



“Finding the best sperm among the millions. For embryologists, this is the unique work of selection, and we feel a great sense of responsibility.”



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Reproduction Clinic Tokyo, a fertility clinic located on the third floor of Shiodome City Center, a state-of-the-art office building in the Shiodome area of central Tokyo, has a large number of patients waiting for treatment, even in the evening on weekdays. We spoke with Shimpei Mizuta and Tomohiro Maekawa, who are using Nikon’s Ti2 inverted microscope for sperm sorting and Intracytoplasmic Sperm Injection (ICSI), about their thoughts on their work and their impressions of the Ti2.



Top-flight clinic in the treatment of male infertility

—What are the features and strengths of the clinic?

Mizuta: We opened our first clinic in Osaka in September 2013 as a fertility clinic. Then, in 2017, we opened a new clinic, the Reproduction Clinic Tokyo, here in Shiodome, Tokyo. One of the reasons we have been able to provide treatment for so many people over the past eight years is because, among the approximately 600 IVF clinics in Japan, we have a proven track record in meeting client expectations in the treatment of male infertility. In addition to examining and treating female infertility patients, our clinic is unique in that we have full-time doctors who can treat male infertility patients, allowing couples to be examined and treated at the same time.

These days, the policy of providing fertility treatment for couples together has become standard practice, but back in 2013, there were not many facilities in Japan that were able to do this. Fertility clinics had an atmosphere that made it difficult for men to enter, but the fact that we were able to put into practice the idea of “seeing the doctor together as a couple” may have been a breakthrough.

—How did you come to focus on male infertility treatment?

Mizuta: It may be related to the fact that Tomomoto Ishikawa, the CEO of our clinic, is a urologist who specializes in male infertility. At our clinic, Dr. Ishikawa, Supervisor Matsubayashi, Director Takeuchi, and others have many years of experience in the United States and Australia, countries at the forefront of in-vitro fertilization (IVF). In those countries, there are a relatively large number of treatment

facilities headed by male infertility doctors, but when our clinic opened, this was very rare in Japan.

Ishikawa is one of the country’s leading experts in the field of Testicular Sperm Extraction (TESE)*, and there are patients all over Japan who want to undergo TESE by Ishikawa. In order to meet this demand and to make it easier for men to come to our clinic, we opened clinics in the central business districts of Osaka and Tokyo. Today, approximately 5-10% of our IVF patients are treated for azoospermia. The doctors and us embryologists travel back and forth between the Osaka and Tokyo clinics, and through repeated discussion and information sharing, are able to maintain the same quality of service at both clinics.

*A procedure performed mainly on azoospermia patients who have no sperm in their ejaculated semen. By extracting the sperm-producing seminiferous tubules from the testes, sperm can be collected from approximately 50% of patients.



—Why do your patients value your clinic?

Mizuta: In 2020, we had 4,600 oocyte retrievals in Tokyo.

Combined with Osaka, we have performed more than 7,000 oocyte retrievals per year, and have performed approximately 2,000 TESEs over the past eight years. This was achieved by about 40 embryologists in Tokyo and Osaka in total.

Another feature of our clinic is that about 70% of our patients have had previous IVF treatment at other facilities. Since so many of our patients come to us because they were unable to achieve satisfactory results at other facilities, we have many difficult cases. That’s why our patients have high expectations, and we are working hard to meet them.

As a “face-to-face embryologist”

—What are some of the challenges of ICSI?

Mizuta: Ultimately, there is a lot of responsibility, or pressure. The name of the embryologist who performed the ICSI procedure is not disclosed, but the name and results will be recorded and managed. If the results are not as good as I had hoped despite my best efforts, I find myself wondering if I could have done more. Patients are also curious about who is in charge of the procedure. In ICSI, we are the ones who actually insert the needle and inject the sperm, so even though our names and faces are not disclosed like those of the doctors, I believe that we are professionals in a position of equal responsibility.

—What are some memorable moments in your work so far?

Mizuta: At our clinic, the embryologists themselves explain the results of cultures to all the patients whose oocytes have been retrieved. This is a real challenge in terms of time, but it allows us to interact with our patients with an honest sense of responsibility. Patients may also find it easier to ask an embryologist about things that they would hesitate to ask doctors about, or technical matters. Being able to talk with a specialist who has actually worked on the culture, and directly see their face, creates a sense of security. In addition, we are able to listen to the voice of each individual, which deepens mutual trust. Many of the patients who have undergone treatment at our clinic appreciate this, and it is one of our main motivations.

There was a couple who had undergone TESE before, who left a lasting impression on us. Although we could only find one motile sperm and only one fertilized oocyte, the fertilized oocyte grew into a good blastocyst, a condition suitable for embryo transfer, and the patient conceived. The other day, they came to our clinic hoping to have a second child. We were thrilled when we found out that they had given birth safely after the first treatment. I think this kind of experience is only possible with “face-to-face embryologists” like us.

Taking time to select the best sperm.

—What is your impression of the Nikon microscope?

Maekawa: The image quality is really good. I can see the morphology of the sperm very clearly. I was a little surprised when I first used it. Our mission as embryologists is to choose the best sperm for an oocyte from the tens of millions of sperm available. We

have to choose sperm that are more active and have better shapes, so we teach our junior embryologists to be strict about taking their time to do this, no matter how busy they are.

Mizuta: When we were preparing to open our clinic in Tokyo, we heard from a salesperson that a good microscope was being developed and, impressed by what he told us and his enthusiasm, we decided to install the microscope without evaluating the actual machine. After using it, we found that this latest model Ti2 allows us to see details of sperm more clearly than previous microscopes. One of the most important things in our work is to make sure that the quality of the oocyte and sperm is not compromised, but selecting sperm for ICSI is the only task where selecting is at the discretion of the embryologist. In this case, having a microscope with a good view is a huge and very important advantage.

Maekawa: When choosing sperm, the first thing we look at is the shape. Sperm does not actually have a flat head, and its shape varies depending on the surface you look at, but with the Ti2, we can really see it in all three dimensions.

With a microscope that does not have a good view, it is impossible to tell whether a sperm head has vacuoles, meaning sperm with vacuoles can be erroneously selected. The Ti2 enables us to see even the tiniest of vacuoles, reducing the number of sperm to choose from, and as a result, sperm selection can take a long time (laughs). This is good for the patient, though.

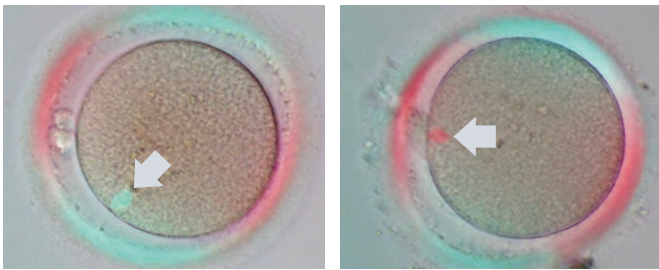
In the past, vacuoles could not be seen without the use of IMSI, a method that uses a special optical system, but nowadays, we can see them clearly in ICSI with the standard user settings of the Ti2.



—What about spindle observation?

Maekawa: We perform spindle observation as required, for example, for patients with slow oocyte maturation or patients with a biased spindle location. By checking the position of spindles, we may be able to avoid future problems.

Mizuta: There are some cases where ICSI can be performed at the correct position and timing without checking the spindle, but checking the spindle means that ICSI can be performed in a more oocyte-friendly manner. With the Ti2, during spindle observation, the position of the spindle can be properly identified by the difference in color without the feeling that there is insufficient light intensity.



Example of the spindle observation system in the Ti2. The spindle is indicated by an arrow.

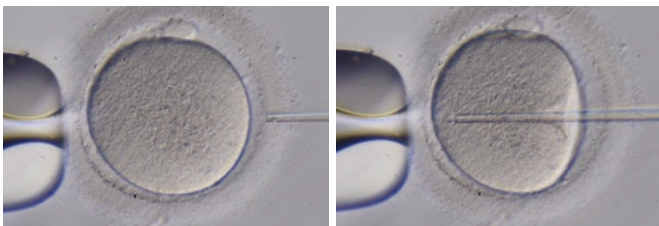
Digitizing of ICSI techniques helps improve accuracy

—What kind of work are Nikon microscopes used in?

Maekawa: About three years ago, we began a joint research project called the Medical Engineering Collaboration with the University of Hyogo in the field of engineering, to develop technology to further improve the accuracy of ICSI. Specifically, we make a video of me performing Piezo-ICSI using the Nikon Ti2, and have hundreds of data points analyzed by simulation and image analysis experts at the university.

For example, we can extract the similarities between ICSI cases where oocyte degeneration damage has occurred and ICSI cases where it has not, determine what triggers the degeneration and where the needle should be inserted to prevent degeneration, and ask them to create a system based on that data. By using this system, we hope to reduce the number of cases of oocyte degeneration to close to zero.

Mizuta: In a facility that follows the basics and has a lot of experience, the fertilization rate has increased to its upper limits, so it is quite difficult to increase it any further. If, however, this technique can reduce the degeneration rate by even another one percent, it can be considered a success. We as embryologists are constantly striving to achieve that one percent.



Intracytoplasmic sperm injection (by Piezo-ICSI). Before sperm injection (left), during injection (right)

Mission to nurture personnel who are active in a wide variety of fields.

—What would you like to achieve in your future work?

Maekawa: The first thing we need to do is to take each case seriously, but I also think that we need to train our junior embryologists and improve our team. In TESE, which is performed in the most difficult cases of azoospermia, we have to look under a microscope for hours to find sperm among the many tissues. The best results can be obtained by splitting up the embryologists and working in teams. For this reason, it is important to increase the number of skilled members who can use a microscope competently. At this clinic, we are able to gain a lot of experience in a wide range of male infertility treatments such as TESE. I think it is important to pass on these skills to younger embryologists.

Mizuta: I believe that our clinic performs some of the highest numbers of TESE cases in the world. Our highly experienced and talented staff members are one of our key strengths.

At our clinic, our staff can experience many cases, so we can see what each staff member wants to do in the future. For example, there are as many ways as there are people, such as being involved in the treatment of patients from a closer distance at a small clinic, working in a facility that takes care of patients through to childbirth, or being active in the world at large. I believe that it is also our mission to nurture human resources who can work in a wide range of fields.

In order to develop excellent human resources, we need to encourage them to continue working for a long time, meaning job satisfaction is also paramount. I believe that it is important, albeit difficult, to provide as many options as possible, determine the individuality and aptitude of each staff member, give them a role, and help them develop their abilities. I continue to make this my mission every day, regardless of the challenges.

Of course, in addition to educating younger staff, I myself do my best to accumulate

achievements such as improving my technical knowledge, developing new technologies, and continuing my research.



The comments and opinions expressed in this article are exclusively those of Mr. Mizuta and Mr. Maekawa, based on their own personal experience with the Nikon Ti2 inverted microscope, in the context of their use of the device for the purposes of IVF fertilization procedures, and do not represent any comments, opinions or claims made by Nikon Corporation with respect to the intended purposes, performance or safety of the Nikon Ti2 inverted microscope. There are no material connections between either Mr. Mizuta or Mr. Maekawa and Nikon Corporation.



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