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Innovation in Neurosurgery: Intellectual Property Strategy and Academia/Industrial Collaboration

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Abstract

Neurosurgery has tremendous possibilities for development of innovative medical devices. However, most of the neurosurgical devices used in Japan are imported products. Promotion and development of domestic medical devices is highly encouraged and it is one of the pillars of Prime Minister Shinzo Abe's growth strategy of Japanese economy. Innovative "Made in Japan" medical devices can be developed by interdisciplinary collaboration between industries and academic institutions. Proper orientation of medical and engineering education, social and administrative awareness of the need of facilitating the medical devices creative process with corresponding regulatory changes, and appropriate medical and technological infrastructure establishment are needed for stimulating medical device innovation.

Key words: innovation, medical device, intellectual property

Introduction

Promotion of medical device development is one of the pillars of Prime Minister Shinzo Abe's growth strategy of Japanese economy. Innovative "Made in Japan" medical devices can be developed by interdisciplinary collaboration between industries and academic institutions. Neurosurgery has tremendous possibilities to generate innovative medical device development. We report the current status of medical technology development in Japan and discuss the key features of a successful device development strategy in the field of neurosurgery.

Current Trends in Medical Device Development in Japan

The Japanese healthcare system places increasing emphasis on improved minimally invasive treatment and quality of aging. Less invasive medical devices and medical information and communication technology (ICT) solutions have been recognized as particularly suited to meeting Japan's healthcare needs. The Japanese market for medical devices is growing and reaching more than $30 billion in recent years. However, approximately 60% of all medical devices approved in Japan were imported products and current Japan export/import rate is over 6,000 million yen in deficit (negative balance). The complexity and difficulty of the Japanese regulatory process has been one of the major limitations to be blamed for the device innovation lag. Japanese government tries to improve regulatory approval process and eliminate the so-called "medical device lags" in Japan.

In 2014, the Ministry of Health, Labor, and Welfare (MHLW) revised the Pharmaceutical Affairs Law (PAL) to ensure safe and prompt provision of medical devices. They revised the law to be able to evaluate the characteristics of medical devices separately from pharmaceuticals, and the medical review process is expected to improve further through this revised PAL and related regulations.

In 2015, a new agency, The Japan Agency for Medical Research and Development (AMED) was established. This agency engages in research and development (R&D) in the field of medicine, establishing and maintaining an environment for innovative R&D, and providing funding in order to promote integrated medical R&D from basic research to practical applications. We believe that in more recent times the Japanese environment of medical device development is certainly changing.

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Role of Innovation in Neurosurgery

In historical perspective, there are many examples of device innovation in collaboration with industry that have strongly advanced in the field of neurosurgery.[1] The author has participated in the development of medical devices in the United States and Japan.[2–13] Based on his personal experience, several key factors of innovation exist and strategic consideration is required for the promotion of any innovation in neurosurgery. For better understanding of the invention process, our previous development, the Matrix 2 detachable coils (Fremont, CA, U.S.A.) was used as an example.[3–8]

Innovation in Neurosurgery: What to Do?

For any medical innovation, there are several steps for its successful development as a medical product. Fig. 1 shows the important steps of idea generation process.

1. Needs finding
2. Need screening
3. Concept generation
4. Concept screening
5. Strategy development
6. Business planning

In the first two phases, neurosurgeons have to identify the clinical problems to be solved. For example, aneurysm recurrence is a major limitation after coil embolization of cerebral aneurysms (Fig. 2A) and it should have been solved by achieving a long-term durability with excellent clinical outcome (1. *Needs finding*). Next, incidence and clinical significance of aneurysm recurrence should be carefully evaluated (2. *Need screening*). If recurrence rate is relatively low, there will be no market for new devices with such application. This first phase is very important before engaging and investing time and effort in actual development. If post-treatment rupture rate is not clinically significant, the need of additional treatment will be minimal.

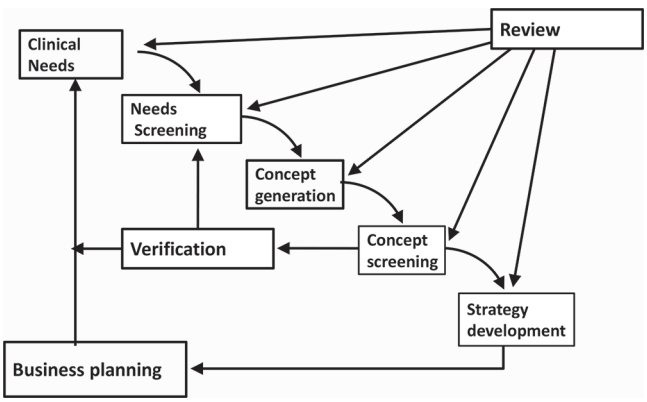

Fig. 1 Idea generation process

After careful evaluation of potential market needs, a new concept should be discussed between researchers and collaborators. For aneurysm recurrence we evaluated three factors to be responsible for recurrence, namely mechanical, biological, and flow dynamic factors. We selected the biological modification of the platinum bare coil as the important one (3. *Concept generation*) (Fig. 2B). This concept was screened through several potential solutions: extracellular matrix coating, ion implantation,[3–4] drug delivery, and bio-absorbed polymer (4. *Concept screening*) (Fig. 2C).[5,6] Next, we examined several basic designs for clinical application (5. *Strategy development*) (Fig. 2D).[7] This phase needs practical consideration of the new device, such as ease of use, product stability, sterilization, packaging, self-life, cost of development, and environmental factors (Fig. 3).

Finally, in collaboration with industry, market strategy was discussed (6. *Business planning*). Key factors are existing regulations on medical devices according to their classification, strategy for approval including clinical trials, and post market studies.[8]

During concept generation/screening process (3 and 4), intellectual property (IP) should be investigated. Ideally, IP will be generated by a patent office or a technology license office of an academic institution. Protection of IP is the most important factor in medical device invention. However, education of IP has not been conducted in the Japanese academic system. Importance of IP education in medical and technological universities should be emphasized.

Collaboration between Neurosurgeons and Engineers

Collaboration between physicians and basic scientists, especially mechanical and other engineering experts, is necessary for the development of innovative medical devices. They need to understand each other and spend efforts for "brain storming" continuously. This process is not always easy because their background and education are different. However, without such efforts it is impossible to develop innovation in medicine. We invite engineering graduate school students to our hospital and they have broader

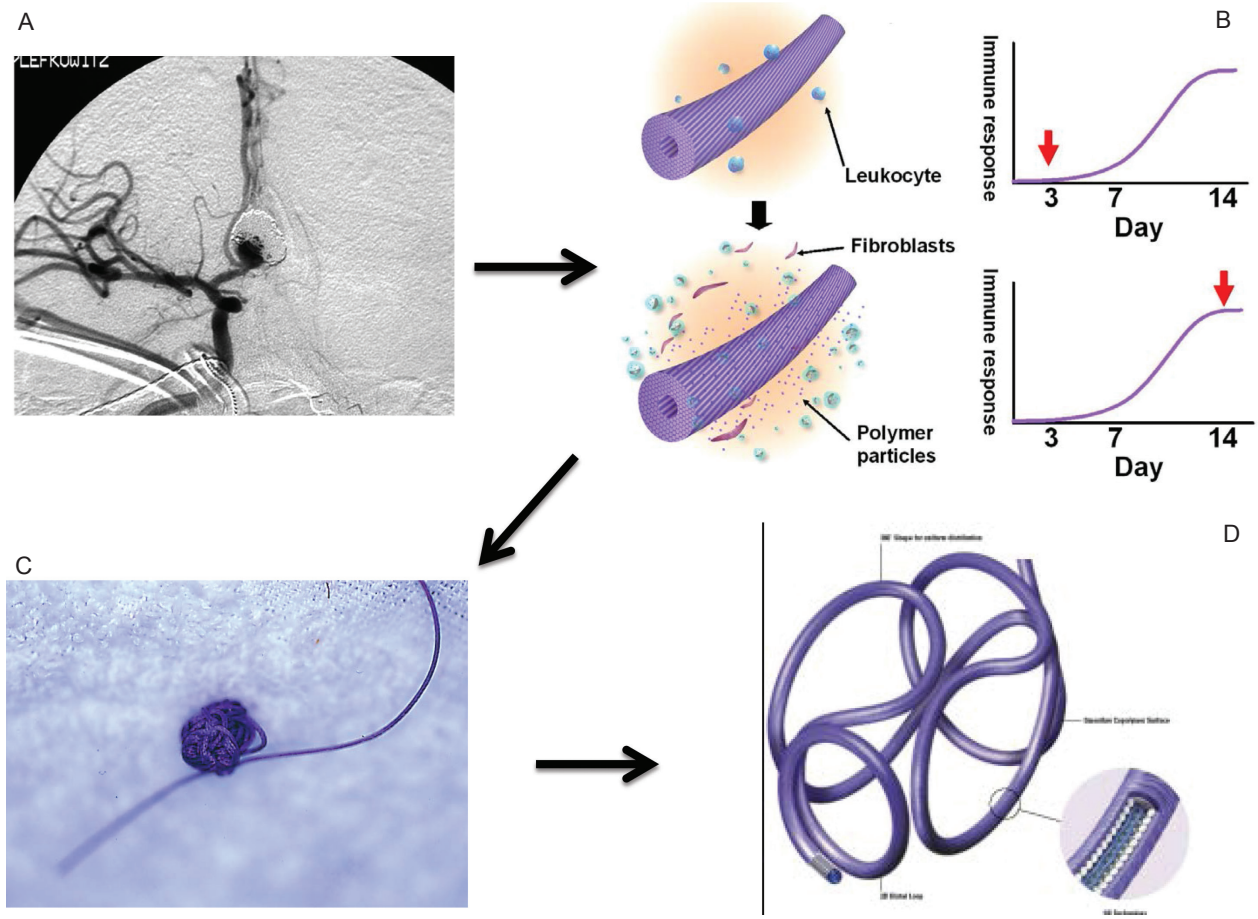

Fig. 2 Idea generation process. An example of matrix coil development idea generation process. A: Needs finding—example of aneurysm recanalization. B: Concept generation—biodegradation of bioabsorbale polymer controls inflammatory reaction. C: Concept screening—bioabsorbable suture (polysorb) simulates embolic material. D: Strategy development—final design of modified Matrix2 coil.

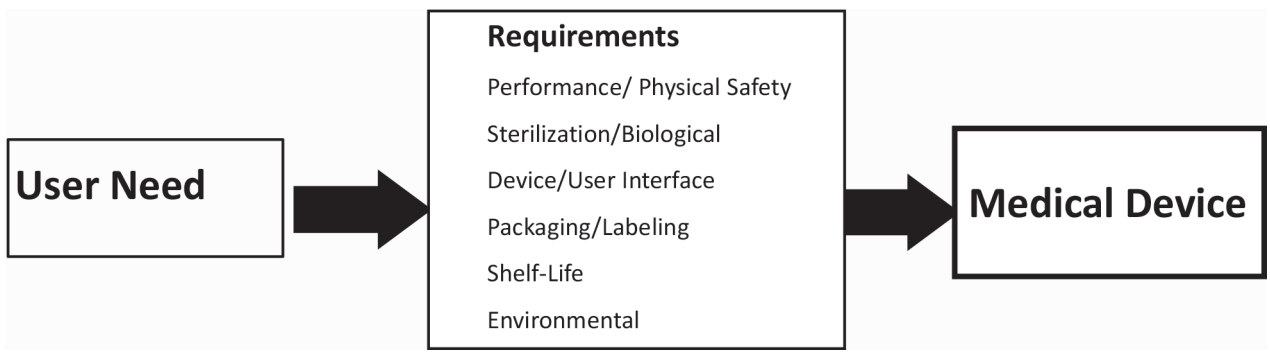

Fig. 3 Product development process

exposure to the real world of medical practice, such as operating rooms, and have the chance to identify technological medical problems. There they can exchange opinion with the physicians for eventual solutions.

Collaboration between Neurosurgeons and Industry

Clinical application of neurosurgical innovation also requires collaboration between neurosurgeons and

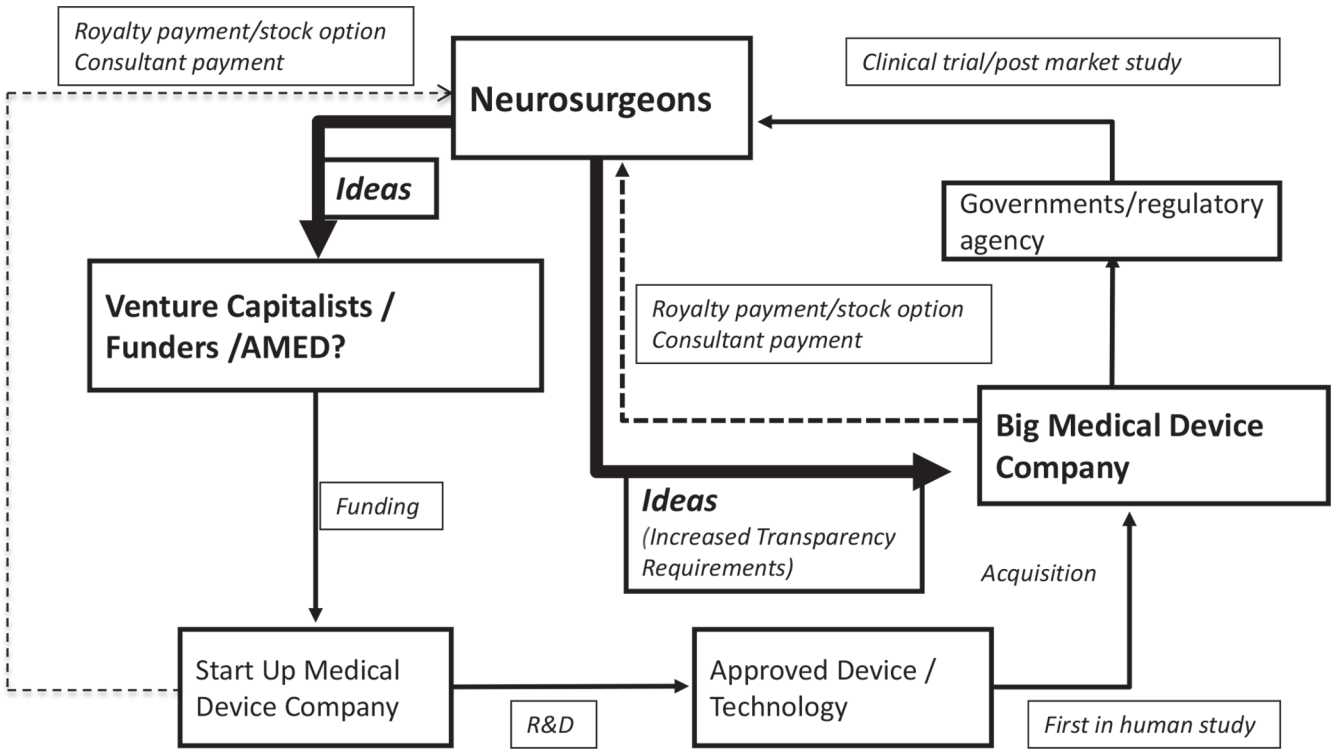

Fig. 4 Cycle of innovation for medical devices. *Thick arrow* showing two possible pathways of a physician's idea to commercialization. *Dotted arrow* showing financial feedback process from industry to physicians.

industries. Ideally, an academic institution should hold the IP and industry should receive exclusive license for production of the devices. Another structure may be joint application of the invention.

Such medico-industrial relationship needs transparency for eventual financial conflict of interest. Babu et al. reported that among 4,868 board certified American neurosurgeons, a total of 147 neurosurgeons (3.0%) hold a total of 582 patents and the total amount of royalties received by neurosurgeons in 2010 was expected to be $13,223,000 (minimum: $7K, maximum: $8.261M).[1)]

In Japan, however, social acceptance of academic institution/industry collaboration is still under development.

There are critics and arguments that financial incentives for physician may influence decision making on device application. Fig. 4 shows two possibilities for physicians to collaborate with industry and their financial relationships. We still do not have the best answer, but based on the fundamentals of medical ethics, physicians should always compare current best treatment to any new device application for the benefit of the patient from the position of their high professional standing.

Balancing Regulation and Innovation in Medical Devices

It is important to maintain and encourage innovation in medical devices. But true innovation requires safety and effectiveness to be proven by adequate scientific study in clinical trials.[14)]

Ideally, innovative medical devices should be approved within an established timeframe fashion without compromise for patient safety. The role of the professional academic society, such as the Japan Neurosurgical Society is more important for post market safety study and transparency for the results. An optimal action plan should be discussed between MHLW/pharmaceutical and medical devices agency (PMDA) and Japan Neurosurgical Society.

Conclusion

Many operative devices have been developed by neurosurgeons and have improved patient care. Most of the devices have been developed in the United States and Europe in the past. However, we believe Japanese neurosurgeons can be innovative and productive to overcome current medical problems in

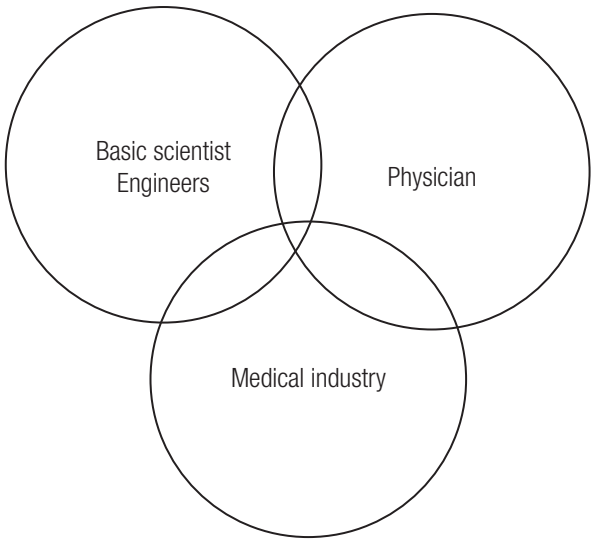

Fig. 5 Representation of medical device development in collaboration with physician, engineer/scientist, and industries

collaboration with engineers and industries (Fig. 5). IP education for medical and technological students is mandatory for innovative environment.

Systematic improvement of regulatory process and support for venture companies will be required for Japan to promote innovation in neurosurgery.

Conflicts of Interest Disclosure

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