Innovation	30-Jun-2014	$375			$48	7.8		Extremity implants
Zimmer	Biomet	24-Apr-2014	$13,350			$3	4.3		Broad orthopedics
Stryker	Pivot Medical, Inc.	19-Feb-2014							Hip arthroscopy
Smith & Nephew	Arthrocare	03-Feb-2014	$1,500	6%	23%	$373	4.0		Sports medicine
Wright Medical	Biotech International	16-Oct-2013	$75			$15	5.0		Extremity implants
Biomet	Lanx	07-Oct-2013							Spine
Stryker	MAKO Surgical	25-Sep-2013	$1,650	86%	105%	$112	14.7		Orthopedic robotics
Microport	Wright Medical Recon	20-Jun-2013	$290			$269	1.1		Hip and knee implants
Zimmer	Knee Creation	02-May-2013							Knee implants
Stryker	Trauson Holdings	17-Jan-2013	$685			$60	11.4		Trauma, spine company in China
Wright Medical	BioMimetics	19-Nov-2012	$190	56%	53%				Bone graft
Medtronic	Kanghui	27-Sep-2012	$755			$52	14.5		Orthopedic company in China
Tornier	OrthoHelix	24-Aug-2012	$135			$29	4.7		Extremity implants
DMS	Kensey Nash	03-May-2012	$360	32%	30%	$90	4.0		Biomaterial
Walter Street HC Partners	Breg Inc. from Orthofix	24-Apr-2012	$158			$109	1.4		Sports medicine. Bracing and cold-therapy products.
Bioventus (Essex Woodland)	Spinoff from Smith & Nephew (S&N retains 49%)	04-Jan-2012	$506			$223	2.3	11.5	EXOGEN, Ultrasound Bone Healing System and orthobiologics
Stryker	Memometal	06-Jun-2011	$150			$30	5.0		Extremity implants
Stryker	Orthovita	16-May-2011	$304	41%		$95	3.2		Ortho biologics
Johnson & Johnson	Synthes	27-Apr-2011	$19,300	10%	30%	$4,371	4.9	13.3	Trauma, CMF, Spine
Medtronic	Osteotech	17-Aug-2010	$135	65%	124%	$96	1.3	25.6	Ortho biologics
Baxter	ApaTech	01-Mar-2010	$330			$60	5.5		Synthetic bone graft ACTIFUSE
Zimmer	Abbott Spine	04-Sep-2008	$360			$109	3.3		Spine
Integra	Theken Spine	24-Jul-2008	$75			$34	2.2		Spine
Medtronic, Inc.	Kyphon, Inc.	27-Jul-2007	$3,235	32%	45%	$444	7.3	42.2	Spine
Blackstone	DJO	16-Jul-2007	$1,600	19%		$413	3.9		Braces and pain management
Smith & Nephew	Plus Orthopedics	12-Mar-2007	$889			$300	3.0	14.0	International recon business
Blackstone, Goldman	Biomet	18-Dec-2006	$11,400			$2,107	5.4	16.0	Broad orthopedics
Kyphon	St. Francis Medical	04-Dec-2006	$725			$58	12.5		Spine
Orthofix	Blackstone Medical	07-Aug-2006	$333			$60	5.5		Spine
Warburg Pincus and	Tornier SAS	21-Jul-2006							Broad orthopedics
Blackstone (PE fund)	Encore Medical	30-Jun-2006	$870	36%		$294	3.0	13.5	Broad orthopedics
Biomet	Interpore International	08-Mar-2004	$280			$68	4.1		Spine
Zimmer	Centerpulse AG	20-May-2003	$3,502	31%	32%	$1,107	3.2	9.6	Broad orthopedics
Average of All Deals							5.6		

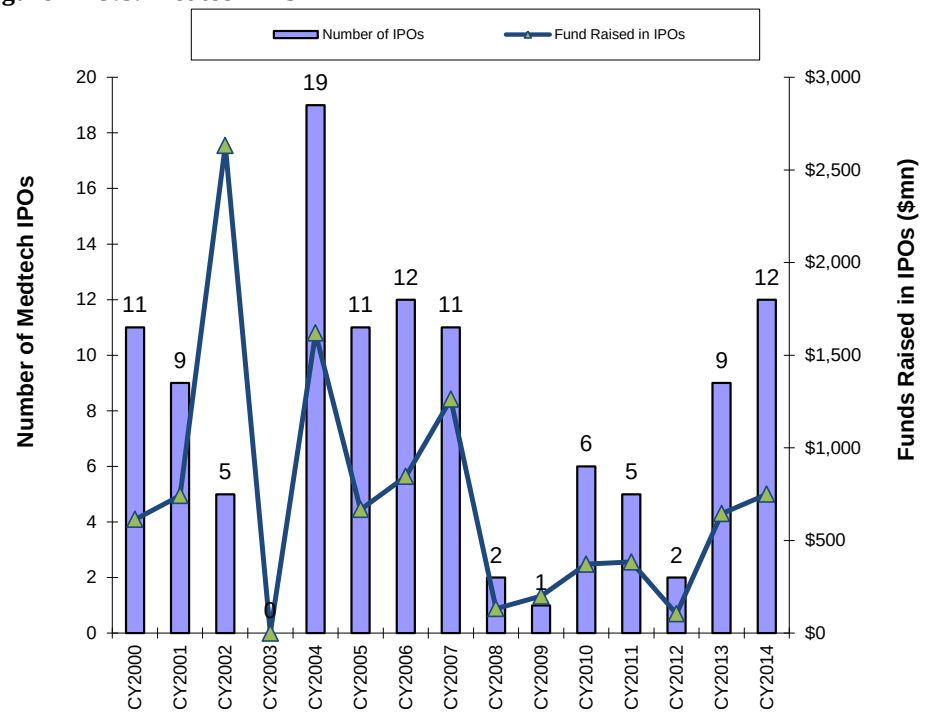
Source: Compiled by MHBK/IRD based on data from Capital IQ

V. U.S. Medtech Industry Capital Market & M&A Updates

A. Medtech IPO Market Review and Outlook

Medtech industry hasn't enjoyed an IPO boom as the biopharma industry has. However, the number of U.S. IPOs did increase from the 2008-2009 trough (see Figure 27).

Figure 27 U.S. Medtech IPO



Source: Compiled by MHBK/IRD based on public company reports

As shown in Table 30, the after-market performance of medtech IPOs has been generally mixed. Of the 2014 class, Nevro, Inogen and Intersect ENT are winners due to their superior technology. But there are quite a number of companies with negative returns, which stands out in the hot healthcare stock market. Performance of the 2013 class was helped by three acquisitions (Foundation Medicine, Cellular Dynamics, and Liposcience), but was nonetheless mixed. We believe private medtech companies face a lukewarm public market. In the current environment, the demand for clinical evidence is very high. So is the bar for reimbursement. Revenue-generating medtech companies need a long runway to achieve a critical level of sales. For development-stage medtech companies, there is a question of whether they are developing truly break-through innovations. Medtronic's expensive acquisition of Ardian was a notable failure in the industry. Investors are somewhat scared of totally new medtech technology aimed at new indications. This is in stark contrast to biopharma where prior gains have spurred investors to seek, rather than to avoid, risk. This dynamic is reflected in the IPO market.

The tepid IPO market combined with relatively subdued M&A landscape means it is hard for venture investors to achieve exits for their portfolio companies. Therefore, VC investors have curtailed funding to start new medtech companies. This trend will have negative repercussion to the medtech industry in the long term as fewer innovative companies are founded. Big medtech companies will have a small field to pick acquisition targets in the future.

Table 30 U.S. Medtech IPO and After-market Performance

Ticker	Company Name	IPO Date	IPO Low	IPO High	IPO Price	IPO Open	Shares Offered	Fund Raided	Current Mkt Cap	Return to Data	Acquired ?	Diagnostics/ Life Science
PEN	Penumbra	9/17/2015	$25.0	$28.0	$30.0		4.0	$120	$1,135	24%		
NTRA	Natera	7/2/2015	17.0	18.0	18.0		10.0	180.0	429	-54%		√
HSGX	Histogenics	12/2/2014	13.0	15.0	11.0	11.8	5.9	64.9	57	-60%		
CAPN	Capnia	11/13/2014			6.5	3.8	1.7	11.1	15	-71%		
NVRO	Nevro	11/5/2014	15.0	17.0	18.0	23.4	6.3	112.5	1,147	125%		
SIEN	Sientra	10/28/2014	14.0	16.0	15.0	17.6	5.0	75.0	70	-75%		
XENT	Intersect ENT	7/24/2014	11.0	13.0	11.0	13.2	5.0	55.0	522	70%		
CDNA	CareDx	41,837.00	15.0	17.0	10.0	9.5	4.0	40.0	53	-55%		√
KTWO	K2M	5/7/2014	16.0	18.0	15.0	15.0	8.8	132.4	743	23%		
TRIV	TriVascular	4/15/2014	13.0	15.0	12.0	11.4	6.5	78.0	138	-48%		
AMDA	Amedica	2/13/2014	8.0	10.0	5.8	6.2	3.5	20.1	21	-95%		
LMNS	Lumenis	2/26/2014	15.0	17.0	12.0	12.5	6.3	75.6	510	17%	√	
EVAR	Lombard Medical	4/24/2014	15.0	18.0	11.0	11.0	5.0	55.0	68	-68%		
INGN	Inogen	2/13/2014	16.0	18.0	16.0	16.0	4.4	70.4	811	164%		
2014								790.0		-6%		
OXFD	Oxford Immunotec	11/22/2013	$13.0	$15.0	$12.0	14	5.4	$65	$269	0%		√
TNDM	Tandem Diabetes Care	11/13/2013	13.0	15.0	15.0	19.5	8.0	120.0	231	-39%		√
VCYT	Veracyte	10/30/2013	13.0	15.0	13.0	13.0	5.0	65.0	181	-51%		√
LDRH	LDR Holding	10/9/2013	14.0	16.0	15.0	18.5	5.0	75.0	704	66%		
FMI	Foundation Medicine	9/24/2013	14.0	16.0	18.0	31.5	5.9	106.2	762	28%	Partly	√
ICEL	Cellular Dynamics	7/25/2013	12.0	14.0	12.0	11.0	3.8	45.6	307	38%	√	√
NSTG	Nanostring	6/26/2013	13.0	15.0	10.0	9.9	5.4	54.0	288	44%		√
CGIX	Cancer Genetics	4/4/2013	10.0	12.0	10.0	10.0	6.9	69.0	72	-36%		√
LPDX	LipoScience	1/25/2013	13.0	15.0	9.0	9.8	5.0	45.0	85	-42%	√	√
2013								644.6		1%		
GMED	Globus	8/3/2012	$12.0	$13.0	$12.0	13.1	8.3	$100	$2,133	88%		
ATOS	Atossa Genetics	10/19/2012	4.0	6.0	5.0	4.7	0.8	4.0	19	-87%		√
2012								104.0		0%		
ZLTQ	Zeltiq	10/19/2011	14.0	16.0	13.0	14.5	7.0	91.0	1,286	158%		
FLDM	Fluidigm	2/10/2011	13.5	15.5	13.5	13.5	5.6	75.6	212	-22%		√
BGMD	BG Medicine	2/4/2011	13.0	15.0	7.0	7.0	5.0	35.0	5	-92%		√
KIPS	Kips Bay Medical Inc.	2/11/2011	7.0	9.0	8.0	8.0	2.1	16.5	0	-100%		
TRNX	Tornier N.V.	2/03/2011	18.0	20.0	19.0	19.0	8.8	166.3	1,584	58%	√	
2011								384.3		0%		
KH	China Kanghui Holdings	8/11/2010	9.3	11.3	10.3	10.3	6.7	68.4	755	200%	√	
GNOM	Complete Genomics	11/11/2010	12.0	14.0	9.0	8.5	6.0	54.0	118	-65%	√	√
PACB	Pacific Biosciences	10/27/2010	15.0	17.0	16.0	16.5	12.5	200.0	544	-55%		√
TASE:OPCT	D Medical Industries Ltd	8/05/2010	10.0	12.0	7.0	6.8	1.5	10.5	12	-85%		
GNMK	GenMark Diagnostics Inc	5/28/2010	5.0	7.0	6.0	5.7	4.6	27.6	304	9%		√
DHRM	Dehaier Medical System	4/15/2010	7.0	9.0	8.0	10.3	1.5	12.0	11	-78%		
2010								372.5		-12%		
AGAM	AGA Medical Holdings Ir	10/21/2009	13.5	15.5	14.5	14.5	13.8	199.4	1,300	43%	√	
2009								199.4		43%		
BEAT	CardioNet Inc.	3/19/2008	17.0	19.0	18.0	18.0	4.5	81.0	357	-28%		
MAKO	MAKO Surgical Corp.	2/14/2008	9.0	11.0	10.0	10.0	5.1	51.0	1,650	200%	√	
2008								132.0		86%		
ETRM	EnteroMedics Inc.	11/15/2007	7.0	9.0	8.0	8.0	5.0	40.0	28	-97%		
BFRM	BioForm Medical Inc.	11/07/2007	7.0	9.0	8.0	8.0	10.0	80.0	253	-32%	√	
PMII	Power Medical Interven	10/30/2007	10.0	12.0	11.0	11.5	3.9	42.4	64	-81%	√	
TSON	TranS1 Inc.	10/17/2007	14.0	16.0	15.0	25.0	5.5	82.5	0	-100%		
MASI	Masimo Corp.	8/08/2007	16.0	18.0	17.0	19.0	11.9	202.6	2,025	136%		
HLCS	Helicos Biosciences	5/24/2007	13.0	15.0	9.0	9.0	5.4	48.6	0	-100%		
PODD	Insulet Corp.	5/15/2007	14.0	16.0	15.0	17.0	7.7	115.5	1,715	100%		
TOMO	TomoTherapy Inc.	5/09/2007	15.0	17.0	19.0	24.0	11.7	223.1	277	-75%	√	√
SENO	SenoRX Inc.	3/29/2007	11.0	13.0	8.0	8.2	5.5	44.0	200	38%	√	
CHIP	VeriChip Corp.	2/12/2007	6.5	6.5	6.5	6.5	3.1	20.2	0	-100%		
ARAY	Accuray Inc.	2/08/2007	14.0	16.0	18.0	21.0	16.0	288.0	473	-63%		
XTNT	XTENT Inc.	2/01/2007	16.0	18.0	16.0	16.2	4.7	75.2	0	-100%		
2007								1,262.0		-40%		

Source: Compiled by MHBK/IRD based on public reports and Capital IQ

B. Medtech M&A Review and Outlook

Medtech M&A has been very active since the beginning of 2014 (see Table 31). This period has seen perhaps unprecedented level of M&A volume in medtech industry. There are a number of forces driving the hot M&A market.

1. To Achieve Greater Economy of Scale

Three mega deals took place in 2014 (Medtronic-Covidien, Zimmer-Biomet and Becton Dickinson-CareFusion). Such huge deals were perhaps unthinkable in the past. The overarching theme of these three deals is to bring total solutions to customers and evolve from product-focused companies to customer-focused companies. This is driven by customers' demand for medtech companies to demonstrate value of their product/service. Whether it is BD-CareFusion's hospital medication management business, Zimmer-Biomet's orthopedic business, or Medtronic-Covidien's vascular business, the acquirers are trying to create a one-stop shop for their customers. Danaher's $2.2bn acquisition of dental implant maker Nobel Biocare also falls into this category. By having a broad product line, they can maximize volume through bundling. Another aspect is to become a customer-focused company by offering services in addition to products. Service is just another way for companies to deliver value. Medtronic is a pioneer in this area. It offers CathLab Management Services for its hospital customers to manage their cath labs. Its CARDIOCOM service combines sensors, telehealth, and various patients support tools to manage patients with chronic diseases. Such close patients monitoring coupled with timely intervention can improve patients' condition and reduce cost to the providers. Similar to Medtronic, Zimmer offers hospital services and solutions that help hospitals optimize operation and reduce costs. In addition to greater economy of scale, penetration into fast-growing emerging markets is another rationale for big mergers. A bigger platform such as Medtronic's can help bring more products to emerging markets. In conclusion, it seems bigger is better for medtech company in the current environment.

2. Tax Inversion

Tax inversion, i.e., to domicile from a high-tax to a low-tax jurisdiction is another driver for merger last year. There were at least four tax inversion deals in medtech – Medtronic-Covidien, Cyberonic-Sorin, Wright Medical-Tornier, and Steris-Synergy Health. For these four cases, the combined companies will be domiciled in Ireland, the U.K., the Netherlands and the U.K. respectively. However, as the U.S. Treasury removed some incentives for tax inversion, this driver of M&A became less potent. Beyond tax inversion, another motivation for U.S. companies to acquire companies outside of the U.S. is to use overseas cash. Under current tax law, U.S. companies cannot bring profits earned from overseas back to the U.S. without paying a tax. Therefore many U.S. medtech companies have large amount of cash overseas but cannot use it to pay dividends or acquire companies in the U.S. Use of overseas cash in a tax-efficient manner is a driver for the Medtronic-Covidien deal.

3. Delivering Value through Lower Price

Faced with growing reimbursement pressure, hospitals are demanding lower cost from device makers. As there is a higher demand for low-cost medical devices, some companies have stepped up to meet that need. For example, the merger of Steris with Synergy Health creates a bigger player in device sterilization market. Hospitals are increasingly reusing the expensive medical devices. Hence there is a greater need for sterilization. Another example is Cardinal Health's acquisition Cordis cardiovascular division from J&J to bolster its portfolio of physician preference items (PPI). By its definition, physician preference items refer to products with limited clinical differentiation, suitable for standardization, yet with some level of physician preference. Cardinal Health hopes to offer a broad portfolio of such products at lower cost to hospital customers.

4. Innovation remains a driver for acquisitions

Medtech companies are always interested in acquiring innovative technology that can boost their product portfolios. True innovations have a number of attractive characteristics such as limited competition and favorable pricing. As large swaths of device categories suffer pricing pressure, the ability to achieve favorable reimbursement is a great attribute. Recently, TAVR received favorable reimbursement from CMS. However, true innovation is hard to find and it often entails high risk (as demonstrated by Ardian in renal denervation field). Therefore, medtech companies have to be very selective in where they place the bets. We believe various areas of "intervention" often present good opportunities. For example, neuromodulation is an attractive area. Peripheral and neurovascular interventions are also quite attractive.

Table 31 Notable Medtech M&A Deals Since 2014

Aquirer	Target	Announce Date	Deal Value ($mn)	Premium 1-Day	Premium 30-Day	Revenue Trailing ($mn)	Price/Sales	EV / EBITDA	Therapeutic Area
Smith & Nephew	Blue Belt Technology	29-Oct-2015	$275			$19	14.5		Orthopedic robotics
Endologix	TriVascular	27-Oct-2015	$211			$35	6.1		AAA
Atricure	nContact	05-Oct-2015	$99						Atrial fibrillation
Medtronic	Lazarus Effect	28-Sep-2015	$100						Neurovascular
Dentsply	Sirona	15-Sep-2015	$5,500	1%		$1,146	4.8	19.6	Dental
Nipro	Infraredx	04-Sep-2015	$59						Vascular imaging
Allergan	AqueSys	03-Sep-2015	$300						Minimally invasive glaucoma surgery (MIGS)
Valeant	Synergetics USA	02-Sep-2015	$160			$80	2.0		Ophthalmology device
Heartware Intl	Valtech Cardio	01-Sep-2015	$800						Mitral and Tricuspid Valve Repair
Medtronic	Medina Medical	31-Aug-2015	$150						Neurovascular (aneurysm coil)
Medtronic	Twelve, Inc.	25-Aug-2015	$458						Mitral valve repair
Greatbatch	Lake Region Medical	27-Aug-2015	$1,730			$806	2.1	11.6	Medical device OEM
Allergan	Oculeve	10-Aug-2015	$125						Medical device for dry eye
St. Jude	Thoractec	22-Jul-2015	$3,400		38%	$473	7.2	43.9	VAD
Medtronic	RF Surgical	16-Jul-2015	$235						Prevention of retained subjects after surgery
Edwards Lifescience	CardiAQ	13-Jul-2015	$350						Transcatheter mitral valve
Integra Lifesciences	TEI Medical	29-Jun-2015	$312			$64	4.9		Wound care, reconstructive surgery
XIO Group	Lumenis	18-Jun-2015	$510	8%	18%	$292	1.7	17.3	Laser based surgical, ophthalmic, devices
Danaher	Pall	13-May-2015	$13,800	28%	29%	$2,853	4.8	20.8	Filtration and purification
St. Jude	Spinal Modulation	20-Apr-2015	$215						Dorsal root ganglion (DRG) stimulation
Boston Scientific	Xlumena	01-Apr-2015	$62.5						GI
Boston Scientific	American Medical Systems (Endo)	02-Mar-2015	$1,650			$400	4.1	12.7	Urology (men's health, prostate health)
Cardinal Health	Cordis (from J&J)	02-Mar-2015	$1,944			$780	2.5		Cardiology, endovascular
Boston Scientific	American Medical Systems	02-Mar-2015	$1,650			$400	4.1	12.7	Urology
Cyberonics (merger)	Sorin (merger)	26-Feb-2015	$2,700			$1,290	2.1		Neurostimulation, CV device
3M	Ivera Medical	19-Feb-2015				$30			Vascular access
Pfizer	Hospira	05-Feb-2015	$17,000	39%	48%	$4,421	3.8	21.1	Infusion pumps, injectable pharmaceuticals
Royal Philips	Volcano	17-Dec-2014	$1,200	57%	62%	$395	3.0		Intravascular imaging
EQT	Siemens Audiology	06-Nov-2014	€ 2,150			€ 693	3.1		Hearing aid
Spectranetics	Stellarex DCB (Covidien)	02-Nov-2014	$30						DCB
Abbott	Topera	29-Oct-2014	$250						Diagnostic catheter and mapping system for AF
Abbott	Advanced Cardiac Therapeutics	29-Oct-2014							Ablation catheter for AF
Wright Medical	Tornier	27-Oct-2014	$1,584	28%		$311	5.1	71.7	Extremity implants
Steris	Synergy Health	13-Oct-2014	$1,800	39%		$627	2.9	10.8	Sterilized devices
Beckton Dickinson	CareFusion	06-Oct-2014	$12,200	26%	25%	$3,842	3.2	14.2	Medication management
Zimmer	ETEX	01-Oct-2014							Bone fillers
Danaher	Nobel Biocare	15-Sep-2014	$2,200			$750	2.9		Dental Implants
Covidien	Reverse Medical	22-Aug-2014							Vascular plug
Tecomet	Symmetry Medical OEM business	04-Aug-2014	$450						OEM for medical device
Danaher	Siemens Microbiology unit	17-Jul-2014	€ 330			€ 150			Antibiotic susceptibility testing
St. Jude	NeuroTherm	14-Jul-2014	$200						Interventional pain management with RF ablation
Coopervision	Sauflon	30-Jun-2014	$1,200			$210	5.7		Contact lenses
Stryker	Small Bone Innovation	30-Jun-2014	$375			$48	7.8		Extremity implants
Merz	Ulthera	27-Jun-2014	$600			$100		6.0	Aesthetics
Medtronic	Covidien	16-Jun-2014	$42,900	29%	29%	$10,329	4.2	15.4	Broad
St. Jude	CardioMEMS	02-Jun-2014	$450						Heart failure monitoring
Volcano	AtheroMed	27-May-2014	$115						Atherectomy for PAD
Spectranetics	AngioScore	27-May-2014	$230			$55	4.2		Specialty balloon for CAD and PAD
Boston Scientific	Bayer Interventional Division	15-May-2014	$415			$120	3.5		Peripheral vascular intervention
Boston Scientific	IoGyn	06-May-2014	$65						hysteroscopic intrauterine tissue removal
Zimmer	Biomet	24-Apr-2014	$13,350			$3	4.3		Orthopedics
Cardinal Health	AccessClosure	04-Apr-2014	$320			$80	4.0		Vascular closure device
Smith & Nephew	Arthrocare	03-Feb-2014	$1,500	6%	23%	$373	4.0	17.3	Sports medicine
Medtronic	TYRX	07-Jan-2014	$160						Antibiotic coated implantable devices

Source: Compiled by MHBK/IRD based on public company reports and Capital IQ

VI. Updates on Diagnostics and Life Science Industry

A. Market Overview

Worldwide in vitro diagnostic (IVD) market is currently worth $55bn and is growing at 4-5% per annum (see Table 32). Aging population and growing importance of diagnostics in medical care are driving growing demand for diagnostic tests. High-growth IVD segments continue to be molecular diagnostics (MDx), pathology, and point of care (POC). Cancer and personalized medicine are the major boosters for IVD market. Specifically, companion diagnostics (CDx), which is to use Dx to guide personalized pharmaceutical therapy is expected to grow very robustly.

Table 32 Major IVD Segment and Projected Growth Rate

IVD Category	2014 Market Size ($bn)	2014-18 CAGR	Key Competitors (not in ranking order)
Clinical Chemistry / Immunoassays	21	4-5%	Siemens, Roche, Abbott, Danaher (Beckman Coulter), OCD
Glucose monitoring	8.5	-3%	Abbott, J&J, Roche, Bayer, Nipro, Arkray, Dexcom
Hematology	3.1	3-4%	Sysmex, Danaher (Beckman Coulter), Abbott, Siemens
Hemostasis (coagulation)	1.8	4-5%	Siemens, Stago, Roche, Sysmex, Danaher (Beckman Coulter)
Point of Care (POC)	7	9-12%	Alere, Siemens, Abbott, Roche, Quidel, BD
Molecular Diagnostic	6	high-single digit to 10%	Roche, Chiron (Novartis), Hologic (Gen-Probe), Siemens, Qiagen, Abbott, Danaher (Beckman Coulter), bioMerieux, Cepheid
Pathology	3	8-10%	Ventana(Roche), Dako (Agilent), Vision (Danaher), Abbott
Microbiology	2.7	Low-Mid single digit	Biomerieux, Becton Dickinson, Danaher, Thermo Fisher, Bio-Rad
Urinalysis	1.0	Low single digit	Sysmex, Arkray, Danaher, Siemens, Roche
Total	**55**	4-5%	

Source: Compiled by MHBK/IRD based on public company reports

B. Major Trends in IVD

1. Regulatory Framework for IVD Is Becoming More Burdensome

FDA announced in July 2014 that it will no longer exercise "enforcement discretion," (i.e., discretion not to regulate) over LDTs (lab developed tests) and plans to phase in regulation of LDTs over a long period of time. LDTs are tests performed in labs and historically have not received FDA oversight. However with increasing complexity of LDTs and the importance of such tests in the patient care, FDA has decided it is time to reverse its historical stance. After a long anticipation by the industry, FDA issued draft guidance for regulation of LDTs in July 2014. In this draft guidance, FDA proposes a risk-based regulatory framework:

- For low-risk LDTs, LDTs for rare diseases, and LDT for unmet needs, FDA will continue to exercise enforcement discretion.
- For high-risk LDTs (Class III devices), companion diagnostic tests and other highest-risk LDTs need to submit PMA within one year of the final guidance date. Other high-risk LDTs will have to submit PMA over the next four years.
- Moderate-risk LDTs will need to submit PMA five years after the guidance is finalized and phased in over the subsequent four years.

Although the long phase-in time seems lenient to the lab industry, the pending regulation still adds substantial burden. ACLA (American Clinical Laboratory Association) and other opponents are fighting the proposal. It seems reaction from the IVD industry is mixed. While getting approval is a burden, it also levels the playfield. Once a big player receives FDA approval, it doesn't have to worry labs develop LDTs to compete with the FDA-approved tests. Every test will get FDA approval on its own. However, small IVD players are often resource-constrained and they often commercialize their tests as LDTs. For them, this regulatory burden will be a lot to bear.

2. Reimbursement of IVD Is Getting Tougher

Reimbursement for IVD is traditionally based on a cost plus basis. Obtaining a CPT code for a new test is very time-consuming. Labs often use "code stack" to get reimbursement. Without a unique identification code for each test, payers often cannot recognize the tests that they are paying and the value associated with the test. At the same time, innovators with FDA approved tests often face competitions from "home-brew" LDTs. This doesn't reward innovators.

The Protection Access to Medicare Act of 2014 (PAMA) was signed in law in April 2014 and will change the situation. The law has three provisions: (1) avoidance of the severe SGR cuts to physician fee schedule, (2) delayed ICD-10 implementation to October 2015, and (3) implanting market-based payments for all tests on the Medicare Clinical Laboratory Fee Schedule (MCLFS) and Advanced Diagnostic Tests. The last provision will have a big impact on IVD reimbursement.

Beginning on January 1, 2016, labs will report to the CMS the payment rates paid by each private payor (including Medicare managed care plans or Medicaid managed care plans) for the test during the previous twelve months. On or after January 1, 2017, MCLFS rates will be based on a weighted median, and any reductions to payments will be phased in over time. The annual reduction will be capped (10% per annum from 2017-2019, and 15% per annum from 2020-2022, no cap after 2023). Private payers are expected to follow CMS reimbursement rate. With this change, IVD reimbursement will move from a cost-plus basis to a market basis.

By 2016, CMS will be required to adopt temporary code to identify new advanced diagnostic tests. Having a designated code will help payer identify innovator's test and thus properly reward innovators.

Beyond changes in reimbursement regulation, in the general market environment, there is an increasing demand for clinical evidence to justify reimbursement. IVD companies are encouraged to run prospective clinical trials to demonstrate the clinical utility of their tests. As a positive example, Exact Sciences ran a robust trial to demonstrate the clinical value of its Cologuard test for colon cancer. As a result, it received favorable reimbursement coverage from CMS. However just as a reflection of the perils of getting reimbursement, in early October the U.S. Preventative Services Task Force (USPSTF) issued a draft guidance on colorectal cancer testing, which classified Cologuard as an alternative test and excluded it from the recommended tests. Had USPSTF recommended Cologuard, the test would be mandatorily covered by all commercial plans. The negative recommendation is likely to significantly curtail the insurance coverage.

Payers increasingly want to be transparent in terms of how they assess the value of a test. For example Palmetto's MolDX program provides for six levels of evidence in its guideline for clinical utility of an IVD test. Tests without meeting a certain level of evidence will be rejected.

3. Next-Gen sequencing will evolve into a huge market.

Led by Illumina, DNA sequencing technology has made improvements in leaps and bounds. Illumina launched the HiSeq X Ten sequencer in early 2014, which dropped the cost of sequencing one human genome to below $1,000. The $1,000 per human genome is a huge landmark in genomic research. Ever since the completion of $3bn human genome project, scientists and the industry have been on a quest to lower the price to below $1,000. With sequencing cost dropped below such a barrier, use of sequencing is becoming more prevalent. At the same time, genomics is becoming increasingly critical in deciding a patient's treatment options. Personalized therapy according to a patient's genomic background is becoming mainstream. So when the increasing market need for sequencing collides with the breakthrough in sequencing technology/cost, the result is a booming market for sequencing in the medical field. Industry leader Illunima estimates the total sequencing market opportunity at $20bn (see Table 33). In contrast, today's sequencing instrument and consumable market (excluding clinical testing with sequencing) is only worth ~$2.5bn. Although $20bn seems a big number, Illumina's estimate appears realistic when examined at the detail level (see Table 33). Some of the major market segments such as NIPT (non-invasive prenatal testing) and Theragnostics (defined as clinical diagnostics and companion diagnostics) are widely recognized as having great growth potential. Only minor sales are projected to come from "new and emerging" segment. Wall Street analysts have been enough more bullish for the future prospect of sequencing. J. P. Morgan analyst projects total market potential for sequencing to be $46bn. UBS analyst estimate the market potential of NGS (next generation sequencing) to be $38bn.

Table 33 Sequencing Market Opportunity through the lens of Illumina

Area	Market Size
Life science	**$5bn**
Research	- $4.5bn
Agriculture	- $0.5bn
Oncology	**$12bn**
Research & Translational	- $2bn
Clinical	- $10bn
Germline analysis	- $1bn
Theragnostics*	- $8.5bn
Molecular monitoring	- $0.5bn
Reproductive and Genetic Health	**$2bn**
NIPT	- $1.1bn
IVF	- $700mn
Newborn neonatal, Genetic Health	- $200mn
New and Emerging	**$1bn**
Forensics	- $400mn
Transplant	- $250mn
Consumer	- $100mn
Total	**$20bn**

Source: Illumina, January 2014 Investor Day
Note*: Defined as clinical diagnostics and companion diagnostics

4. Companion Diagnostics Is Having Exponential Growth

Personalized medicine is a major trend in healthcare. Currently, most of pharma R&D programs have a biomarker component. Companion diagnostic (CDx) market will have exponential growth. One industry source cites CDx market will expand at 25% CAGR from $1.6bn to $6.2bn from 2015 to 2021. There have been numerous partnerships between IVD companies and pharma companies to develop CDx. In general, pharma have three complementary, but not mutually-exclusive, approaches to tap IVD expertise

(see Table 34). Firstly, Roche and J&J have IVD businesses, which make it easy for them to leverage in-house IVD expertise for pharmaceutical business. Secondly, pharma companies have acquired MDx businesses to bring some expertise in house. Even with its might in IVD, Roche acquired a majority stake in Foundation Medicine early this year. At the end of 2014, AstraZeneca acquired tumor biomarker company Definiens AG for $150mn. Celgene acquired Quanticel, which has a single-cell genomic analysis technology for cancer research. Thirdly, big pharma companies have partnered with various MDx companies to develop CDx. To get a drug with biomarker section approved, drug company needs the FDA to approve the companion diagnostic (CDx) together or before the approval of drug. Not to risk a potential delay in drug approval, big pharma have often gone to the leaders in CDx development such as Qiagen, Dako (Agilent), and Roche. Other IVD companies sometimes involved in CDx partnerships include Thermo Fisher, Abbott, Myriad Genetics, and certain specialized IVD companies.

Table 34 Various Approaches Big Pharma Use to Tap IVD Expertise

Approach	Company	Examples	Pros	Cons
Internal expertise	Roche, J&J	At Roche, over 60% of drugs in development have paired CDx developed in house. J&J's Veridex division (CTC technology) has played a positive role in the development of Zytiga.	In-house expertise makes collaboration easy	A company must have Dx in legacy business
Acquire	Roche	Acquired Ventana Medical; Made a unsuccessful hostile bid for Illumina. Acquired a majority stake in Foundation Medicine in 2015.	Often have to pay a big premium or do a hostile	Can go after the most attractive company
	Novartis	Acquired Genoptics		
	Amgen	Acquired DeCode Genetics		
	Eli Lilly	Acquired Avid Radiopharmaceuticals		
	Celgene	Acquired Quanticel (single cell genomics)		
	AstraZeneca	Acquired Definiens, AG (cancer biomarker)		
Partner	Pfizer,	Partned with Abbott Molecular to launch Xalkori simulaneously with a CDx test; signed master collaboration with Dako	Flexible	Lack of control
	Eli Lilly	Signed master collaboration agreements with Qiagen and Dako		
	AstraZeneca	Partnered with Ventana (Roche)		
	BMS	Life Technologies, Roche.		
	Amgen	Collaborate with Dako for oncology		
	Novartis	Master collaboration agreement with Qiagen		

Source: Compiled by MHBK/IRD based on public company reports

5. Test Decentralization Boosts POC Market

More IVD tests are performed at decentralized places. Tests are migrating out of central labs, to hospital labs, and to physician offices. Many diagnostic companies have developed innovative POC instruments. Molecular testing for infectious disease is an area where point-of-care testing has gained popularity.

C. M&A Trends in IVD and Life Science Industry

As IVD and life science tools are sibling industries, we will discuss M&A trends jointly in this section. Table 35 lists the M&A deals with size above $1bn in the industry. On average, acquirers pay ~4x sales and 15.5x EBITDA. We noticed a creep-up in valuation in recent years. For example, recently Danaher is paying 21x EBITDA to acquire Pall. Pall has a very similar business to Millipore, which Merck KGaA acquired in 2010 for ~18x EBITDA. Merck KGaA recently also is paying 20x EBITDA to acquire Sigma Aldrich. We note historically companies pay 20x EBITDA multiples for highly innovative assets (e.g., Agilent's acquisition of Dako and Hologic's acquisition of Gen-Probe). In comparison, Sigma Aldrich has a more mundane businesses. Roche recently paid 30x sales to acquire a majority stake in Foundation Medicine, which is a very high valuation.

Table 35 Diagnostic / Life Science Deals with Valuation Above $1bn

Acquirer	Target	Announce Date	Total Invested Capital ($mn)	Revenue LTM ($mn)	Price/ Sales	EV / EBITDA
Danaher	Pall	13-May-2015	13,800	2,853.0	4.8	20.8
Merck KGaA	Sigma Aldrich	22-Sep-2014	17,000	2,738.0	6.2	20.4
Carlyle	J&J Ortho-Clinical Diagnostics	31-Mar-2014	4,000	1,885.0	2.1	
Thermo Fisher	Life Technologies	15-Apr-2013	15,800	3,800	4.2	
Grifols	Novartis blood transfusion Dx	11-Nov-2013	1,675	565.0	3.0	
Agilent	DAKO	17-May-2012	2,200	358	6.1	19.8
Hologic	Gen-Probe	30-Apr-2012	3,700	587.0	6.3	21.4
TPG Capital	Immucor	05-Jul-2011	1,698	329	5.2	11.7
Thermo Fisher Scientific	Phadia	19-May-2011	3,500	525.0	6.7	16.8
Danaher	Beckman Coulter	07-Feb-2011	6,800	3,663	1.9	8.5
Danaher Corp.	Beckman Coulter, Inc.	07-Feb-2011	7,282	3,663	1.9	8.9
Thermo Fisher	Dionex	13-Dec-2010	2,093	432	4.7	19.6
Merck KGaA	Millipore	01-Mar-2010	7,200	1,654	4.4	17.8
Agilent	Varian	27-Jul-2009	1,500	893	1.7	9.6
Invitrogen Corp.	Applied Biosystems	12-Jun-2008	6,543	2,173	3.0	12.3
Average					4.1	15.6

Source: Compiled by MHBK/IRD based on public company reports

Table 36 and Table 37 list the historical acquisitions in the IVD industry and life science industry respectively. We note in IVD, recent acquisitions have been focused on companion diagnostics, sequencing, and POC. In life science, sector consolidation has been an ongoing theme. Long-time industry stalwarts such as Pall and Sigma Aldrich had been taken out.

Table 36 Acquisitions of IVD Companies

Aquirer	Target	Announce Date	Deal Value ($mn)	Premium 1-Day	Premium 30-Day	Revenue ($mn)	Price/Sales LTM	EV / EBITDA
Sinocare	Nipro Diagnostics	27-Oct-2015	$272					
NeoGenomics	Clarient Inc. (GE)	21-Oct-2015	$205			$127	1.6	15.8
Becton Dickinson	Cellular Research	25-Aug-2015						
Roche	Kapa Biosciences	19-Aug-2015						
Roche	GeneWEAVE	13-Aug-2015	$190					
Panasonic Healthcare (KKR)	Bayer Diabetes Care	10-Jun-2015	$1,150			$1,025	1.1	
Opko Health	Bio-Reference Labs	04-Jun-2015	$1,470	60%	59%	$860	2	12.7
Celgene	Quanticell	27-Apr-2015	$100					
Roche	CAPP Medical	13-Apr-2015						
Roche	Signature Diagnostics	09-Feb-2015						
Roche	Foundation Medicine	12-Jan-2015	$1,030	109%		$61	30	
Adaptive Biotech	Sequenta	07-Jan-2015						
Roche	Ariosa Diagnostics	02-Dec-2014						
AstraZeneca	Definiens AG	04-Nov-2014	$150					
Bio-Techne	CyVek	03-Nov-2014	$60					
Becton Dickinson	GenCell	13-Oct-2015						
LabCorp	LipoScience	25-Sep-2014	$63	65%	80%	$46	1.4	
Danaher	Siemens Microbiology unit	17-Jul-2014	€ 330			€ 150		
Roche	Genia	03-Jun-2014	$125					
Bio-Rad	GnuBIO	11-Apr-2014	$40					
Roche	IQuum	07-Apr-2014	$275					
Carlyle	J&J Ortho-Clinical Diagnostics	31-Mar-2014	$4,000			$1,885	2.1	
Myriad Genetics	Crescendo Biosciences	04-Feb-2014	$270					
Quest	Solstas Lab	14-Jan-2014	$570			$350	1.6	
Grifols	Novartis blood transfusion Dx	11-Nov-2013	$1,675			$565	3.0	
bioMerieux	BioFire	03-Sep-2013	$450			$70	6.4	
ITC	Accumetrix	30-Aug-2013						
Trinity Biotech	Immco Diagnostics	23-Aug-2013	$33			$13	2.6	
Roche Diagnostics	Constitution Medical	02-Jul-2013	$220					
Thermo Fisher Scientific	Life Technologies	15-Apr-2013	$15,800			$3,799	4.2	13.2
Danaher's Radiometer	HemoCue from Quest	25-Feb-2013	$300			$116	2.6	
Illumina	Verinata	07-Jan-2013	$350					
Amgen	DeCode Genetics	11-Dec-2012	$415					
BGI	Complete Genomics	17-Sep-2012	$118		54%	$19	6.1	
Danaher	Iris International	17-Sep-2012	$355	45%	58%	$118	3.0	50.0
Life Technologies	Pinpoint Genomics	25-Jul-2012						
Life Technologies	Navigenics	16-Jul-2012						
Thermo Fisher Scientific	One Lambda	16-Jul-2012	$925			$182	5.1	
Luminex	GenturaDx	09-Jul-2012	$50					
LabCorp	Medtox	04-Jun-2012	$241	37%	36%	$108	2.2	18.1
Agilent	DAKO	17-May-2012	$2,200			$358	6.1	19.8
Hologic	Gen-Probe	30-Apr-2012	$3,700	19%	25%	$587	6.3	21.4
Alere	eScreen	29-Feb-2012	$270			$120	2.3	
Alere	Arriva	23-Nov-2011	$83			$46	1.8	
Opko Health	Claros	21-Oct-2011	$30					
Bio-Rad Laboratories	QuantaLife	05-Oct-2011	$162					
Miraca Holdings	Caris Diagnostics	05-Oct-2011	$725			$207	3.5	
Danaher (Leica)	Aperio Technologies	21-Aug-2012						
bioMerieux SA	Argene SA	19-Jul-2011	€ 38			€ 10	3.8	
Roche Holding AG	mtm Laboratories AG	19-Jul-2011	€ 130					
Alere	Axis-Shield	06-Jul-2011	£235	40%	41%	£102	2.3	15.4
TPG Capital	Immucor	05-Jul-2011	$1,698	30%	37%	$329	5.2	11.7
Qiagen	Ipsogen S.A.	15-Jun-2011	€ 70	71%	70%	€ 8	8.3	
Nestle	Prometheus Laboratories	24-May-2011				$519		
bioMerieux SA	AES Laboratories	19-May-2011	€ 183			€ 76	2.4	
Thermo Fisher Scientific	Phadia	19-May-2011	$3,500			$525	6.7	16.8
Myriad Genetics	Rules-Based Medicine	28-Apr-2011	$80			$25	3.2	
LabCorp	Orchid Cellmark	06-Apr-2011	$85	39%		$64	1.3	
Qiagen	Cellestis	04-Apr-2011	$374			$42	8.9	
Quest	Celera	18-Mar-2011	$344	28%	23%	$128	2.7	
Quest	Athena Diagnostics	24-Feb-2011	$740			$110	6.7	
Danaher	Beckman Coulter	07-Feb-2011	$6,800	11%	45%	$3,663	1.9	8.5
Novartis	Genoptix	24-Jan-2011	$330	27%	39%	$197	1.7	6.4
Sekisui Chemical	Genzyme Diagnostics	18-Nov-2010	$265			$167	1.6	
GE Healthcare	Clarient	22-Oct-2010	$570	34%	43%	$92	6.2	
LabCorp	Genzyme Genetic Testing	13-Sep-2010	$925			$371	2.5	
Fujirebio	Innogenetics	20-Jul-2010	$113					
PerkinElmer	Signature Genomic Laboratories	14-Apr-2010	$90					
Cinven	Sebia	15-Mar-2010	€ 800					
Alere	Kroll Laboratories	03-Feb-2010	$110			$40	2.7	
Nipro	Home Diagnostics	03-Feb-2010	$215	90%	85%	$121	1.8	
Medco	DNA Direct	02-Feb-2010						
Quidel	Diagnostic Hybrids	20-Jan-2010	$130			$51	2.5	
Inverness	Standard Diagnostics	11-Jan-2010	$216		33%	$36	6.0	
Inverness Medical	Epocal	05-Jan-2010	$255.0					
Average							**4.2**	**17.5**

Source: Compiled by MHBK/IRD based on Capital IQ and public

Table 37 Acquisitions of Life Science Companies

Acquirer	Target	Announce Date	Total Invested Capital ($mn)	Premium 1-Day	Premium 2-Day	Revenue LTM ($mn)	Price/Sales LTM	EV / EBITDA
Agilent	Seahorse Biosciences	09-Sep-2015	235			49.0	4.8	
Affymetryx	Eureka Genomics	14-May-2015	15					
Danaher	Pall	13-May-2015	13,800	28%	29%	2,853.0	4.8	20.8
Fujifilm	Cellular Dynamics	30-Mar-2015	307	108%	204%	16.7	18.4	
Beckton Dickinson	CareFusion	06-Oct-2014	12,200	26%	25%	3,842.0	3.2	14.2
Merck KGaA	Sigma Aldrich	22-Sep-2014	17,000	38%	36%	2,738.0	6.2	20.4
Techne	ProteinSimple	17-Jun-2014	300			57	5.3	38.0
Roche	Genia	02-Jun-2014	125					
Fluidigm	DVS	29-Jan-2014	208					
Thermo Fisher	Life Technologies	15-Apr-2013	15,800			3,800	4.2	
Bio-Rad	AbD Serotec from Morphosys	10-Jan-2013	70				3.0	
Affymetryx	eBiosciences	30-Nov-2011	330			70	4.7	14.0
Bio-Rad	QuantaLife	05-Oct-2011	162					
EMD Millipore	Amnis	30-Aug-2011	111			14	7.9	
Becton Dickinson	Accuri Cytometers, Inc.	07-Feb-2011	205			20	10.3	
Danaher Corp.	Beckman Coulter, Inc.	07-Feb-2011	7,282	11%	11%	3,663	1.9	8.9
IDEX Corp.	Microfluidics International	11-Jan-2011	19	59%	69%	17	1.0	20.4
Thermo Fisher	Dionex	13-Dec-2010	2,093	21%	33%	432	4.7	19.6
PerkinElmer	Caliper Life Sciences	08-Sep-2011	600	42%	46%	124	4.9	
Caliper	Cambridge Res. & Instru.	09-Dec-2010	19			13	1.3	
Life Technologies	Ion Torrent	17-Aug-2010	375					
Olympus	Innov-X	02-Jul-2010	78					
Thermo Fisher	Proxeon A/S	15-Apr-2010				10		
Merck KGaA	Millipore	01-Mar-2010	7,200	50%		1,654	4.4	17.8
Thermo Fisher	Finnzyme	02-Feb-2010				20		
Thermo Fisher	Ahura Scientific	19-Jan-2010	145					
Danaher	Genetix Group PLC	18-Dec-2009	82			42	2.0	
Thermo Fisher	BRAHMS AG	02-Sep-2009	€ 330			€ 75	4.4	
Danaher	MDS Analytical Division	02-Sep-2009	1,100			650	1.7	
Agilent	Varian	27-Jul-2009	1,500	33%	33%	893	1.7	9.6
Roche	Innovatis AG	16-Mar-2009	€ 15					
Millipore	Guava Technologies	02-Feb-2009	23			22	1.0	
Invitrogen Corp.	Applera Corp.	12-Jun-2008	6,543	17%	19%	2,173	3.0	12.3
General Electric	Whatman	04-Feb-2008	£363			£116	3.1	13.8
PerkinElmer	ViaCel	01-Oct-2007	282	54%	69%	59	4.8	
Eppendorf	New Brunswick Scientific	11-Jul-2007	108	43%	46%	76	1.4	15.5
Roche	NimbleGen Systems	19-Jun-2007	273					
Qiagen	Digene	03-Jun-2007	1,500	35%	36%	191	7.9	35.9
Bio-Rad	DiaMed Holding AG	16-May-2007	406					
Agilent	Stratagene	06-Apr-2007	249	29%	30%	96	2.6	16.6
Roche Holding AG	454 Life Sciences	29-Mar-2007	140					
MDS	Molecular Devices	29-Jan-2007	589	49%	57%	186	3.2	20.5
Average							4.4	18.6

Source: Compiled by MHBK/IRD based on Capital IQ and public company reports

Appendix – Company Valuation and Financial Tables

Table 38 U.S. Med Tech Industry Company Valuation Sheet

Company					EPS (USD)			P/E			Growth		
October 29, 2015	Price (USD)	52-wk Hi	52-wk Low	Market Cap (USD in mn)	2014	2015E	2016E	2014	2015E	2016E	'14-16	EV/ '14 Sales	EV/ '14 EBITDA
S&P 500	**2091.2**	**2130.8**	**1867.6**		**102.6**	**119.6**	**129.7**		**17.5**	**16.1**			
Cardiovascular Device													
Medtronic plc	73.78	79.50	55.54	103,957	3.82	4.34	4.36	19.3	17.0	16.9	6.9%	7.1	19.9
Boston Scientific Corporation	18.15	18.62	12.56	24,729	0.83	0.92	1.05	22.0	19.8	17.3	12.6%	4.1	17.2
St. Jude Medical Inc.	63.63	80.84	60.34	17,722	3.98	3.93	4.32	16.0	16.2	14.7	4.2%	3.6	11.5
Edwards Lifesciences Corp.	154.99	157.61	118.89	16,563	3.38	4.50	4.79	45.8	34.4	32.4	18.9%	6.9	29.6
Cardiovascular Device	**51.79**			**162,971**	**2.46**	**2.76**	**2.87**	**21.0**	**18.8**	**18.0**	**8.0%**	**5.8**	**18.5**
Orthopedics													
Zimmer Biomet Holdings, Inc.	105.25	121.84	88.77	19,903	6.05	6.76	7.81	17.4	15.6	13.5	13.6%	6.4	16.5
Stryker Corporation	95.74	105.34	86.16	36,010	4.74	5.11	5.61	20.2	18.7	17.1	8.7%	3.7	13.9
Smith & Nephew plc	16.70	18.60	15.33	15,005	0.81	0.83	0.94	20.5	20.0	17.8	7.4%	3.6	12.9
Wright Medical Group N.V.	19.86	23.46	18.03	1,994		-1.63	-0.97					7.1	-84.3
Globus Medical, Inc.	22.39	28.99	20.48	2,124	0.97	1.05	1.18	23.2	21.2	19.0	10.4%	4.1	11.5
NuVasive, Inc.	46.83	56.61	38.17	2,332	1.13	1.26	1.47	41.5	37.2	31.8	14.3%	3.1	14.4
Orthofix International N.V.	34.44	42.10	27.85	666	0.83	0.69	0.99	41.7	49.9	34.7	9.7%	1.5	9.6
Integra LifeSciences Holdings Corporation	59.25	70.32	46.55	2,141	2.90	3.06	3.42	20.4	19.4	17.3	8.5%	2.9	14.5
Exactech Inc.	17.77	26.20	16.11	255	1.14	1.02	1.19	15.6	17.4	14.9	2.3%	1.0	5.7
Orthopedics	**44.86**			**78,034**	**2.18**	**2.30**	**2.61**	**20.5**	**19.5**	**17.2**	**9.3%**	**4.3**	**14.8**
Hospital Supplies													
Baxter International Inc.	37.55	75.29	32.18	20,321	4.87	1.24	1.42	7.7	30.3	26.5	-46.1%	1.7	6.4
CR Bard Inc.	186.47	202.47	158.93	13,607	7.44	8.12	8.96	25.1	23.0	20.8	9.8%	4.2	14.5
Becton, Dickinson and Company	143.44	154.98	125.35	29,850	6.23	7.11	8.39	23.0	20.2	17.1	16.1%	4.9	18.4
Abbott Laboratories	45.29	51.74	39.00	66,712	2.03	2.16	2.39	22.3	21.0	19.0	8.5%	3.2	13.5
Johnson & Johnson	101.44	109.49	81.79	278,058	5.95	6.19	6.43	17.0	16.4	15.8	3.9%	3.5	10.2
Teleflex Incorporated	132.95	140.50	107.45	5,404	5.69	6.23	7.17	23.4	21.4	18.5	12.3%	3.4	13.9
Hospital Supplies	**80.71**			**413,952**	**4.73**	**4.56**	**4.85**	**17.1**	**17.7**	**16.6**	**1.3%**	**3.3**	**10.8**
Small-Cap CV Medical Device													
ABIOMED, Inc.	70.56	110.68	26.50	4,146	0.53	0.53	0.69	132.3	134.4	102.0	13.9%	21.7	392.5
AngioDynamics Inc.	12.59	19.80	11.80	456	0.61	0.59	0.62	20.6	21.4	20.2	1.1%	1.6	11.2
AtriCure, Inc.	18.50	28.15	15.89	606	-0.70	-0.98	-1.09	-	-	-	24.7%	5.2	-
Cardiovascular Systems Inc.	14.11	41.28	11.80	469	-2.24	-2.23	-1.63	-	-	-	NA	2.9	NA
Endologix Inc.	8.68	18.07	8.42	616	-0.37	-0.60	-0.43	-	-	-	NA	4.2	NA
Heartware International Inc.	42.71	95.59	34.70	1,517	-2.24	-2.23	-1.63	-	-	-	NA	2.5	-
LeMaitre Vascular, Inc.	14.65	14.82	6.81	248	0.21	0.37	0.40	71.5	39.4	36.6	39.7%	3.1	23.1
Merit Medical Systems, Inc.	19.20	26.42	13.88	846	0.73	0.86	0.93	26.3	22.3	20.8	12.6%	2.1	14.0
The Spectranetics Corporation	12.29	37.04	10.65	510	-0.28	-0.97	-0.81	-	-	-	NA	3.5	169.4
Stereotaxis Inc.	0.93	2.97	0.65	21									NA
Hansen Medical, Inc.	3.65	12.30	3.47	68	-4.60	-3.60	-2.60	-	-	-	NA	3.1	-
Vascular Solutions Inc.	32.38	40.33	22.92	581	0.75	1.04	1.19	43.0	31.2	27.2	25.8%	4.3	22.2
Small-Cap CV Medical Device				**10,083**								**4.4**	

Source: Compiled by MHBK/IRD based on public data from Capital IQ

Table 39U.S. Med. Tech Industry Financial Metrics

Company October 29, 2015	Ticker	Sales (USD in mn) 2014	2015E	2016E	Sales Growth '14-16	EBITDA (USD in mn) 2014	2015E	2016E	EBITDA Growth '14-16	Net Income (USD in mn) 2014	2015E	2016E	N. I. Growth '14-16	Net Cash (USD in mn)
Cardiovascular Device														
Medtronic plc	MDT	17,013	20,623	28,941	30.4%	6,108	8,459	10,021	28.1%	3,065	6,076	6,457	45.1%	-17,613
Boston Scientific Corporation	BSX	7,392	7,495	8,059	4.4%	1,760	2,054	2,278	13.8%	1,115	1,242	1,415		-5,509
St. Jude Medical Inc.	STJ	5,622	5,574	6,193	5.0%	1,759	1,663	1,842		1,152	1,121	1,200		-2,525
Edwards Lifesciences Corp.	EW	2,306	2,481	2,701	8.2%	537	711	748	18.0%	367	496	520	19.1%	646
Cardiovascular Device		**32,332**	**36,173**	**45,893**	**19.1%**	**10,164**	**12,887**	**14,888**	**21.0%**	**5,699**	**8,934**	**9,593**	**29.7%**	**-25,001**
Orthopedics														
Zimmer Biomet Holdings, Inc.	ZBH	4,694	6,213	7,672	27.8%	1,822	2,379	2,966	27.6%	720	1,312	1,594	48.8%	-10,104
Stryker Corporation	SYK	9,675	9,944	10,483	4.1%	2,597	2,645	2,831	4.4%	1,177	1,923	2,057	32.2%	-116
Smith & Nephew plc	LSE:SN.	4,635	4,653	4,916	3.0%	1,280	1,412	609	-31.1%	15	743	786	625.9%	-1,510
Wright Medical Group N.V.	WMGI	298	356	499	29.4%	-25	-23	8	#NUM!	-267	-93	-81		-132
Globus Medical, Inc.	GMED	474	529	577	10.3%	168	184	203	9.9%	92	102	106	7.2%	200
NuVasive, Inc.	NUVA	761	811	872	7.0%	165	202	223	16.5%	-17	64	69		-35
Orthofix International N.V.	OFIX	404	393	408	0.5%	63	59	68	3.6%	-9	6	13		56
Integra LifeSciences Holdings Corp	IART	920	880	968	2.5%	184	213	250	16.5%	34	106	118	86.6%	-523
Exactech Inc.	EXAC	249	242	250	0.4%	45	42	45	-0.3%	16	14	16	-2.8%	-4
Orthopedics		**20,941**	**22,898**	**25,427**	**10.2%**	**6,070**	**6,858**	**6,907**	**6.7%**	**1,712**	**4,058**	**4,544**	**62.9%**	**-11,642**
Hospital Supplies														
Baxter International Inc.	BAX	16,536	9,904	10,060	-22.0%	4,373	1,526	1,643	-38.7%	2,497	680	740	-45.6%	-7,550
CR Bard Inc.	BCR	3,303	3,416	3,577	4.1%	963	1,026	1,089	6.3%	295	611	648	48.3%	-407
Becton, Dickinson and Company	BDX	8,406	10,290	12,741	23.1%	2,245	2,696	3,516	25.1%	1,185	1,471	1,779	22.5%	-11,574
Abbott Laboratories	ABT	20,376	20,563	21,606	3.0%	4,781	4,910	5,319	5.5%	2,284	3,258	3,530	24.3%	2,399
Johnson & Johnson	JNJ	74,650	70,214	72,418	-1.5%	25,755	23,055	24,752	-2.0%	16,323	17,374	17,573	3.8%	14,647
Teleflex Incorporated	TFX	1,837	1,804	1,912	2.0%	445	485	556	NA	188	256	323	NA	-786
Hospital Supplies		**125,107**	**116,191**	**122,314**	**-1.1%**	**38,563**	**33,698**	**36,874**	**-2.2%**	**22,771**	**23,649**	**24,592**	**3.9%**	**-3,271**
Small-Cap CV Medical Device														
ABIOMED, Inc.	ABMD	184	225	310	29.8%	10	26	48	117.3%	7	22	37	125.5%	176
AngioDynamics Inc.	ANGO	354	358	363	1.2%	51	58	57	5.3%	3	21	24		-115
AtriCure, Inc.	ATRC	108	130	161	22.4%	-4	-12	-65		-16	-27	-35		48
Cardiovascular Systems Inc.	CSII	134	183	190	19.0%	-21	-18	-23	NA	-35	-34	-42		84
Endologix Inc.	ELGX	147	155	175	9.2%	-22	-23	-2	NA	-32	-41	-32		-5
Heartware International Inc.	HTWR	277	283	305	4.9%	-10	-9	-2	NA	-19	-40	-32		59
LeMaitre Vascular, Inc.	LMAT	71	78	84	8.7%	10	16	16	30.1%	4	7	7	33.2%	24
Merit Medical Systems, Inc.	MMSI	510	544	583	7.0%	75	84	94	12.1%	23	35	39	30.5%	-204
The Spectranetics Corporation	SPNC	204	245	265	14.2%	4	-13	-13		-41	-41	-39		-211
Stereotaxis Inc.	STXS									-5				-15
Hansen Medical, Inc.	HNSN	19	22	31	25.9%	-45	-44	-43	-2.2%	-54	-44	0		7
Vascular Solutions Inc.	VASC	126	147	164	14.0%	24	26	33	16.3%	13	19	20	26.4%	40
Small-Cap CV Medical Device		**2,134**	**2,369**	**2,632**	**11.1%**									**-112**

Source: Compiled by MHBK/IRD based on Capital IQ and public company reports

Table 40 U.S. Diagnostic and Life Science Industry Valuation Sheet

Company					EPS (USD)			P/E			Growth		
October 29, 2015	Price (USD)	52-wk Hi	52-wk Low	Market Cap (USD in mn)	2014	2015E	2016E	2014	2015E	2016E	'14-16	EV/ '14 Sales	EV/ '14 EBITDA
S&P 500	**2091.2**	**2130.8**	**1867.6**		**102.6**	**119.6**	**129.7**		**17.5**	**16.1**			
Diagnostics													
Abaxis, Inc.	51.63	66.89	41.53	1,215	0.65	0.94	1.30	79.0	55.2	39.7	41.1%	6.2	38.1
Accelerate Diagnostics, Inc.	17.37	31.29	14.77	803									
Becton, Dickinson and Company	143.44	154.98	125.35	29,850	6.23	7.11	8.39	23.0	20.2	17.1	16.1%	4.9	18.4
BG Medicine, Inc.	0.56	4.88	0.34	5	-1.04	0.00	0.00					2.2	
Cancer Genetics, Inc.	6.85	12.75	4.83	73	-1.75	-1.77	-1.11					5.7	-
Cepheid	34.14	63.69	29.21	2,415	0.13	0.00	0.29	260.9		119.2	47.9%	5.1	381.1
Danaher Corp.	93.10	94.61	78.74	63,457	3.74	4.28	4.97	24.9	21.8	18.7	15.3%	3.9	17.2
Foundation Medicine, Inc.	22.27	54.28	17.51	793	-1.90	-2.46	-2.01					8.8	-
Genomic Health Inc.	21.13	37.75	20.05	718	-0.81	-0.75	0.02					2.1	-
Hologic Inc.	38.55	43.00	25.26	11,142	1.46	1.66	1.82	26.4	23.2	21.1	11.8%	5.7	14.8
T2 Biosystems, Inc.	11.14	24.04	8.45	237	-3.33	-2.27	-2.14						
Myriad Genetics, Inc.	41.16	42.99	30.30	2,977	2.40	1.46	1.63	17.2	28.2	25.3	-17.6%	3.6	9.3
Nanosphere, Inc.	1.74	9.94	1.58	14	-9.40	-5.14	-3.48					0.7	
Alere Inc.	46.13	55.99	35.81	3,944	2.01	2.42	2.78	23.0	19.0	16.6	17.7%	2.7	14.3
Meridian Bioscience, Inc.	19.05	20.28	15.56	789	0.86	0.86	0.90	22.2	22.3	21.2	2.4%	3.9	11.5
Luminex Corporation	18.11	21.16	15.05	801	0.57	0.65	0.59	31.6	28.1	30.6	1.6%	3.0	14.2
Qiagen NV	24.07	28.53	22.11	6,117	1.05	1.11	1.22	22.9	21.7	19.8	7.7%	5.0	15.6
Trinity Biotech plc	11.59	20.24	10.83	269	0.74	0.44	0.55	15.7	26.5	21.1	-13.9%	2.5	
Quidel Corp.	20.28	29.38	17.16	581	0.17	0.47	0.56	119.3	43.5	36.1	81.8%	2.9	17.7
Oxford Immunotec Global PLC	11.93	15.61	10.01	265	-1.33	-1.17	-0.82					3.6	
Veracyte, Inc.	6.52	12.47	4.59	190	-1.32	-1.31	-1.11					3.8	
NanoString Technologies, Inc.	14.78	19.81	9.95	290	-2.35	-2.31	-1.80					5.7	
GenMark Diagnostics, Inc.	7.12	14.40	4.63	292	-1.01	-1.07	-1.17					8.1	
Tandem Diabetes Care, Inc.	7.58	17.98	7.26	226	-3.45	-2.84	-2.24					3.2	
Diagnostics				**127,463**								**4.2**	**18.0**
Life Science Industry													
Agilent Technologies Inc.	37.73	55.41	33.12	12,434	3.06	1.70	1.97	12.3	22.2	19.1	-19.7%	1.7	7.9
Affymetrix Inc.	8.96	13.11	7.90	775	0.25	0.41	0.41	35.8		22.1		2.2	16.0
Albany Molecular Research Inc.	18.28	23.95	13.73	667	0.68	0.92	1.11	26.9	19.9	16.5	27.8%	3.0	16.3
Bio-Rad Laboratories, Inc.	140.48	152.38	102.71	4,132	3.53	3.52	4.10	39.8	39.9	34.3	7.8%	1.8	12.0
Enzo Biochem Inc.	4.00	5.38	2.26	184	-0.27	-0.30	-0.20	-				1.8	
Fluidigm Corporation	7.40	46.38	7.20	215	-1.30	-1.77	-1.48	-				2.7	
Harvard Bioscience Inc.	3.05	6.84	3.30	126	0.26	0.21	0.25	11.7	14.5	12.2		1.3	
Illumina Inc.	145.64	242.37	130.00	21,265	2.65	3.31	3.79	54.9	44.0	38.4	19.6%	11.3	34.4
Mettler-Toledo International Inc.	309.86	350.11	254.04	8,514	11.64	12.82	14.24	26.6	24.2	21.8	10.6%	3.6	16.4
NanoString Technologies, Inc.	14.78	19.81	9.95	290	-2.35	-2.31	-1.80					5.7	-
Pacific Biosciences of California, Inc.	7.19	8.78	3.58	550	-0.91	-0.69	-0.85					8.7	-
PerkinElmer Inc.	51.05	54.45	40.62	5,781	2.40	2.58	2.87	21.3	19.7	17.8	9.4%	2.9	15.6
Thermo Fisher Scientific, Inc.	131.44	141.25	14.00	51,505	6.91	7.39	8.24	19.0	17.8	15.9	9.2%	3.8	15.9
Waters Corporation	128.44	137.39	109.17	10,629	5.40	5.88	6.41	23.8	21.8	20.1	8.9%	5.0	15.5
Bruker Corporation	18.28	22.32	15.78	3,065	0.75	0.75	0.87	24.5	24.3	21.1	7.8%	1.6	12.5
Qiagen NV	24.07	28.53	22.11	6,117	1.05	1.11	1.22	22.9	21.7	19.8	7.7%	5.0	15.6
Bio-Techne Corp.	87.41	114.56	83.90	3,251	3.37	3.40	3.42	25.9	25.7	25.6	0.7%	9.3	17.7
Charles River Laboratories International, Inc.	66.40	84.69	59.99	3,157	3.36	3.64	4.10	19.8	18.2	16.2	10.4%	2.9	12.9
Life Science Industry				**132,658**				**20.1**	**20.1**	**18.0**	**5.5%**	**3.6**	**15.8**

Source: Compiled by MHBK/IRD based on data from Capital IQ and public company reports

Table 41 U.S. Diagnostic and Life Science Industry Financial Metrics

Company October 29, 2015	Ticker	Sales (USD in mn) 2014	2015E	2016E	Sales Growth '14-16	EBITDA (USD in mn) 2014	2015E	2016E	EBITDA Growth '14-16	Net Income (USD in mn) 2014	2015E	2016E	N. I. Growth '14-16	Net Cash (USD in mn)
Diagnostics														
Abaxis, Inc.	ABAX	175	217	226	13.4%	28	39	52	35.9%	14	21	32	49.4%	133
Accelerate Diagnostics, Inc.	AXDX							-90						48
Becton, Dickinson and Company	BDX	8,406	10,290	12,741	23.1%	2,245	2,696	3,516	25.1%	1,185	1,471	1,779	22.5%	-11,574
BG Medicine, Inc.	BGMD	3	0	0	-100.0%					-8	0	0		-1
Cancer Genetics, Inc.	CGIX	10	21	41	103.1%	-18	-17	-68	97.0%	-17	-19	-16		16
Cepheid	CPHD	464	539	620	15.6%	6	2	21	84.6%	-50	-2	7		41
Danaher Corp.	DHR	19,886	20,826	23,370	8.4%	4,471	4,708	5,521	11.1%	2,598	2,941	3,216	11.3%	-13,179
Foundation Medicine, Inc.	FMI	60	92	140	52.4%	-46	-76	-70		-52	-83	-75		264
Genomic Health Inc.	GHDX	279	291	334	9.6%	-18	-23	10		-25	-24	-6		120
Hologic Inc.	HOLX	2,510	2,695	2,843	6.4%	956	1,010	1,083	6.4%	17	482	538		-3,057
T2 Biosystems, Inc.	TTOO	0	3	20	939.5%	-30	-42	-38		-31	-46			32
Myriad Genetics, Inc.	MYGN	777	721	757	-1.2%	304	187	213	-16.2%	176	107	116	-18.9%	145
Nanosphere, Inc.	NSPH	14	21	25	33.4%	-36	0	0		-39	-34	-31		6
Alere Inc.	ALR	2,810	2,569	2,653	-2.8%	539	581	605	5.9%	-38	225	253		-3,134
Meridian Bioscience, Inc.	VIVO	191	193	200	2.2%	65	65	66	0.8%	35	36	37	3.7%	46
Luminex Corporation	LMNX	227	235	249	4.7%	48	51	49	1.2%	39	28	23	-23.9%	121
Qiagen NV	QGEN	1,355	1,304	1,394	1.4%	432	396	472	4.6%	117	258	280	55.0%	-629
Trinity Biotech plc	TRIB	105	101	112	3.1%	24	20	23	-0.7%	17	10	14	-11.4%	5
Quidel Corp.	QDEL	183	208	227	11.5%	30	46	50	29.6%	-7	18	16		59
Oxford Immunotec Global PLC	OXFD	49	62	80	27.6%	-20	-23	-17		-22	-26	-24		90
Veracyte, Inc.	VCYT	38	50	66	31.7%	-27	-33	-29		-29	-34	-35		46
NanoString Technologies, Inc.	NSTG	48	61	86	34.7%	-40	-40	-31		-50	-44	-38		21
GenMark Diagnostics, Inc.	GNMK	31	39	49	26.7%	-40	-41	-43		-38	-45	-53		44
Tandem Diabetes Care, Inc.	TNDM	49	73	101	43.4%	-74	-72	-61		-80	-81	-82		68
Diagnostics		**37,669**	**40,609**	**46,334**	**10.9%**	**8,800**	**9,434**	**11,236**	**13.0%**	**3,712**	**5,160**	**5,948**	**26.6%**	**-30,268**
Life Science Industry														
Affymetrix Inc.	AFFX	348	358	371	3.2%	48	55	258	132.5%	-4	35	37		13
Albany Molecular Research Inc.	AMRI	280	408	504	34.2%	51	73	0	-100.0%	-3	31	35		-160
Bio-Rad Laboratories, Inc.	BIO	2,170	2,069	2,156	-0.3%	321	294	317	-0.6%	89	103	114	13.4%	292
Enzo Biochem Inc.	ENZ	95	97	103	3.8%	-8	-9	0		-10	0	-10		14
Fluidigm Corporation	FLDM	116	113	131	6.2%	-33	-43	226		-53	-51	-49		-96
Illumina Inc.	ILMN	1,856	2,200	2,558	17.4%	609	771	890	20.9%	353	493	538	23.4%	329
Mettler-Toledo International Inc.	MTD	2,481	2,386	2,479	-0.1%	548	569	1,536	67.4%	338	362	386	6.8%	-479
NanoString Technologies, Inc.	NSTG	48	61	86	34.7%	-40	-40	-31		-50	-44	-38		21
Pacific Biosciences of California, In	PACB	58	91	83	19.5%	-58	-38	-18		-66	-47	-50		44
PerkinElmer Inc.	PKI	2,233	2,274	2,375	3.1%	422	450	486	7.3%	158	294	312	40.7%	-796
Thermo Fisher Scientific, Inc.	TMO	16,778	16,870	17,642	2.5%	4,040	4,179	4,527		1,894	2,968	3,179	29.5%	-12,807
Waters Corporation	WAT	1,986	2,038	2,146	4.0%	640	673	717	5.9%	432	488	515	9.2%	681
Bruker Corporation	BRKR	1,817	1,609	1,674	-4.0%	235	229	258		57	127	133	53.4%	129
Qiagen NV	QGEN	1,355	1,304	1,394	1.4%	432	396	472	4.6%	117	258	280	55.0%	-629
Bio-Techne Corp.	TECH	357	452	482	16.2%	188	204	226		111	129	127	6.9%	-81
Charles River Laboratories Internati	CRL	1,288	1,346	1,441	5.8%	294	322	356	10.1%	127	173	185	20.7%	-604

Source: Compiled by MHBK/IRD based on data from Capital IQ and public company reports

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