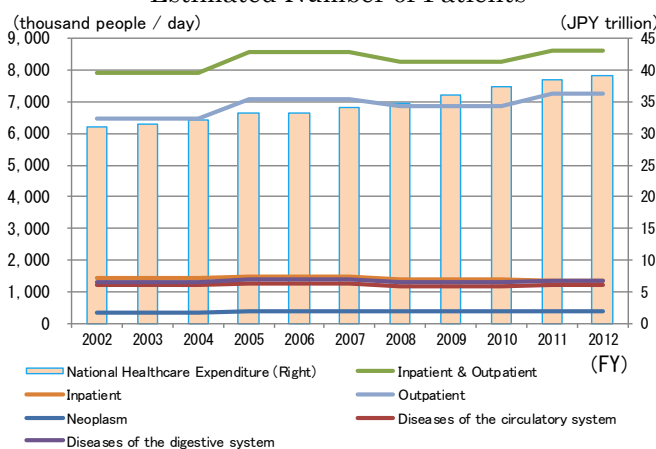


Method of Innovation for Japanese Med-Tech Industry — Essence of Silicon Valley Style and How Japan Can Tap IT —

1. Overview of Japanese Medical Devices (Med-Tech) Industry

- In Japan, government is taking the lead to solve a "device lag" and promote med-tech industry. At the same time, aggressive corporate reorganization like Medtronic's acquisition of Covidien is ongoing worldwide. Under these circumstances, referring to US companies, we study a method of innovation for Japanese medical devices industry.
- In Japan, national healthcare expenditure is expanding gradually along with the aging population. Nevertheless, due to increasingly sophisticated medical treatment, which results in shorter hospitalization stays and, thus, fewer hospital beds, we are successfully avoiding a rapid increase in the number of inpatients. There are many types of medical devices (Figure 1-2) and the market size of the industry is growing, especially for catheters and in the medical endoscope field.
- The portion of imports in Japan's med-tech market is large (49%), mainly from the US. The portion of imports has stayed between 46% and 49% over the last ten years; thus, domestic production and imports grew at approximately the same proportion.
- Japanese med-tech companies are doing well, as we see on page 5, but US med-tech companies are still leading the market worldwide. One of the reasons seems to be a technological ecosystem in which innovation is partly driven by venture companies that are then acquired by major companies. We studied the mechanism and released the report *Silicon Valley's "Ecosystem" for the Development of Medical Devices*. Tapping the network we developed in the course of this study, we consider a new way for increased Japanese participation in this sector's innovation.

Figure 1-1 National Healthcare Expenditure and Estimated Number of Patients



Sources. Patient surveys and the Ministry of Health, Labour and Welfare's triennial *Estimates of National Medical Care Expenditure*.

Figure 1-2 Classification of Major Medical Devices

Category	Broad classification	Middle classification
Treatment devices	Manipulation devices	Injection and puncture devices, Tubes and catheters, Blood donor and transfusion devices, surgical needles etc
	Artificial internal organ apparatus and assistance devices	Pacemakers/Artificial blood vessels/Stents, Prosthetic joints, Dialyzators, Artificial lungs, Respirators etc
	Treatment and surgical devices	Equipment for use with radiotherapy equipment, Low and high frequency therapy equipment, Laser therapy devices etc
Diagnostic devices	Image diagnostic devices	X-ray inspection device, CT, MRI, Thermography, X-ray image diagnostic device, Diagnostic ultrasound imaging systems etc
	Measuring and monitoring systems for bio-phenomena	Clinical thermometer, Sphygmomanometer, Percussion device, Heart rate rheometer, Tonometer, Endoscopes etc

Figure 1-3 Domestic Market Size of Medical Devices

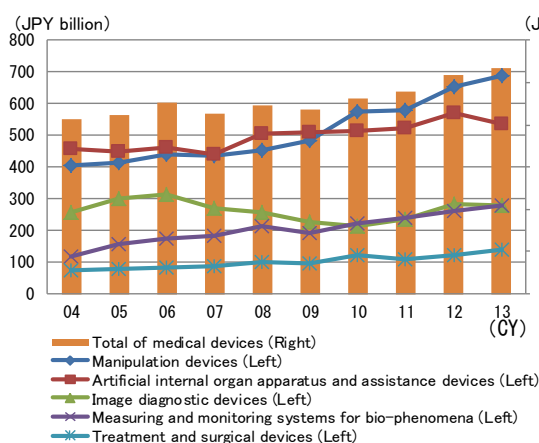
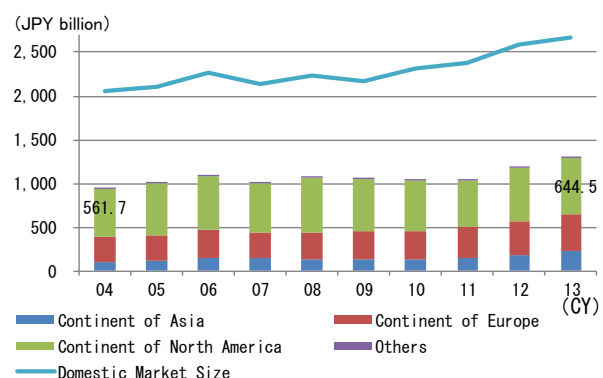


Figure 1-4 Trend of Medical Device Imports

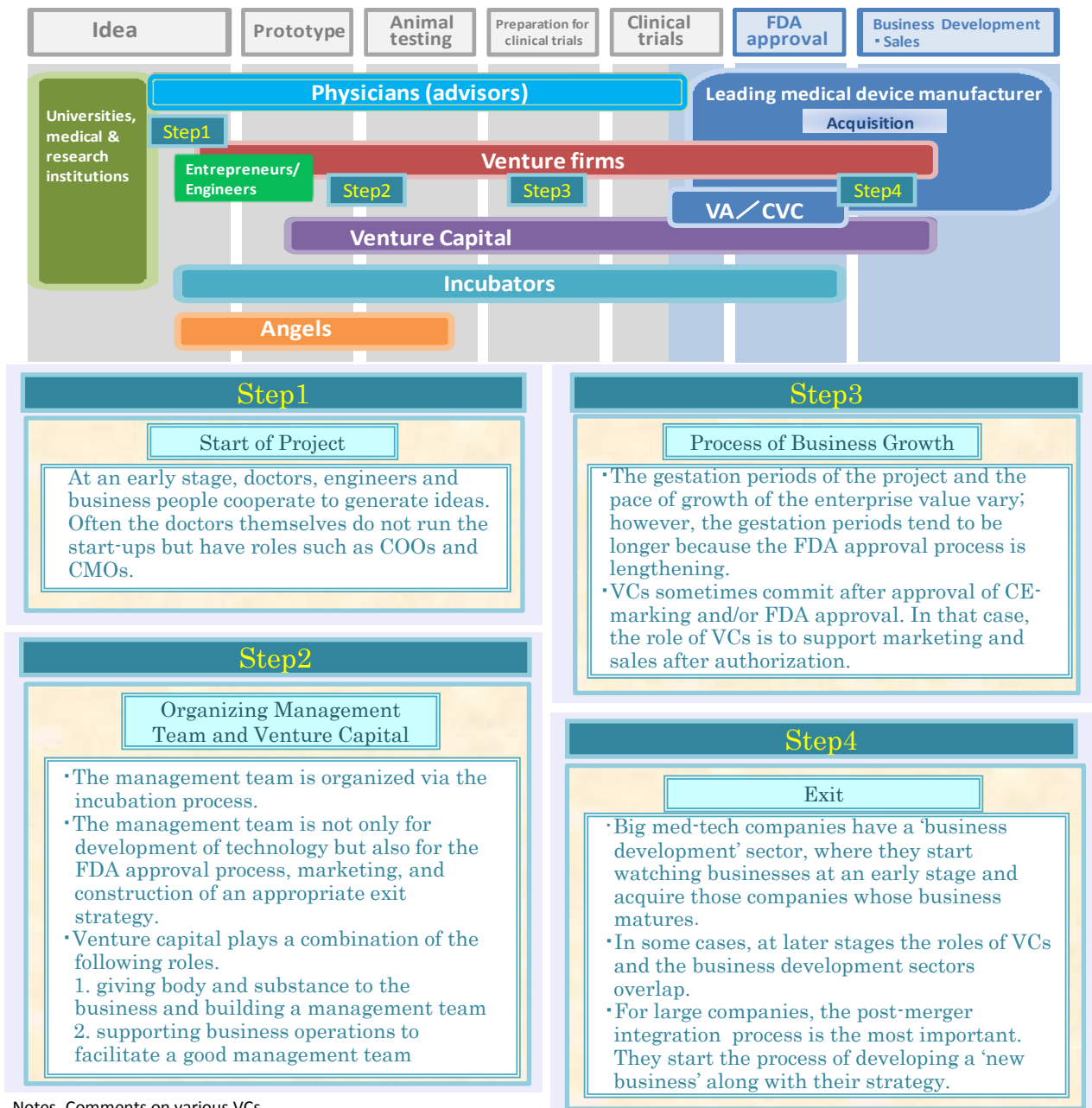


Notes. The source for Figs.1-2, 1-3 and 1-4 is the Ministry of Health, Labour and Welfare's *Statistics of Production by Pharmaceutical Industry*. Market size is estimated by Domestic products + Imports - Exports.

2. 'Ecosystem' for Med-Tech Development (part 1)

- We study again the Silicon Valley "Ecosystem" regarding the process of business development. We have invested (2014/9) in one med-tech fund, Emergent Medical Partners II, L.P. (http://www.dbj.jp/en/topics/dbj_news/2014/html/0000017115.html)
Since then, we have interviewed various venture funds regarding actions taking place in the Ecosystem and re-plotted the system as per Figure 2. The exits of med-tech startups are mainly through takeovers by large-size or middle-size med-tech companies. In Silicon Valley, there are an especially large number of acquisitions. It can be said that this constitutes a part of the world's business development.
- This process is established by the US labor market and culture, and the key factors are the following.
 1. a management team that implements 'Concept'
 2. mutual understanding of business operators and investors
 3. existence of financial providers at each stage
 4. continuous relationships between venture companies and acquired companies

Figure 2 Ecosystem in Silicon Valley Focusing on 'Business Operators' and 'Financial Provider'



Notes. Comments on various VCs.

3. 'Ecosystem' for Med-Tech Development (part 2)

- We interviewed some Silicon Valley venture capitalists to hear about their way of thinking about the business process. We integrate the essence of the interviews below. This report includes the opinions of both the early-stage and the later-stage VCs we interviewed, despite their frequent differences.
- Every comment is important, but the following are more essential.
 1. When VCs consider investment in a venture business, they take into account **what the VB is trying to accomplish**. VCs consider valuable a VB's desire for a big change.
 2. VC's take into account the experience of the members of the VB's management team.
 3. Regarding exit strategy, important characteristics include longtime relationships and a sense of special fit between acquiring and acquired companies.
- Of course, ecosystems exist in other regions—for example, Minnesota. However, this time we glean the Silicon Valley VCs' comments for some clues to this sector's uniqueness.
- Also, major US med-tech companies have business development sectors that monitor the exits of VBs continuously and start to raise new 'business' worldwide through acquisitions, as we discuss later.

Figure 3 Interview Comment (opposing opinions included)

(1) How important is 'experience' in running start-up companies?		(3) As for exit strategy, what is the image of the 'acquiring company'?	
Experience is important	• Technologically skilled team members are helpful when generating new ideas, but it is more important to organize an experienced management team. Without experience, commercialization doesn't work. • Because med-tech has numerous regulations and patents, it is difficult for people lacking experience to deal with the issues.	Aspect of fit when acquiring a company	• The sense of fit is the most important aspect. No matter how large the acquiring company is, the project's results depend on how the new management team deals with the project. An inappropriate fit can lead to damaging defections from a VB team.
Various opinions	• For example, competence in digital health might not depend on healthcare experience. As long as it includes a technologically skilled person, a team can be assembled appropriately.	Various opinions	• Only large-size companies can afford to make acquisitions. Even middle-size companies are not able to pay for them.
(2) Important points in terms of investment *1		(4) Can Japanese companies be startup-'acquiring companies'?	
What you want to accomplish?	• The most important point is 'patients first'-- that is, how the product works for patients. Market size differs from project to project. The bigger the market is, the more difficult the project is. • The first priority is market size, and the second is the solution. So, can you make a big change for the market? The third priority is cost of development, and the fourth is sales force. The technology is the last priority; thus, big change comes not from technology itself, but rather from ideas. • The most important thing is the kinds of problems to be solved. 'Unmet needs' must be the focus. For example, mere improvements in 'stent' quality are not critical to increasing the size of their market. Market size depends more on the impact of the solution to the problem.	Promoting confidence-building	• It is important to build mutual trust. Credibility at critical moments is key, and that is why frequent contact is necessary. • Japanese companies need to clarify what they want to accomplish. Long-time relationships are also important, as are actual track records of actual transactions.
Evaluate the management team	• Management is the most important aspect, followed by clinical efficiency. • Key components of management are team composition, first, and corporate size, second, followed by technology and financial status.	Severe opinion	• Japanese companies' decision-making is slow and their leaders' committedness is weak. Also, their sales focus is Japan-centric, whereas their foreign competitors sell globally; so, their respective evaluations of start-ups are also from different standpoints. That contributes to pricing differences between companies, because when foreign companies in the US really want to penetrate that country's market, they incur heavy costs for investment in capital, both human and financial.

*1 We asked about order of priority: The level of technology, Market size, Cost of development, Sales Force, etc.

Notes : Comments on various VCs

4. Technology Trend & M&A Cases in Silicon Valley and the US

- Below we organize some trends of med-tech VB from Silicon Valley. Both major companies and venture companies are major players and the main trend is 'minimally invasive'.
- First, in the circulatory system, for ischemic cardiac disease such as angina pectoris and cardiac infarct, we usually do catheter intervention called PCI. That field develops many kinds of products--from bare metal stents to drug-eluting stent and bioabsorbable vascular scaffold systems. For tachyarrhythmia, the evolution of ablation electrodes and ICDs is ongoing.
- Also, the incidence of aortic valve stenosis is increasing in line with the aging population; and as for valve replacement, TAVI is spreading in the US and Europe. Products for TAVI and transcatheter products for mitral valve insufficiency are also being developed actively.
- In addition, you can see various other kinds of development: intravascular treatment for lower extremity arteries etc, intravascular treatment for neurosurgical operations such as stent retrieval, ENT in the area of sinusitis, and SCS for chronic pain. Trends in exits in California are represented by the cases highlighted in Figure 4-1.
- At the same time, major US med-tech companies are aggressively engaging in M&A outside Silicon Valley, both in and outside the US (Figure 4-2), and driving innovation and the scale of sales.

Figure 4-1 Exit Cases via M&A (subset of California exit cases between 2009 and 2015)

Company	Acquiring Company	Year	Products	Field
Spinal Modulation	St.Jude Medical	2015	A form of spinal cord stimulation that targets a neural structure within the spine called the dorsal root ganglion	Chronic pain
Reverse Medical	Covidien(*1)	2014	Vascular embolization plugs etc	Vascular disease
WaveTec Vision	Alcon(Novartis)	2014	Ophthalmic surgical guidance system	Ophthalmology
Nanostim	St.Jude Medical	2013	Miniaturized, leadless pacemakers	Irregular pulse
Loma Vista Medical	C.R.Bard	2013	Aortic valvuloplasty products, which use noncompliant fiber-based balloon technology	Valvular disease
Crux	Volcano (*2)	2012	Filter technology for the vascular, cardiovascular and interventional radiology	Peripheral
Vessix Vascular	Boston Scientific	2012	A catheter-based renal denervation system for the treatment of uncontrolled	Hypertension
Newport Medical Instruments	Covidien(*1)	2012	Dependable, life improving ventilators that are affordable for caregivers	Respiratory disease
Cameron Health	Boston Scientific	2012	Implantable Cardioverting Defibrillator without intravenous leads	Irregular pulse
BÂRRX Medical	Covidien(*1)	2012	Esophageal ablation	Digestive system
Ardian	Medtronic	2011	Catheter-based treatment for hypertension(high blood pressure)	Hypertension
Concentric Medical	Stryker	2011	Minimally invasive products for the treatment of acute ischemic stroke	Neurosurgical
Acclarent	Ethicon(J&J)	2010	Balloon Sinuplasty technology	ENT
InSound Medical	Sonova	2010	Hearing system which is placed deep in the ear canal	ENT
Evalve	Abbott	2009	Percutaneous mitral valve repair system	Valvular disease

Figure 4-2 Major US Companies' M&A Deals

Acquiring Company/ Assignee	Acquired Company/ Assignor	Contents/Location		Acquiring Company/ Assignee	Acquired Company/ Assignor	Contents/Location	
①M&A or business transfer of large-size med-tech companies							
Medtronic	Covidien	Acquisition		Boston Scientific	Bayer	Interventional division	
Zimmer	Biomet	Acquisition		Boston Scientific	C.R.Bard	Electrophysiology	
Becton Dickinson	CareFusion	Acquisition					
②Offshore M&A							
Medtronic	NGC Medical	Italy	Hospital managed services	Stryker	Berchtold HD	Germany	Surgical tables etc
Covidien(*1)	Given Imaging	Israel	Swallowed optical endoscopy	St.Jude Medical	Endosense	Switzer- Land	Ablation catheter
Stryker	Trauson HD	China	Trauma-related manufacturer				
③Acquisition inside US (excluding California)							
Covidien(*1)	Sapheon	NC	Venous disease treatment	St.Jude Medical	NeuroTherm	MA	Interventional pain management
Medtronic	Visualase	TX	Laser ablation	Medtronic	TYRX	NJ	Surgical site infections
Stryker	MAKO Surgical	FL	Robotic arm	Medtronic	Cardiacom	MN	Telehealth

Note. Sources for Figs. 4-1 and 4-2 are IR and other press release materials.

*1 Medtronic at present.

*2 Philips at present.

5. Characteristics and Possibilities for Japanese Med-Tech Makers

- We survey capital investment and R&D trends of Japanese companies via their financial statements to compare with those of major US med-tech companies. In Japan, 'medical devices makers' are not always purely medical device companies; in some cases they are branches of electronics or materials makers and play big roles in the industry. The survey and this paper focus on the balance sheets of companies for which med-tech sales occupy a high proportion of their total sales between 2004 and 2013/14. Also, some companies in the US have strong sales both in med-tech and in, for example, medicine; however, we eliminate those companies for this survey. Therefore, Figure 5 does not include data on all major med-tech companies.
- In one decade, annual Japanese national healthcare expenditure went roughly from 32.1 (2004) to 39.3 (2013) trillion yen, an increase of 22%. OECD data shows annual US total healthcare expenditure increasing from 1.79 to 2.75 trillion dollars over the same period, growing at 54%.
- Sales and operational profits of ten major Japanese companies doubled during that same period. The total asset and cash position also increased in line with sales and profits. Intangible assets, including goodwill from acquisitions, was very small in 2004 but grew at a very high rate over those same ten years. On the other hand, the ratio of R&D to sales, or the amount of capital investment from operating CF, did not change at the same rate.
- The growth rate of sales in US companies is not different from that of Japanese companies; their operating profit to sales went down. But unlike their sales and profits, their intangible assets increased strongly. Also, R&D cost for US companies is composed of both self-development and additional R&D for acquired technology.
- As of 2013, US companies had high R&D costs to sales; however, their operating profit to sales was higher than that of Japanese companies. Regarding the ratio of capital investment to operating CF, US and Japanese companies are similar, but in terms of intangible assets to total assets, US companies' ratios are higher than Japanese companies'. Note, certain differences (for example, in the ownership structure of the manufacturing sector and in the accounting system) make comparison difficult.
- Over these ten years, Japanese companies invested in overseas factories because domestic demand was supposed to grow slowly. Some companies engaged in offshore M&A. Consequently Japanese companies overall realized higher sales growth than did the Japanese med-tech sector. Additionally, the growth rate of international sales and profits was also higher than the domestic figure (the effort should be highly appreciated). The disclosed offshore sales data of Japanese companies indicate that the international contribution to sales growth over these ten years was less than 80% and the domestic contribution was more than 20%.
- There are still big differences between US and Japanese companies in terms of the R&D cost-to-sales ratio and the investment for M&A. The huge R&D expenditure and acquisition investment must be the sources of US companies' added value. US companies' growth rates and profitability are decreasing somewhat and they should see some limits to investment. Japanese companies, on the other hand, instead of being so highly focused on improvement of existing products and on international distribution, should also find ways for their financial successes to lead to new business seeds. Now would be a good time to start.

Figure 5 Summary of Med-Tech Companies' Financial Statements Focusing on Capital Investment

Sum of ten Japan med-tech companies						Sum of eight Us med-tech companies		
	(JPY 100 million)					(USD million)		
	2004fy	2013fy	2014fy	2013/ 2004	2014/ 2004	2004fy	2013fy	2013/ 2004
Sales	7,726	13,760	14,831	1.8	1.9	32,739	56,443	1.7
Operating profit	955	1,619	1,803	1.7	1.9	7,302	9,703	1.3
Ratio of Operating profit to Sales	12.4%	11.8%	12.2%			22.3%	17.2%	
Ratio of R&D cost to Sales	4.3%	5.0%	4.7%			8.0%	8.7%	
Cash equivalent (A)	1,884	3,196	4,018	1.7	2.1	6,029	8,790	1.5
Intangible assets (B)	308	3,852	4,141	12.5	13.4	15,856	43,105	2.7
Total assets (C)	10,294	21,883	25,143	2.1	2.4	46,673	109,986	2.4
=A/C	18.3%	14.6%	16.0%			12.9%	8.0%	
=B/C	3.0%	17.6%	16.5%			34.0%	39.2%	
Operating cash flow (D)	930	1,999	1,937	2.1	2.1	8,240	13,192	1.6
Investment cash flow (E)	-561	-1,459	-1,193	2.6	2.1	-5,004	-8,103	1.6
=E/D	60.3%	73.0%	61.6%			60.7%	61.4%	

Sources. IR materials of the companies below.

Ten Japan med-tech companies

Top ten companies in 2014 in which the proportion of med-tech sales to total sales was high over the previous 10 years: Terumo, Nipro, Sismex, Nihon-Koden, Fukuda Electronics, JMS, Hogi Medical, Nakanishi, Kawasumi Chemical, Asahi Intecc

Eight US med-tech companies

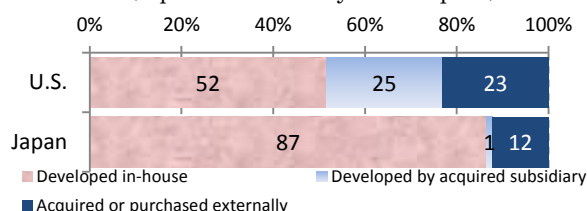
Top eight companies in 2013 in which the proportion of med-tech sales to total sales was high over the previous 10 years: Medtronic (Irish at present *), Stryker, Becton Dickinson, Boston Scientific, St.Jude Medical, Zimmer, C.R. Bard, Edward Lifesciences

*Medtronic is an Irish company now, but was a US company during almost all the period above; thus, we analyze the company as a US company for this report.

6. New Initiatives for Development of Human Resources

- In Japan, the R&D sector plays a main role in developing new med-tech products (Figure 6-1). The reason for imports surpassing exports is not only this structure; another key factor is underdevelopment of Japan's med-tech sector human resources.
- As a part of Japan's national healthcare strategy, Osaka University, Tohoku University and the University of Tokyo launched the Japan Biodesign program in cooperation with Stanford University in October 2015. The Biodesign program, started by Dr. Paul Yock and others, is to cultivate human resources capable of medical device innovation based on 'design thinking'. Its uniqueness is the process for innovation (Figure 6-3). We interviewed Dr. Fumiaki Ikeno about the core idea of the program (Figure 6-4).
- Also, Tohoku University has already started a program that returns medical assets to society (Figure 6-5).
- In addition to these nascent movements, Dr. Atsuhiko Nakagawa from Tohoku University and Dr. Ikeno from Stanford University share the opinion that 'implementation' is a key to developing human resources in Japan. Here 'implementation' means that product developers must take care to hear about needs firsthand, on-site from stakeholders directly connected to the business and then start actual trials. The initiatives below should foster effective methods in Japan.

Figure 6-1 Comparison of Patent Holdings by Japanese and US Medical Device Makers (reprint from 'Ecosystem Report')



Notes.

1. Prepared from data issued by Intellectual Property Information Services Co., Ltd.
2. Covers all US medical device patents held by the 3 top-selling firms as of June 30, 2013.
3. "Acquired subsidiaries" refers to subsidiaries acquired since 1990.

Figure 6-2 Healthcare Policy (excerpt)

Cultivating personnel in 'medical devices development' field

To cultivate leaders in medical device development, Osaka University, Tohoku University and the University of Tokyo as well as the Japan Federation of Medical Devices Associations are collaborating with Stanford University on matters concerning the introduction of the Japan Biodesign program – a program that introduces practical ways of thinking and skills for 'problem solving type' innovation based on the identification of clinical needs

Note. "To execute the existing healthcare policy as well as policies developed by the Cabinet in 2015. "

Figure 6-3 Processes of the Biodesign Program

Biodesign and the Japan Biodesign Program are guiding projects through the process illustrated

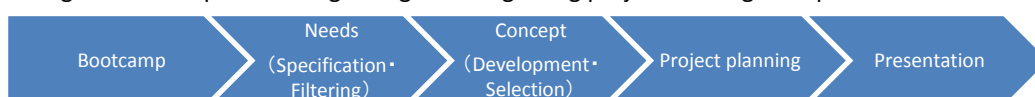


Figure 6-4 Stanford University Biodesign Program: Points Drawn from the Dr. Fumiaki Ikeno Interview

Merely hearing from doctors about needs doesn't lead to the development of good products. So, most important in the process outlined above is that product developers physically go to medical sites and identify needs through firsthand observation. Interviews with doctors illuminate the critical areas of need. With this information, team members and mentors of diverse backgrounds brainstorm on how to address the needs, leading to the development of original solutions. In addition, persons that understand the whole process must be cultivated.

Major US med-tech companies acquire many technologies from start-ups, but the technology is not matured at the time of acquisition; thus, the major companies' role is to build businesses from those immature products.

Figure 6-5 Tohoku University CRIETO

Tohoku University is committed to Japan Biodesign as well as to a hospital bedside-focused solution program designed by the Clinical Research, Innovation and Education Center (CRIETO), part of the university's Academic Science Unit (ASU) started in March 2014. In this program, teams of R&D partners who have passed a series of tests and training accompany doctors to patients' bedsides, where they get firsthand exposure to what is needed in these medical environments.

Medical technology is a broad category that includes, for example, the fields of IT and new materials, as well as areas existing between medical industry and other industries.

From interviews with Dr. Atsuhiko Nakagawa, deputy director of CRIETO's Bedside Solution Program, Tohoku University

7. Utilizing the US Ecosystem

- A process like that depicted in Figure 7-1 exists in the US, where major med-tech companies comprise a so-called business development sector. In contrast, in Japan basically all the processes take place within the individual companies.
- As we saw on slide 5, US companies invest in both acquisition and their R&D. This R&D includes further development of acquired technology. It leads to their global growth.
- Approaches to bridge the gap between the Japanese and US models are thought to be in two steps.
1st: Introduce a biodesign program to stimulate R&D progress in Japanese companies and Universities.
2nd: Use the already existing US ecosystem.
- The essential issue of utilizing the US ecosystem is whether Japanese companies can incubate a way of thinking and activity that the US business development sector might have. Figure 7-2 shows problems to address in order to use the US ecosystem.
- First, based on VC comments, key points in whether Japanese companies can be good 'acquiring companies' are 'fitting feeling' and 'mutual trust'. In the process, Japanese companies need to clarify their 'want lists' along with their business strategies. This is actually somewhat difficult because Japanese company board members are not accustomed to straightforwardly declaring their 'wants'.
- Next, in terms of the 'problems to be solved' identified on the right side of Figure 7-2, item a. is what VCs typically do, and companies might learn the process through making investments in venture funds. On the other hand, items b. through e. are the points that acquiring companies need to learn on their own.
- Some issues other than acquisition, from the perspective of global business, include (1) securing sales channels for existing products, (2) considering M&A for scale merit and (3) nurturing new business opportunities. However, Japanese companies sometimes downplay the business opportunity nurturing aspect. Another contrast is that US companies evaluate enterprises based on their global business. Japanese companies need to address these issues points as part of their growth strategies.

Figure 7-1 Business Development Process

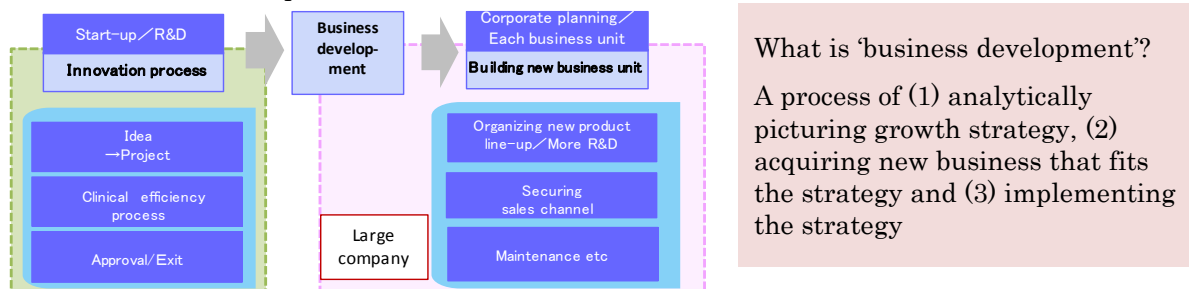
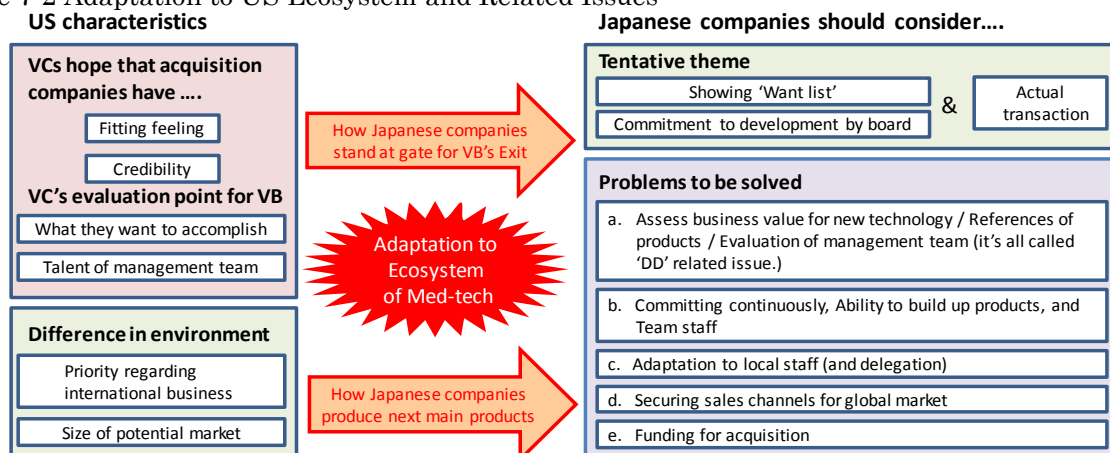


Figure 7-2 Adaptation to US Ecosystem and Related Issues

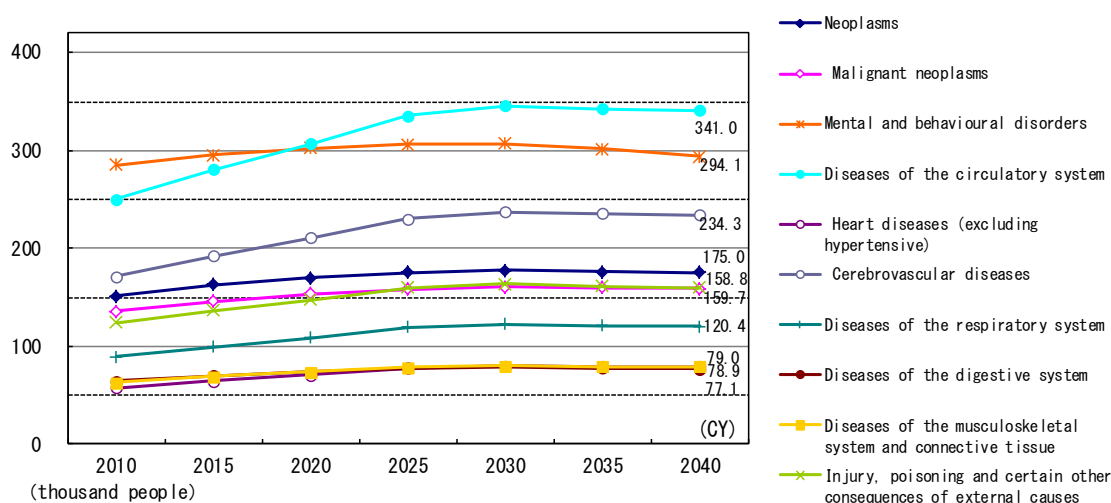


Note. Fig. 7-1 and 7-2 data were obtained from various sources.

8. Japan's Way, Based on Its Domestic Medical Market

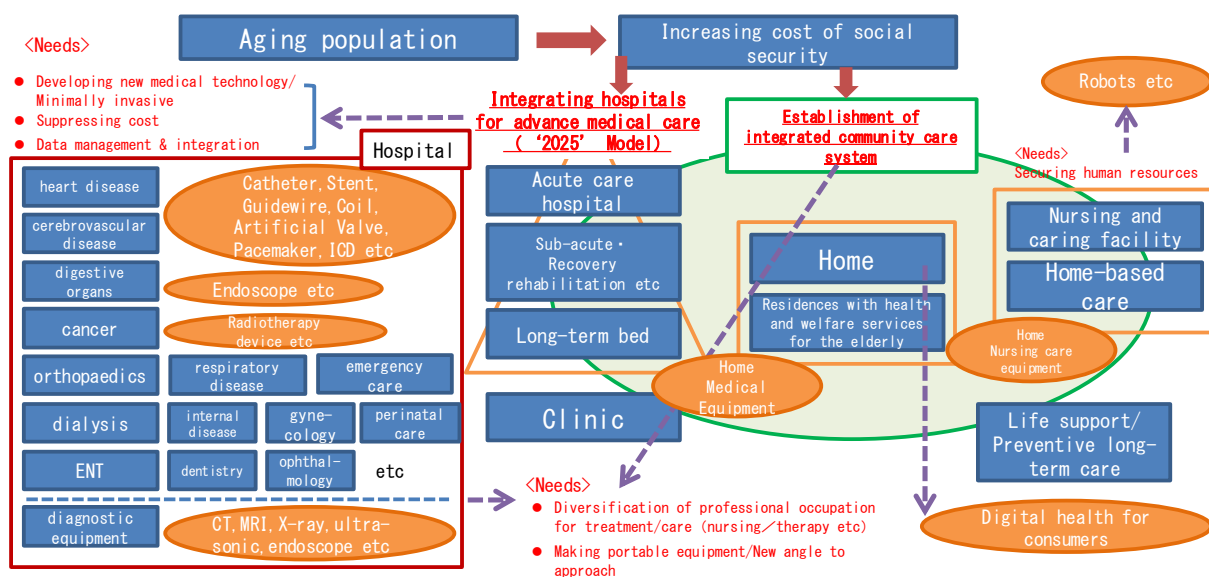
- As we show on slide 5, Japanese companies realize steady growth through global development of their own existing products. Nevertheless, the drive to innovate is not so strong in Japan; thus, we suggest that cultivation of new human resources and utilization of the US ecosystem might be needed. The question that arises is, are those initiatives good for the domestic medical market trend?
- Figure 8-1 shows potential inpatient trends for various major disease categories (this estimation doesn't account for a shortening of hospitalization stays and an increase in the shift to home healthcare). The numbers of heart-diseased and cerebrovascular-diseased inpatients will grow to some extent and those areas are directly connected to med-tech development. As we show on page 4, many new developments are occurring in the circulatory organ, brain, peripheral and other fields. Developing minimally invasive products for aging society is a goal all over the globe.
- As for the market for care (well-being, medical) domestically in Japan, to prevent increases in social security costs, we will renew the medical structure via the '2025 model', the name of which refers to the fact that by the year 2025, all baby-boomers will be over 75 years old. It mainly calls for advanced medical care through government integration of hospitals and for a 'shift to home healthcare' based on Community General Support Centers. Figure 8-2 depicts many hospital departments in which minimally invasive procedures are being developed. In this environment, individual companies in Japan are trying to expand their business horizontally and also develop portable products for home healthcare. The Japanese government also pushes such development by shortening the time it takes for the Pharmaceuticals and Medical Devices Agency to approve new medicines and medical devices.
- Japan has some strict regulations about the information that medical institutes can directly provide but, in general, advanced medical care and shifts to home healthcare are challenges that must be addressed worldwide. And if Japanese med-tech companies want to produce novel technologies like those depicted in Figure 4-1, they must critically examine not only doctors' and engineers' technological desires but also the implementation process. After that, they can proceed to refining their global penetration focus, which will have to include taking their corporate cultures based on precise procedural processes and creating innovative methods that can be useful in other countries that face similar issues.
- As for new med-tech technology, a broad range of businesses are entering this industry, frequently through alliances. There is constant demand for new materials and processing technologies in this field. And although the med-tech companies typically are developing methods best-suited to their own specific purposes, they should not hesitate to look for possible new markets. It is key that they resist being satisfied with the relatively safe practice of merely adopting popular developmental trends.

Figure 8-1 Potential Inpatient Trends (per day), by Type of Medical



Note: These estimations by DBJ are based on 'Patient Survey' data of the Ministry of Health, Labour and Welfare and 'Population Projections for Japan' of the National Institute of Population and Social Security Research.

Figure 8-2 Needs in Japan's Domestic Market for Care (Well-being and Medical)



Note. Sources for Fig. 8-2 are various data.

All inquiries should be directed to the Economic & Industrial Research Department,
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