Column

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Keeping the Light of Hope Alive
Bringing Retinal Regenerative Therapies to Patients: Social Implementation and New Business Models

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"Incurable diseases" deprive people of their "lives": retinal disorders as a societal challenge

Vision profoundly influences human quality of life. Losing vision is not merely a functional impairment of "not being able to see"; it also undermines the foundations of social life, including employment, education, mobility, and communication. In particular, blindness caused by retinal diseases constitutes a serious challenge in developed countries facing rapid population aging. In Japan as well, retinal degenerative diseases—such as age-related macular degeneration (AMD), diabetic retinopathy, and retinitis pigmentosa (RP)—are major causes of visual impairment. Because the retina does not spontaneously regenerate once it degenerates and therapeutic options are limited, these diseases have long been regarded as "incurable."

Ten years since the world's first iPS-RPE transplantation: safety and "sustaining visual function"

Against this backdrop, the advent of induced pluripotent stem (iPS) cell technology brought about a major turning point in ophthalmology. It remains fresh in our memory that Professor Shinya Yamanaka received the Nobel Prize in 2012, drawing global attention to iPS cell research. Subsequently, in 2014, the world's first transplantation of a retinal pigment epithelium (RPE) cell sheet derived from iPS cells was performed, making the potential of regenerative medicine a reality[1] (Figure 1).

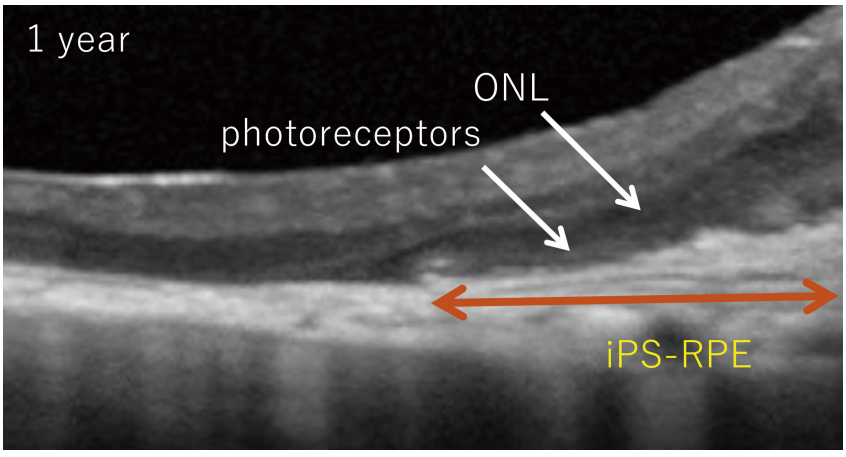

Figure 1 Optical coherence tomography image from the first clinical application of iPS cells. At 1 year after transplantation, the photoreceptor layer is preserved only above the iPS cell–derived RPE cell sheet, and visual function is maintained.

The first clinical study of iPS cell–derived RPE transplantation was designed to demonstrate the safety of iPS cells, which the world had regarded as potentially dangerous because of their resemblance to infinitely proliferating cancer cells. To this end, we generated more than 200 iPS cell lines and conducted exhaustive safety verification[2]. The therapy itself was also designed and implemented as the scientifically best, highly symbolic treatment. Its success became major news worldwide at the time[3]. Ten years later, it has been shown that the transplanted cells engraft safely over the long term and maintain the survival of photoreceptors—which cannot survive in areas where the RPE has atrophied and disappeared—thereby preserving visual function. In other words, a single transplantation of an iPS cell–derived RPE sheet reconstructs retinal structure and sustains retinal function permanently, conferring substantial clinical value from the perspective of "prolonging" visual function. Notably, beyond the medical domain, this was also the year in which the Act on the Safety of Regenerative Medicine and the Pharmaceuticals and Medical Devices Act were formulated alongside the progress of our project and subsequently came into force. These were the world's first laws specialized for regenerative medicine, and the year also impressed upon us the societal power of science—namely, that a technology such as iPS cells could even give rise to new legislation.

"Cells as products" are not sufficient: the "healthcare system" that determines standard-of-care adoption

However, this success does not immediately translate into establishment as standard-of-care. To deliver therapy broadly, not only "cells as products" but also a development model as a medical treatment is indispensable. The success factors for regenerative medicine are not limited to the cell product as one key success factor; rather, success is achieved only when optimization of clinical protocols and surgical techniques, an explanatory framework that supports patients' understanding and informed acceptance, postoperative follow-up, and linkage to insurance systems are all in place. Put differently, regenerative medicine is not a "product" but a "treatment," and social implementation is itself the construction of a comprehensive healthcare system. In other words, it is necessary to transform treatment development from a focus on "things" to a focus on "services/experiences."

The path by which new technologies reach social implementation is never smooth. As illustrated by Gartner's hype cycle, innovative technologies attract excessive expectations, then pass through a trough of disillusionment, and only later mature into practical use through steady, incremental applications. Regenerative medicine is no exception; scientific success alone is insufficient. Multifaceted challenges—such as safety, manufacturing stability, cost, institutional design, patient care, and technology transfer to healthcare professionals—must be addressed (Figure 2).

This reflects the difficulty of developing a new modality—surgical regenerative medicine using cells—which differs fundamentally from pharmaceuticals.

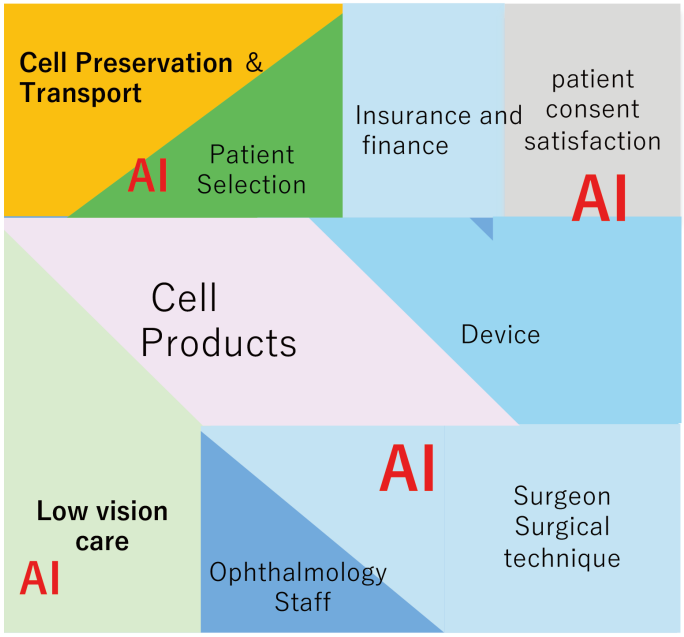

Figure 2 Elements required for the success of surgical regenerative medicine.

Scaling up cell manufacturing and ensuring uniform quality: automation and AI-driven process optimization

One of the critical challenges for accelerating implementation is scaling up cell manufacturing and ensuring uniform quality. Traditionally, cell manufacturing has tended to depend heavily on the skills of experienced technicians; this not only increases labor costs but also makes it difficult to ensure reproducibility. In this context, manufacturing automation using the humanoid robot "Maholo"[4] and process optimization through AI-based analysis improved yield and opened a path to manufacturing cells for 700–800 people per batch. This is not merely labor saving; it resolves the instability inherent in manufacturing in which individual staff members—each with different tendencies—culture cells that are constantly changing, thereby contributing to product stabilization. It may also help suppress future treatment prices and represents a key to evolving regenerative medicine from "advanced medicine for a limited number of people" into "standard medicine disseminated throughout society."

Improving the formulation of transplant products: reducing surgical and immunosuppression risks

In addition, improving the formulation of transplant products was also important. Since the first autologous iPS cell–derived RPE sheet transplantation, formulations have evolved to an allogeneic (donor-derived) iPS cell–derived RPE suspension and further to an RPE aggregate strip, thereby reducing surgical risk and immunosuppression risk[5]. To date, long-term engraftment has been achieved in a total of 10 cases without serious complications, and maintenance of visual function has been confirmed in all cases. In particular, in two cases, improvements were observed that would be impossible under the natural course of the disease, strongly indicating the clinical potential of regenerative medicine. Overall, a characteristic of our therapy development has been that improvements derived from information obtained from each individual case have enabled both reduction of surgical risk and greater certainty of efficacy.

Institutional innovation for dissemination: beyond conventional clinical trial–approval pathways

Meanwhile, innovation in institutional design is also necessary for regenerative medicine to become widespread. Surgical regenerative medicine tends to be costly, and relying solely on conventional clinical trial and approval models carries risks of failure midstream and prolonged timelines before reaching the full population of patients in need. Therefore, we are pursuing treatment development that is not limited to conventional clinical trials, based on the view that new development tracks are important to deliver therapies to patients earlier by leveraging mechanisms such as the Advanced Medical Care system, combined use of insured and uninsured medical services, and combinations of public and private insurance. In regenerative medicine, rather than "entering clinical trials quickly," there are cases in which it has greater societal value—similar to surgical treatments—to "deliver better treatments while continuously improving them." Institutional design to enable this is required.

The reality beyond treatment: low vision care and designing "expectations"

Now that regenerative medicine—once a "dream therapy"—has become "reality," in both positive and challenging senses, patient care is indispensable. Visual impairment cannot be resolved by treatment alone; support is also required to help patients reconstruct daily life beyond the medical domain (low vision care). In particular, what is expected from the term "regenerative medicine" is "seeing well," yet in reality, recovery of visual function is limited. Expecting "seeing well" is akin to expecting a bedridden person to sprint 100 meters; however, in the case of vision, such expectations are often placed on patients, with a high risk of disappointment. Accordingly, we established the Kobe Eye Center and built an integrated framework that unifies healthcare, research, support, and social implementation: patient follow-up by the Public Interest Incorporated Association NEXT VISION; introduction of devices that people with visual impairment can use, which often advance faster than medical care; optimization of surgical methods and clinical protocols by Kobe Eye Center Hospital; and the development of Kobe i Clinic (KiC), which provides online medical care primarily for overseas patients. Now in its eighth year since establishment, each division is operated autonomously and has received a certain level of recognition in its respective field (Figure 3).

From Japan to the world: an international dissemination model built on hospital leadership × local regulations

Broadening our perspective further, collaboration not only within Japan but also with Asia, Europe, and the United States will become increasingly important. Plans to advance outbound and inbound treatments through partnerships with overseas medical institutions—such as Thomas Jefferson University and Wills Eye Hospital in the United States, and a stem cell center in Indonesia—hold the potential to expand regenerative medicine originating in Japan to the world. By conducting hospital-led clinical practice in compliance with local regulations and further supporting the transition to clinical trials, it is possible to form an international dissemination model for the therapy.

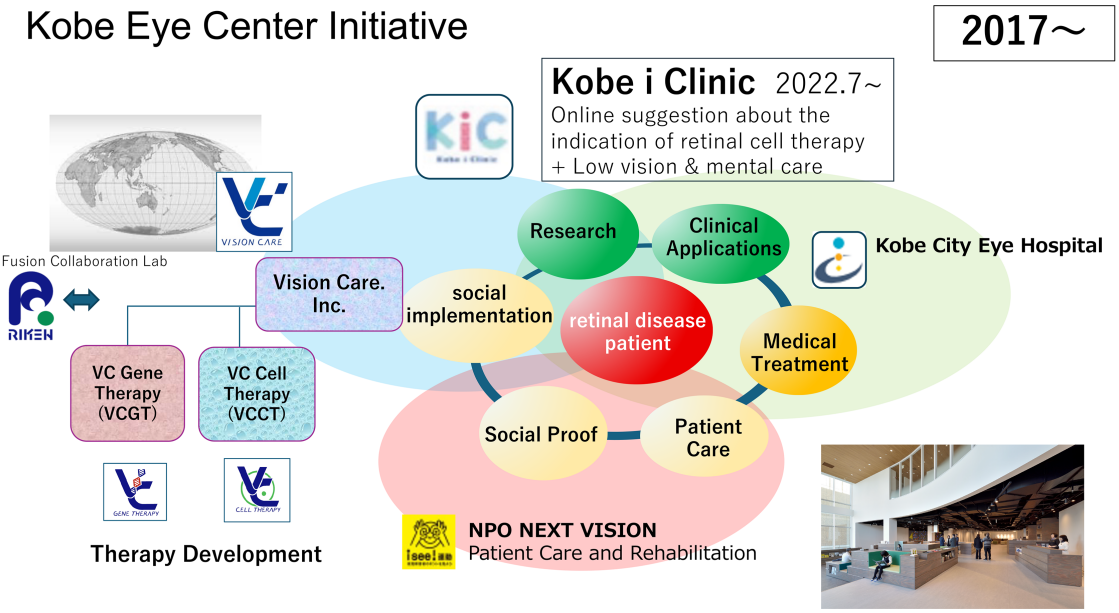

Figure 3 Structure of the Kobe Eye Center.

In 2025, *Nature* reported that "Japan's big bet on stem-cell therapies might soon pay off"[6]. This is not mere optimism; it reflects the cumulative result of many years of research, trial and error, and challenges toward social implementation

Conclusion

To ensure that the "medicine of dreams" does not extinguish the light of hope even after it becomes reality, it is necessary to build a comprehensive medical-economic ecosystem that encompasses not only innovation in cell technologies but also manufacturing, institutions, insurance, patient support, and international expansion. When science and society function as two aligned wheels, regenerative medicine will, for the first time, shift from a "special treatment" to an "ordinary treatment." Going forward, we will continue to build new business models that connect the clinical frontlines with industrial frontlines, in order to realize a society in which patients can live without giving up on the future.

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