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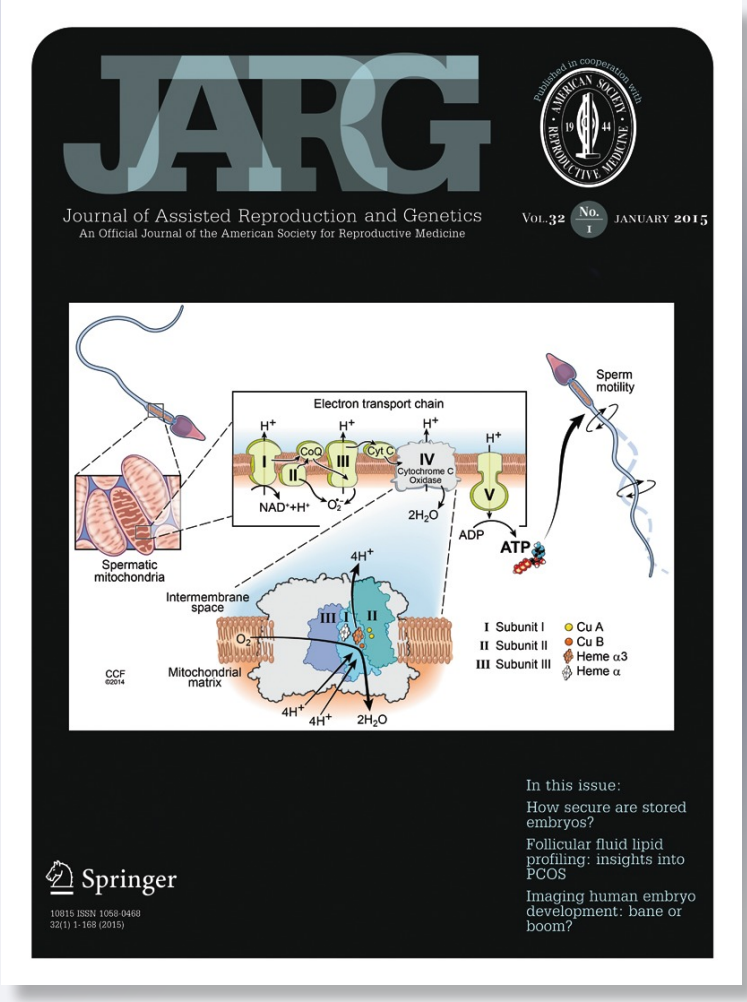

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TECHNOLOGICAL INNOVATIONS

Development of a security system for assisted reproductive technology (ART)

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Abstract
Purpose In the field of assisted reproductive technology (ART), medical accidents can result in serious legal and social consequences. This study was conducted to develop a security system (called IVF-guardian; IG) that could prevent mismatching or mix-ups in ART.
Materials and methods A software program was developed in collaboration with outside computer programmers. A quick response (QR) code was used to identify the patients, gametes and embryos in a format that was printed on a label. There was a possibility that embryo development could be affected by volatile organic components (VOC) in the printing material and adhesive material in the label paper. Further, LED light was used as the light source to recognize the QR code. Using mouse embryos, the effects of the label paper and LED light were examined. The stability of IG was assessed when applied in clinical practice after developing the system. A total of 104 cycles formed the study group, and 82 cycles (from patients who did not want to use IG because of safety concerns and lack of confidence in the security system) to which IG was not applied comprised the control group.
Results Many of the label paper samples were toxic to mouse embryo development. We selected a particular label paper (P touch label) that did not affect mouse embryo development. The LED lights were non-toxic to the development of the mouse embryos under any experimental conditions. There were no differences in the clinical pregnancy rates between the IG-applied group and the control group (40/104=38.5 % and 30/82=36.6 %, respectively).
Conclusions The application of IG in clinical practice did not affect human embryo development or clinical outcomes. The use of IG reduces the misspelling of patient names. Using IG, there was a disadvantage in that each treatment step became more complicated, but the medical staff improved and became sufficiently confident in ART to offset this disadvantage. Patients who received treatment using the IG system also went through a somewhat tedious process, but there were no complaints. These patients gained further confidence in the practitioners over the course of treatment.

Keywords Mix-up · Mismatching · Security system · Assisted reproductive technology (ART)

Capsule We have developed a security system called IVF-Guardian (IG) that uses QR (quick response) codes for ART (assisted reproductive technology) treatment. IG helped the medical staff gain the confidence and trust of their patients.

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Introduction

Medical accidents occur in medical centers for a variety of reasons, such as not refining the treatment process, inexperienced personnel or working processes or insufficient management caused by a surge of patients [1]. There is always the possibility of mistakes based on the daily health, moods, and activities of practitioners, as well as their individual skills. Medical accidents are directly linked to patient health and can result in serious consequences. Mistakes or errors in assisted reproductive technology (ART) can occur because

practitioners are involved in the entire process of ART. Wrong ART results can cause serious suffering and irreparable long-term injury, as well as legal and ethical issues, for babies, parents and various third parties associated with the babies.

The mixing of gametes between patients during ART, usually referred to as a "mix-up," includes the woman's egg and the man's sperm being misplaced or an embryo transfer into someone who is completely unrelated to the embryo [2]. The first report of an ART mix-up occurred in the United States in 1987, and mix-up cases have been reported several times worldwide [3, 4]. The majority of these cases have included parents of babies born with skin colors that differ from the parents. The presence of undiscovered cases of mix-ups is likely to become more common. Despite the fact that mix-up cases have not officially occurred in the Republic of Korea, the possibility of undiscovered mix-ups cannot be denied. Because international marriages frequently occur in the Republic of Korea, it is time to examine the safety of ART.

All ART processes must be performed perfectly. Currently, most ART organizations worldwide have established their own preventive measures. ART-related organizations, such as the European Society for Human Reproduction and Embryology (ESHRE), the Federacion Latinoamericana de Sociedades de Esterilidady Fertilidad (FLASEF) of Europe and South America and the Human Fertilisation and Embryology Authority (HFEA) of the United Kingdom (UK), have recommended guidelines to prevent mix-ups [5–7]. These guidelines include naming and recording the patients on all surgical materials, with confirmation by at least two practitioners, which is called a “double witness” process in ART [8]. However, in accordance with these recommendations, procedures cannot be guaranteed to be safe. Therefore, verification machines have been recently developed to prevent mix-ups during ART. Among verification machines, barcode systems and radio frequency identification (RFID) systems are common [9]. However, the introduction of such a system has not yet occurred in the Republic of Korea. It has been difficult to introduce systems that have mainly been developed in Europe into the Republic of Korea.

The aim of this study was to develop a verification machine that can make both the patients and medical staff more confident in the ART process. We called this system the “IVF-guardian,” and it was intended to ensure the stability of the ART process by continuously comparing QR (quick response) codes generated on the basis of the patient's identification during each key step, throughout the entire ART procedure.

Methods

Development of the software program

The development of the software program was undertaken in collaboration with outside vendors (Dual Information Technology, Seoul, Republic of Korea). It was necessary to describe the entire ART process to the application developers to ensure that they understood the steps involved in it. Then, we developed a program that was based on a flow chart of each step in the entire ART process. In some cases, there was insufficient information in the flow chart for certain steps; thus, a complete work program was established using the detailed descriptions and by repeating the steps. Fig. 1 shows a flow chart of the general IVF process. Since this flow chart shows a typical process, specific processes including frozen oocytes and sperm or their donation are omitted. Briefly, frozen oocytes or sperm were used after the QR code verification process during thawing. When using donor oocytes or sperm or a surrogate mother, the consultant identified the donor, surrogate mother and couple before treatment. The IVF-guardian program was designed to be able to record not only the couple, but also the contents of the donor or surrogacy (Fig. 2). We used Visual Basic to develop the software program.

Registration of the biometric information and patient identification

For ART, all patients visiting Maria Fertility Hospital went through the existing process of submitting proof of family relationships to identify the couple. Couple that is married in Korea can get a legal document to prove family relationships from legal authority. They then completed the ART legal forms to consent to treatment. Some of the consent forms also included personal information, including the registration of biometric information. When patients register their fingerprints, priority was given to the index finger of the right hand; if it was difficult to detect a fingerprint, then the middle finger or ring finger was used. In some patients, a fingerprint was not possible, or the patient did not agree to provide biometric information. In such cases, the patients were guided through a general identity check to receive ART. This study was conducted with the approval of the Institutional Review Board of Maria Fertility Hospital (Approval no. 2013–009).

QR code generation

QR codes were generated based on the personal information and fingerprint information from each couple (Fig. 3). QR codes were recorded on the left side, and the names of the couple were recorded on the right side of a paper label. Then, depending on the treatment step, the doctor's name and a treatment day were recorded. Depending on what was convenient for a particular treatment step, different label sizes (upon which the QR codes were printed) were used. The largest label, label A (40x20 mm), was placed on the semen collection cup to make it easier to view the name of the couple and the person in charge. Label B (28x12 mm) was used for sperm

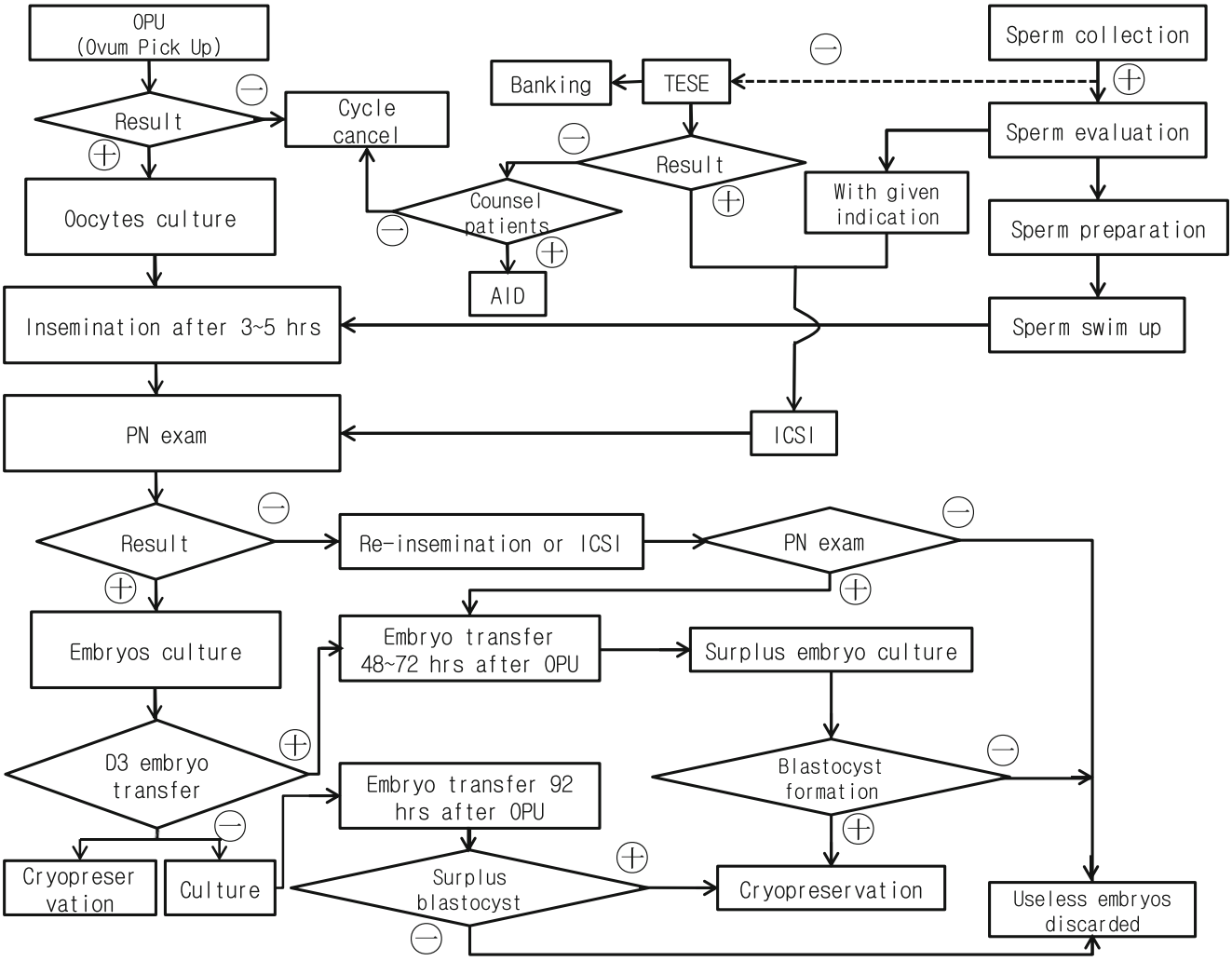

Fig. 1 A flow chart of the general IVF process

preparation and was attached to the sperm preparation tubes. The smallest label, Label C (20x6 mm), was used for the embryo culture step and was attached to the bottom of the culture dish (the reasons for label attaching to the bottom of the culture dish was described following sentences); Label C was selected to minimize the effects of volatile organic compounds (VOCs) that were likely to occur in an incubator. Label D (38x12 mm) was applied to the frozen and thawed sperm, oocytes and embryos. The effects of VOCs on embryonic development are described below.

When recognized by the code reader, the QR code was represented by a value expressed as a 13-digit number (Fig. 4). Regarding the 13-digit number, the "01" double-digit at the end referred to the treatment step, and this number increased when the treatment was repeated. Regarding the three previous digits, "1" indicated artificial insemination, "2" indicated IVF, "3" indicated thawing embryo transfer, and "4" indicated cryopreservation of semen. An "11" at the beginning of the number referred to the ART institution, which was Maria Fertility Hospital. The 8-digit number in the middle was the registration number given to the patient. Both the QR code and the read value were interchangeable in the software program.

Hardware for IVF-guardian

With the ART process divided into several steps, we analyzed the equipment that was needed for each step. On the original PC, we installed the IVF-guardian software program. In situations in which it was difficult to install the hardware on a PC, we used a tablet PC. All PCs were connected either with or without wires. In conjunction with the electronic medical record (EMR) data server at the hospital, basic patient information was shared with the IG program. The IG data were stored in a dedicated SQL server. The IG equipment included a fingerprint sensor (Suprema, Biomini, Republic of Korea), Label printer 1 (TSC, TTP-245plus, Taiwan), Label printer 2 (Brother International Korea, PT-9700PC, Republic of Korea), Code reader 1 (Honeywell international Inc., Xenon, 1900, USA), Code reader 2 (Datalogic, matrix210, Italy),

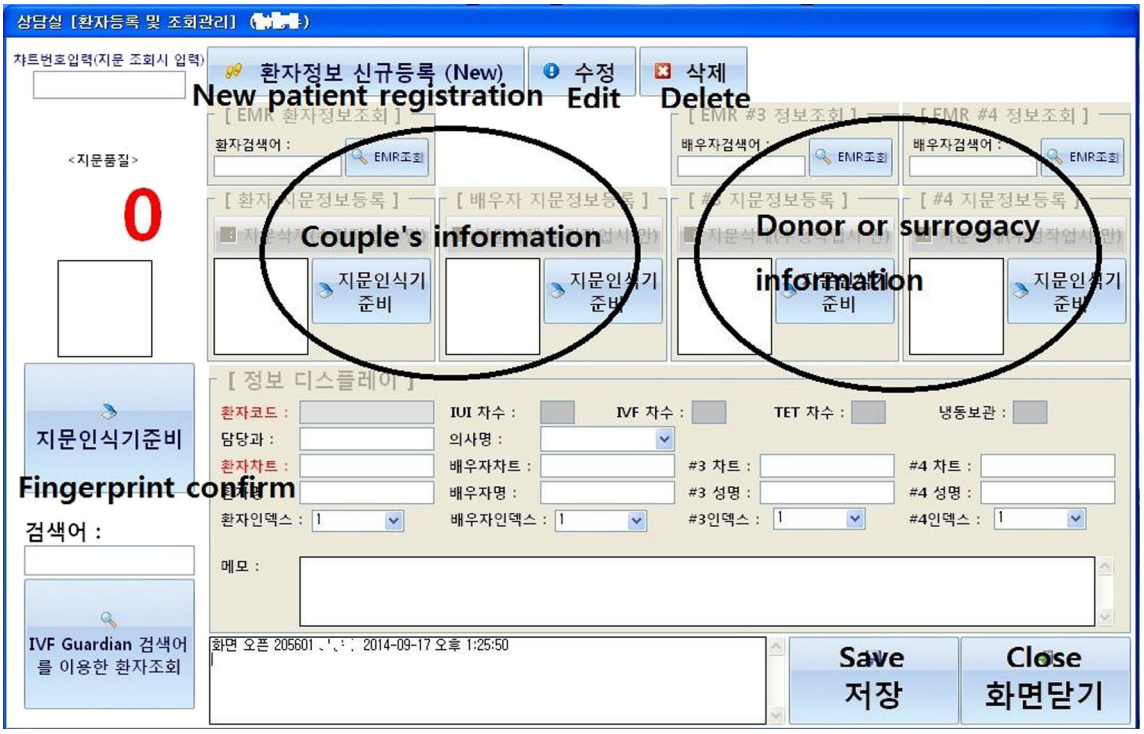

Fig. 2 Initial screen of consultation

tablet PC (Gigabyte, S1080, Taiwan), cuff band (IVF, green color; IUI, red), PDA (M3 mobile, MC-6700S, Republic of Korea), SQL data server and wireless network equipment (Fig. 5).

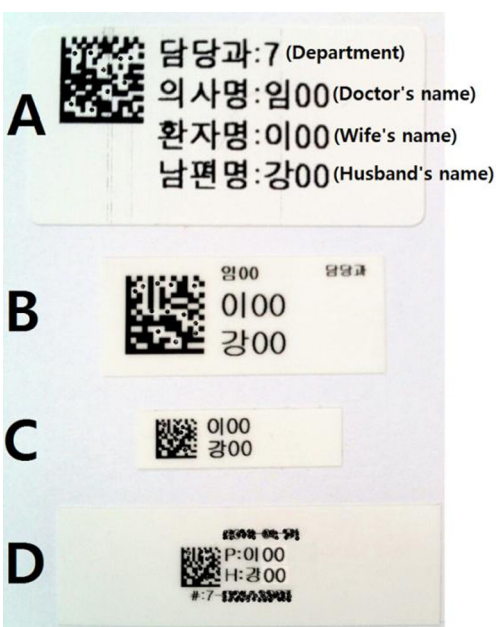

Fig. 3 The four types of labels used in IUI and IVF procedures; this QR code was modified to protect the patients' personal information (**a**: label for sperm collection; **b**: label for sperm preparation; **c**: label for the culture dish; **d**: label for cryopreservation)

Operator records

Most of the laboratory work was performed by a main operator and a sub-operator for each step. The main operator and sub-operator helped one another and double witnessed each step of the process. IVF-guardian used a process to input the name of the main operator, and it added a process to input the name of the sub-operator, depending on the step. The main operator saved the data after completed each step. Data include working time, worker's name of the step and patient's information can be seen by searching from the server at any time.

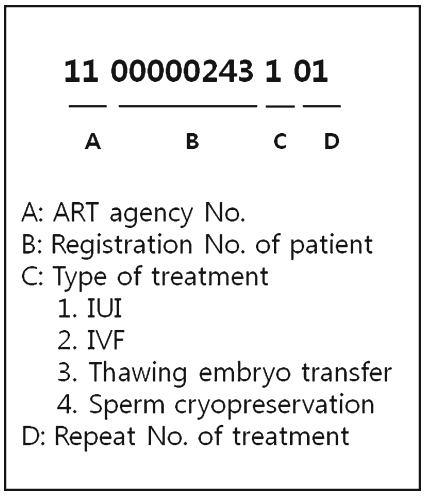

Fig. 4 The reading values of the QR code

Fig. 5 Some equipments used for IVF-guardian. **a**. A tablet PC; **b**. Label printer 1 for information; **c**. A fingerprint sensor; **d**. Code reader 1 for sperm preparation or cryopreservation; **e**. Code reader 2 for reading the QR code at the bottom of the culture dish; **f**. A PDA for reading the QR codes for IUI

Each IVF-guardian step

1) Consultation: A consultant identified the couple, registered their fingerprints, and then created a QR code (Figs. 2 and 6).
2) Information: Guidance personnel identified the couple once again and printed the QR code label (Easy solution, Repulic of Korea) after performing the registered fingerprint verification process. The fingerprint verification process was a process to determine whether the fingerprint on the day to treatment matched the enrolled fingerprints of the couple. Using the cuff band (green color), the QR code label was worn by the woman. Guidance personnel pasted the same QR code label to the lid and body of a semen collection cup. Guidance personnel had the husband check his name and the woman's name and guided the man to collect his sperm (Fig. 6).
3) Ovum pickup (OPU room+culture lab.): Recognizing the patient's QR code at the entrance to the OPU room, a voice speaking the phrase "It is the enrolled patient; please admit" could be heard. Simultaneously, information on patient admission appeared on the monitors of the OPU room and laboratory. Then, the doctor and nurses would check the patient's information on the tablet PC monitor in the OPU room, and the main operator and sub-operator would also check the patient's information and print the same QR code label (P touch recyclable cassette, Brother Industries, China) in the laboratory. The QR code label was attached to the bottoms of out-well and oocytes or embryos placed at inner-well of 2-well culture dishes (Fig. 6). There were several reasons for attaching QR code label to the bottom of culture dishes. The first, we were able to compare the patient's information of bottom label and information handwritten on lid. We could read the print of bottom label in bright microscope. The second, it was possible to prevent "mix-up" because label was attached to the bottom even when lid was replaced by others. Of course, other patients were prohibited from entering the handling chamber before a step of a patient was completed; the possibility that such a thing to occur was low. The third, there was no need to worry about QR code damage attached at the bottom of culture dish. Because QR code and image-based scanner has advanced algorithms to overcome code damage that cause barcode the most trouble [10].
4) IVF sperm preparation: The operator recognized the QR code on the semen cup that contained ejaculated sperm and checked the patient's information on the monitor of the tablet PC. Then, the operator printed the same QR code labels for sperm preparation and attached the QR

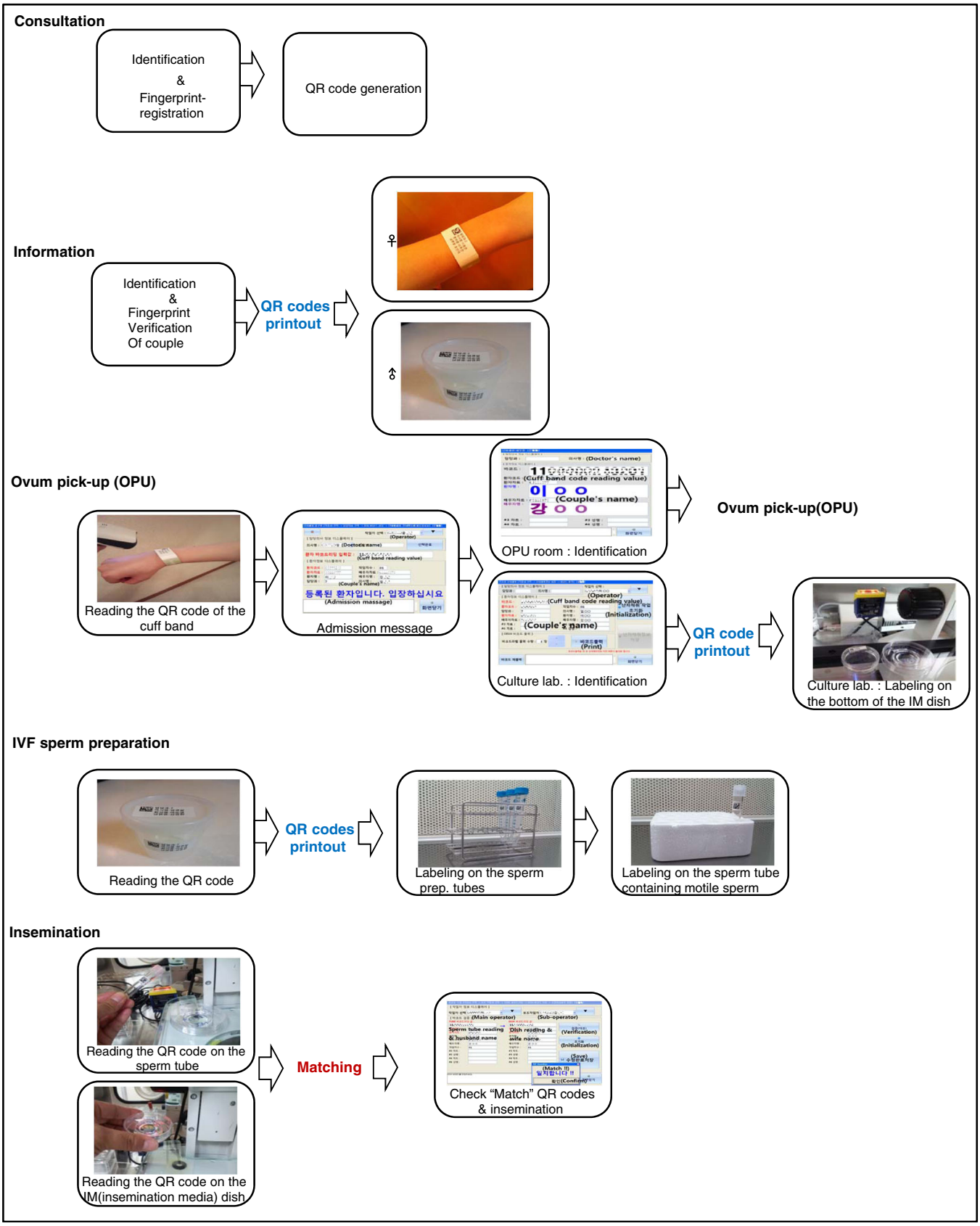

Fig. 6 The collection procedures from consultation to insemination; registration numbers and names were modified to protect the patients' personal information

code labels to the sperm preparation tubes (Fig. 6). Donor sperm were also treated in the same process after identification at information. To prevent mix-ups during the matching process of following insemination step, when an operator recovered motile sperm, he or she transferred carefully the sperm to a new tube at the final stage of sperm preparation. Other patients were prohibited from entering before the sperm preparation for one patient was completed (Fig. 6).

5) Insemination: The main operator took the dish that contained the oocytes from the incubator and checked the QR code on the bottom of the dish in the chamber. The sub-operator also checked the QR code of the man's sperm. Then, both the main operator and sub-operator checked whether the QR codes matched. If a match occurred, the "match" message was heard, and insemination was performed. Otherwise, a beep was heard. In such cases, insemination was interrupted, and the cause of the problem was investigated (Fig. 6).
6) 2PN identification: The following day, the sub-operator removed the cumulus cells of the embryos and passed the embryos to the main operator. The main operator checked the QR code and the patient's information. Further, the main operator selected only normally fertilized embryos, transferred them to new culture dishes and then attached the same QR code label to the bottom of the dishes, which were in an incubator. The main operator verified that the same QR codes were attached when there was more than one culture dish due to the number of oocytes retrieved or the combination of conventional insemination and ICSI. Other patients were prohibited from entering the handling chamber before the PN identification of a patient was completed (Fig. 7).
7) Embryo observation: The main operator checked the QR code, and both the main operator and sub-operator checked the patient's information. When the culture dish was replaced with a new culture dish, the main operator checked the existing QR code to print the same QR code label, and both the main operator and sub-operator checked the patient's information and attached it to a new culture dish. Before the end of embryo observation for one patient, the embryo observation for another patient was prohibited (Fig. 7).
8) Embryo selection for transfer: The main operator checked the QR code and the patient's information. After the selection of embryos, surplus embryos were transferred to a new culture dish, to which the same QR code label was attached. Surplus embryos for cryopreservation were also transferred to a new culture dish, to which the same QR code label was attached.
9) Embryo transfer (ET): Recognizing the QR code of a patient at the entrance of the ET room, a voice speaking the phrase “It is the enrolled patients; please admit” could be heard. Information about patient admission simultaneously appeared on the monitors of the ET room and laboratory. Thus, the doctor and nurses could check the patient's information in the ET room, and both the main operator and sub-operator could also check the patient's information in the laboratory. The main operator removed the dish containing the embryos for transfer from the incubator and checked the QR code attached to the bottom of the dish in the chamber. Then, the operators checked whether the codes matched. If a match occurred, the "match" message was played, which could be recognized by the patient, as well as the doctor and nurses in the ET room, and the ET was performed. Otherwise, a beep was heard. In such cases, ET was interrupted, and the cause of the problem was investigated (Fig. 7).
10) Embryo cryopreservation: After embryo transfer, surplus embryos were frozen at the cleavage stage or were cultured to the blastocyst stage. The operator went to the cryopreservation room with the culture dish containing the embryos for freezing, checked the QR code and the patient's information, and then printed the same QR code labels to attach to the cryo-vials, cryo-canes, and cryo-lists. The operator completed the freezing process by validating the QR code on the culture dish and the QR code that was printed (Fig. 8). In this figure, QR code label had been designed according to cryo-vials. When using other cryo-container, it is preferable to change the print program accordingly. Before the cryopreservation of a patient's embryos was completed, other patients were prohibited.
11) Thawed embryo transfer (TET): The operator checked the patient's information on the cryo-lists and removed the cryo-cane containing the patient's embryos from the LN_2 tank. Then, the operator checked the QR codes on both the cryo-cane and cryo-lists and checked whether the codes matched (Fig. 8). Thawed embryos were transferred to a warming dish with the same QR code label attached, and the embryos were cultured in an incubator. The embryo transfer of thawed embryos used the same process for embryo transfer described earlier. The oocytes were thawed used the same process as that for embryo thawing. Before the end of thawing a patient's embryos or oocytes, other patients were prohibited.
12) Sperm cryopreservation: The operator checked the QR code on the semen cup and the patient's information and then printed the same QR code labels to attach to the cryo-vials, cryo-canes, and cryo-lists. The operator completed the freezing process by validating the QR code on the semen cup and the QR code that was printed. This verification process was very similar to the process of confirmation for embryo cryopreservation. Before the end of cryopreservation of a patient's sperm, other patients were prohibited.

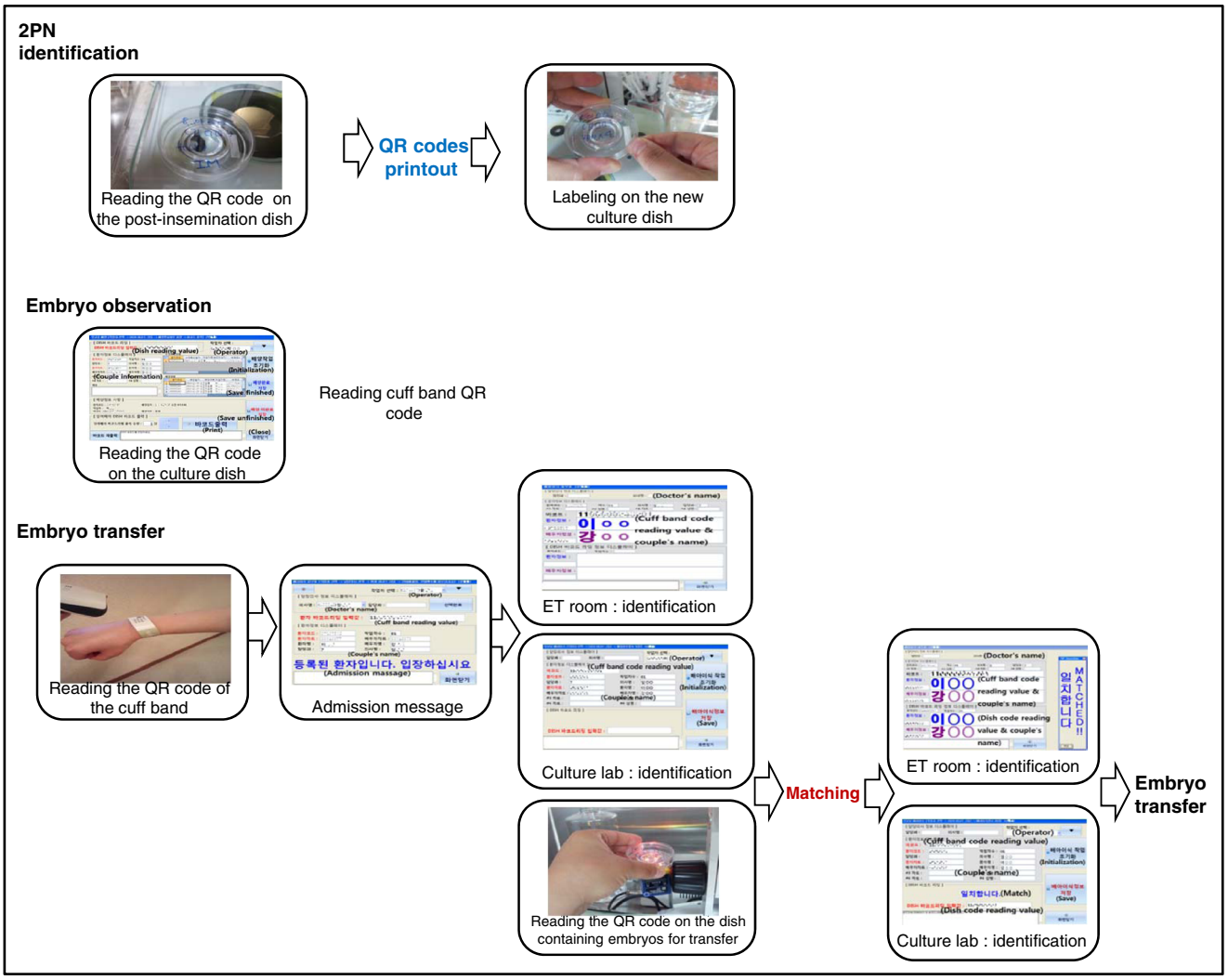

Fig. 7 Collection procedure from 2PN identification to embryo transfer; registration numbers and names were modified to protect the patients' personal information

13) Sperm thawing: The operator checked the patient's information on the cryo-lists and removed the cryo-cane that contained the patient's sperm from the LN_2 tank. Then, the operator checked the QR codes on both the cryo-cane and cryo-lists and determined whether the labels matched. Then, the operator printed the same QR code labels for sperm preparation and attached these labels to the tubes for sperm preparation. This verification process was similar to the process for the confirmation of embryo thawing. Before the end of thawing of a patient's sperm, other patients were prohibited.
14) Artificial insemination: Sperm preparation for artificial insemination used the same process as that used for IVF sperm preparation, which was described earlier. Using the cuff band (red color), the QR code label was worn by the woman. The operator checked the QR codes on both the cuff band and tube and determined whether the labels matched. If a match occurred, the "match" message played on the PDA, and the operator asked the woman to confirm the "match" message on the PDA screen. Then, artificial insemination was performed (Fig. 9).

Toxicity testing

Toxicity testing of the label paper

There was a possibility that the development of the embryo could be affected by volatile organic components originating from the printing material or adhesive material used in the label paper. Labels can be classified into those based on acrylic, rubber-based and hot melt adhesives. There are some differences in the composition of the chemical compound employed by the manufacturer in order for the mass of the adhesive to be kept the same. Labels also can be divided into the ink-jet and laser printing varieties. Most labels are made for business rather than for biological environments.

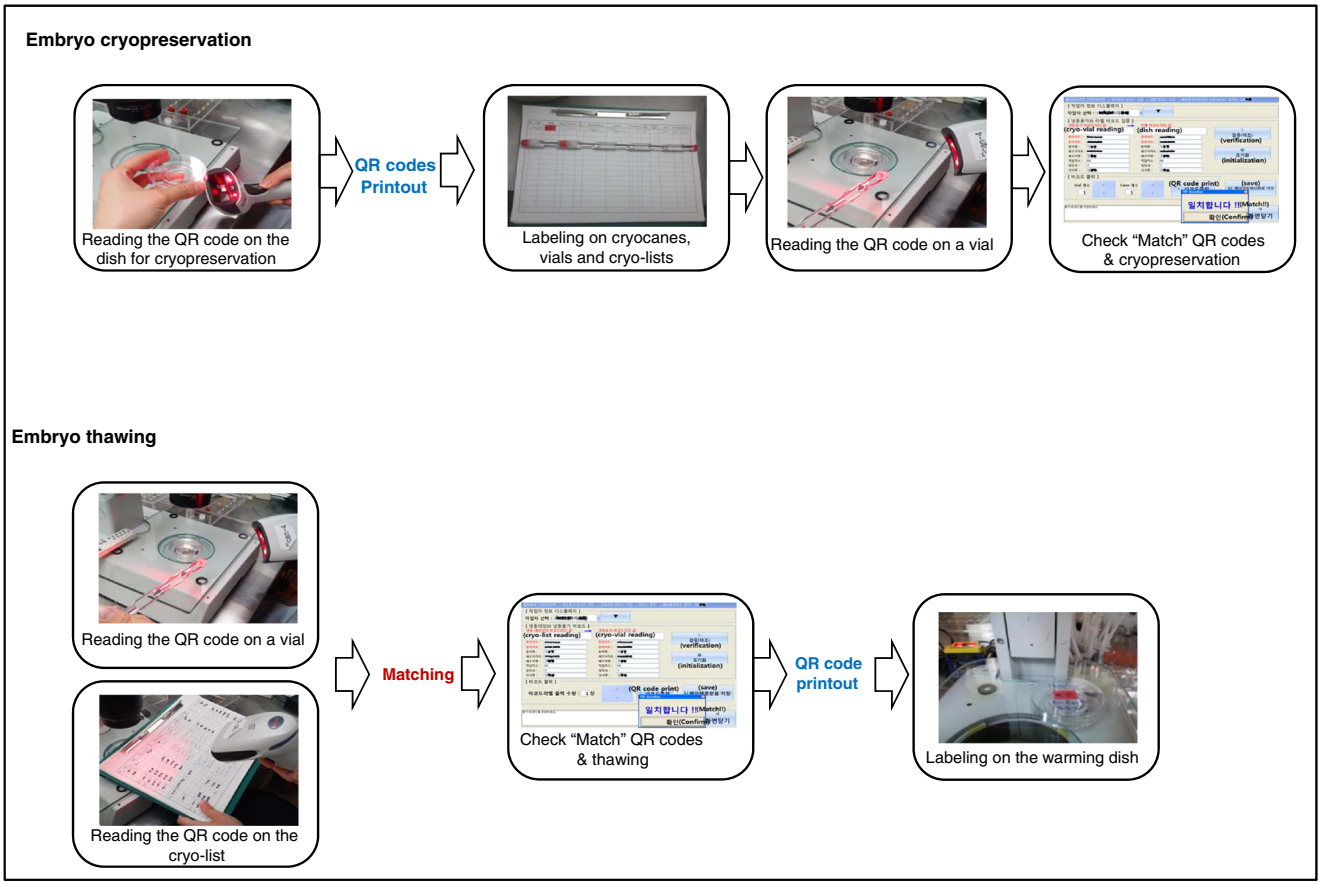

Fig. 8 The validation processes for embryo cryopreservation and thawing; registration numbers and names were modified to protect the patients' personal information

We tested a wide variety of labels including several series of Zebra labels, some hot melt labels from China, P touch labels (Brother Industries, China), etc. Toxicity studies were performed using mouse embryos to verify whether the

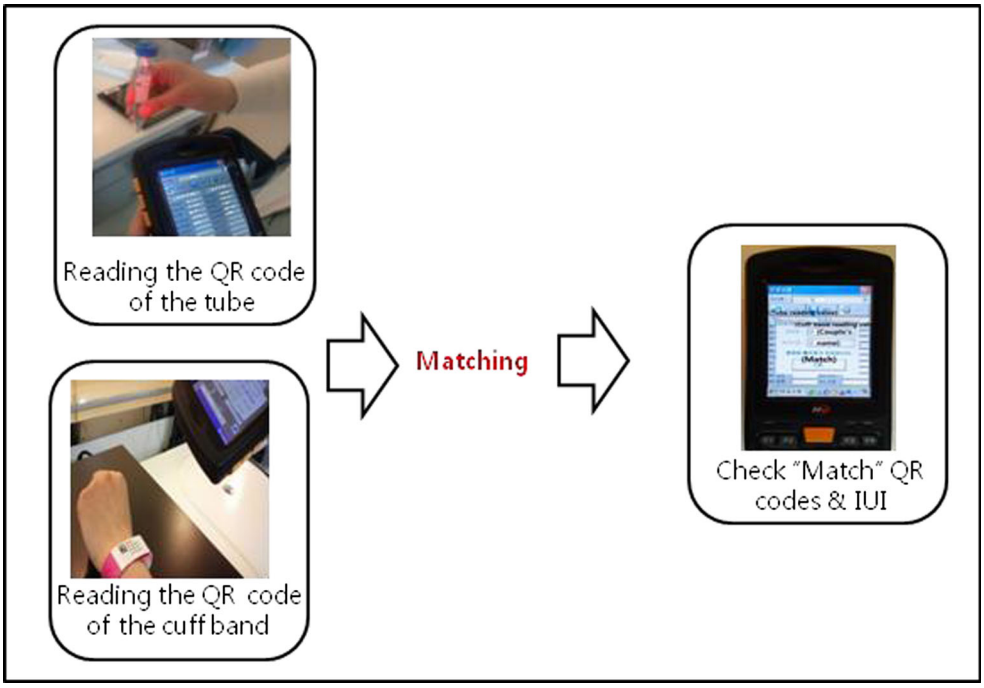

Fig. 9 The validation process before artificial insemination; registration numbers and names were modified to protect the patients' personal information

development of the embryo was affected. The protocol for handling the mouse embryos is as follows. Briefly, 6-week-old B6D2 F1 mice were superovulated with pregnant mareserum gonadotrophin (PMSG) and human chorionic gonadotropin (hCG). After administration, the female mice were mated with males and the copulation plugs were checked the following morning. Twenty hours after the injection of hCG, the female mice were sacrificed and single-cell zygotes were collected and cultured into mouse tubal fluid (MTF) +4 mg/mL human serum albumin medium at 37 °C in an atmosphere of 5 % CO_2. Each 50 μL MTF droplet contained 5 mouse embryos and was cultured. Observation of the embryonic development of the mice was performed on days 2 (at 46 h post hCG), 3 (at 70 h post hCG), 4 (at 94 h post hCG) and 5 (at 120 h post hCG). The embryos were evaluated for their quality and cell stages. On day 5, the blastocyst was graded as the hatching blastocyst (HgB), expanded blastocyst (EdB), intermediate expanded blastocyst (MeB), early blastocyst (ErB) or pre-morula stage. The test results were compared under the condition of increasing the label paper (3.6 cm^2) from one to three. The label sizes that were used in the experiment were larger than the label sizes (20x6 mm) that were used in clinical practice.

Light toxicity testing of the code reader

Code reader 1 (Xenon1900, USA Honeywell International Inc.) was an area image scanner commonly used in the medical field and was not used during the process of embryo culture. Therefore, for code reader 1, there was no need to test for light toxicity. Code reader 2 (Matrix210, Italy Datalogic) was a type of image-based ID scanner; the light source used LED light instead of a laser. Image scanning includes the process of comparing many images taken in a short period of time. Therefore, to accurately perform image analysis, LED light is used rather than conventional light. Generally, it took only about 1 to 2 s to read the QR code and the LED light was always shining in while the scanner was powered on. There was a possibility that the LED light could affect the development of the embryo. Using mouse embryos, the effects of the LED light were examined. The handling protocol and observation time of the mouse embryo was the same as that of the label toxicity test. The development of the mouse embryo was monitored after exposure to LED light once or twice with or without a cover. Reading it twice meant reading the QR code two times successively. The cover was a half-moon shaped cover used to protect the mouse embryos from the LED light when reading the QR code. The QR code label was attached to the bottom of the out-well and the mouse embryos were placed at the inner-well of the 2-well culture dish. Therefore, we protected the mouse embryos from exposure to LED light with the half moon-shaped cover when reading the QR code. In order to determine the influence of the light exposure time on their development, the mouse embryos were exposed to LED light for 10–30 s. The quality and cell stages of the embryos were evaluated.

Clinical application of IVF-guardian

After developing the system, we inspected the stability of IG in clinical practice. We fully described the requirements and functions of IG to the patients during the consultations. The patients were classified into two groups based on whether or not they wished to participate in IG for approximately 8 weeks. The IG applied and control groups consisted of 104 and 82 cycles, respectively. The distribution of the patients according to the insemination method in each group was conventional insemination (IG applied group 6/104=5.8 %, control group 5/82=6.1 %, respectively), half ICSI (IG applied group 41/104=39.4 %, control group 34/82=41.5 %, respectively) and all ICSI (IG applied group 57/104=54.8 %, control group 43/82=52.4 %, respectively). Embryo transfer was performed on day 3 or 5.

Cryopreservation of cleavage-stage embryos (day3) and blastocysts (day5, 6) was performed. The cleavage-stage embryos were equilibrated with 7.5 % ethylene glycol (EG, Sigma) and 7.5 % 1,2-Propanediol (PROH, Sigma) dissolved in Dulbecco's phosphate buffered saline (d-PBS) supplemented with 20 % serum substitute supplement (SSS, Irvine Scientific) for 5 min. The cleavage-stage embryos were then transferred into a vitrification solution consisting of 15 % EG, 15 % PROH and 0.5 M sucrose (Sigma) dissolved in d-PBS supplemented with 20 % SSS for 40 s. The blastocysts were equilibrated with 20 % EG dissolved in d-PBS supplemented with 20 % SSS for 45 s. After initial shrinkage, the embryos were transferred into a vitrification solution consisting of 40 % EG, 18 % Ficoll (Sigma) and 0.3 M sucrose dissolved in d-PBS supplemented with 20 % SSS for 20 s. All of the steps were performed at room temperature. After the exposure to the vitrification solution, the embryos were quickly loaded into an EM grid and plunged into LN_2.

Statistical analysis

The mouse and human embryonic development rates were analyzed using the χ^2 test and *t* test. The clinical data were compared using the χ^2 test.

Results

Label paper toxicity

We observed that many types of labels, including all of the Zebra labels and hot melt labels, affected the development of the mouse embryos in the toxicity test. It was decided not to

publish the internal data regarding the toxicity associated with each label. Only the P touch label did not affect the development of the mouse embryos.

There were no differences in the developmental rates of the mouse embryos when cultured without labels or cultured with one, two, or three labels on day 2 (>3 cell; 100 % vs. 100 % vs. 100 % vs. 100 %, respectively), on day 4 (>EdB; 95.8 % vs. 92 % vs. 92 % vs. 100 %, respectively) or on day 5 (>HgB; 95.8 % vs. 92 % vs. 88 % vs. 100 %, respectively). Furthermore, there were also no differences in the degeneration rate between the mouse embryos without labels and the mouse embryos cultured with 1, 2 or 3 labels on day 2, 4 or 5. It was confirmed that there were no effects on the development of the mouse embryos (Table 1).

Light toxicity

Compared to the control group, we observed no effects on the development of the mouse embryos when they were exposed once or twice to LED light. There were no influences on the developmental rates of the mouse embryos when they were exposed for 10–30 s with or without the cover (Table 2). In clinical practice, when checking the QR code of the culture dish, the exposure of the embryo in a culture dish to LED light is much less than that under experimental conditions. It took only about 1 to 2 s to read the QR code

Clinical results of IVF-guardian

When IG was used in clinical practice, some bugs were discovered in the operating program; however, they were corrected each time and the operating program was completed. Then, when the operating program failed in the field of wireless communications, no problem was found in the operating program; rather, the problem was solved by improving the communication line. We did not encounter any "mix-up' accidents when the IG system was introduced in clinical practice. One of the advantages obtained by using IG was a reduction in the misspelling of the patients' names. There were no between-group (i.e., those patients who participated in IG or not) differences in the patient's age, number of oocytes, 2PN, or number of embryos transferred. We found that there was no difference in the clinical pregnancy rates between the groups (Table 3). The cryopreservation rates of surplus embryos were also similar between the groups. The use of IG in ART processes had no effects on the clinical outcomes or embryonic development.

Discussion

Accidents in medical institutions often lead to fatal results or results that directly affect the health and lives of the patients. Because of the need for a system capable of preventing medical accidents, solutions have been steadily developed in the past. More recently, by fusing advanced technology and high-speed information communication environments, many safety systems that attempt to prevent medical errors are in active development [11]. In the case of ART, irreparable mistakes that occur in treatment can cause prolonged emotional distress for the patient. Because the potential for error is always present, even in the case of researchers and medical staff with many years of experience, the introduction of a safety system that could prevent such mistakes is required.

Barcode systems are in development, but they are not in widespread use in Asia [9]. Bar codes are generally not easy to read and require greater storage capacity than a QR code. Barcodes are one dimensional numeric codes and consist of up to 20 characters, whereas QR codes are two dimensional codes capable of storing data horizontally and vertically. Therefore, QR codes can hold up to 7,100 characters of data, rather than the much lower number which barcodes hold [12]. QR codes are now being used for the patient's 13-digit number, but we expect them to be used more widely in the future. IVF Witness™ using RFID has been introduced in several countries in Asia and it is likely to be introduced in the

Table 1 A comparison of the mouse embryo developmental rates using P touch label paper

	No. of Zygotes	No. (%) of embryos on D2		No.(%) of embryos on D4		No. (%) of embryos on D5	
	Total	>3 cells	Deg.[a]	>EdB[b]	Deg.	>HgB[c]	Deg.
0 label	24	24(100)	0(0)	23(95.8)	1(4.2)	23(95.8)	1(4.2)
3.6 cm^2 1 label	25	25(100)	0(0)	23(92.0)	2(8.0)	23(92.0)	2(8.0)
3.6 cm^2 2 label	25	25(100)	0(0)	23(92.0)	2(8.0)	22(88.0)	3(12.0)
3.6 cm^2 3 label	25	25(100)	0(0)	25(100)	0(0)	25(100.0)	0(0)
P- value				0.517		0.324	

No significant differences in the development or degeneration rates of embryos were detected among the different label numbers ($P>0.05$)

[a] Deg.: Degenerated embryo

[b] EdB: Expanded blastocyst

[c] HgB: Hatching blastocyst

Table 2 The results of LED light toxicity

	No. of Zygotes	No. (%) of embryos on D2		No. (%) of embryos on D3		No. (%) of embryos on D5	
	Total	>4 cells	Deg[a]	>M[b]	Deg.	>HgB[c]	Deg.
Control	81	81(100)	0(0)	81(100)	0(0)	77(95.1)	4(4.9)
Once reading	82	81(98.8)	1(1.2)	81(98.7)	1(1.2)	77(93.9)	3(3.7)
Once reading+cover[d]	80	80(100)	0(0)	79(98.8)	1(1.3)	74(92.5)	3(3.8)
Twice reading	82	81(98.8)	1(1.2)	80(97.6)	2(2.4)	73(89.0)	6(7.3)
Twice reading+cover	81	81(100)	0(0)	81(100)	0(0)	74(91.4)	4(4.9)
10 s exposure	81	81(100)	0(0)	81(100)	0(0)	76(93.8)	2(2.5)
10 s exposure+cover	82	82(100)	0(0)	81(98.8)	1(1.2)	74(90.2)	5(6.1)
30 s exposure	82	82(100)	0(0)	82(100)	0(0)	81(98.8)	1(1.2)
30 s exposure+cover	82	82(100)	0(0)	82(100)	0(0)	78(95.1)	3(3.7)
P- value		0.541		0.472		0.685	

No significant differences in the development or degeneration rates of the embryos were detected between the LED light exposure methods and times ($P>0.05$)

[a] Deg.: Degenerated embryo

[b] M: Morula

[c] >HgB: Hatched and hatching blastocyst

[d] cover : half-moon shaped bottom cover were used for protection embryos from LED light

Republic of Korea at a later date [13]. However, RFID chips are not recycled and are currently expensive and, in the case of long-term use, they could cause a financial burden for patients and hospitals. With the further development of RFID technology, the price could decrease. The stability and safety of the electromagnetic waves used in RFID systems have been demonstrated. However, a lot of research papers reported that exposure to electromagnetic waves alters the reproductive endocrine hormones, embryonic development and fetal development. These effects vary and differ according to the frequency, exposure time, and strength of the electromagnetic waves [14]. Therefore, a careful approach is required, because no studies with sufficiently long durations have been performed to ensure that there are no effects of electromagnetic waves [15–19]. Recent studies have investigated direct insertions into the zona pellucida and perivitelline space in each embryo using a barcode made of polysilicon with the goal of preventing mix-ups [20–24]. It has been reported that polysilicon barcode tagging can be used to identify individual mouse embryos. They could also be applied clinically, and it has been reported as a new method for preventing mix-ups. However, the effects of polysilicon barcodes on fetal development or problems that might occur after transferring them into the human body must be examined in future studies.

The IVF-guardian system is a unique system that can facilitate the verification process through the necessary treatment stages. The IG system uses a QR code for identification. A combination of the QR code and image-based scanner increases the read rate. The read rate is the number of barcodes read divided by the number of attempts [10]. When many patients are crowded together, easy and fast reading the barcode is a small but important factor to improve the work efficiency. The QR code label is attached to the bottom of the out-well of the two-well culture dish in the IG system.

Table 3 A comparison of the clinical outcomes between IG applied group and control group

	No. of ET	Mean age	Mean oocytes	Mean 2PN	Mean TE[a]	% of embryo freezing[b]	% of bla. freezing rates[c]	% of clinical preg.
IG group	104	36.5±4.2	8.9±2.2	6.1±1.2	2.3±0.4	42.9 (170/396)	36.5 (130/356)	38.5 (40/104)
Control group	82	36.8±4.4	8.3±2.2	5.7±1.1	2.4±0.3	41.0 (112/273)	34.9 (81/232)	36.6 (30/82)
P- value						0.624	0.692	0.793

Clinical pregnancy rate: in utero gestation sac visualized by sonography (6–7 weeks)

No significant differences in any block ($P>0.05$)

[a] Mean TE : The average number of embryos transferred

[b] % of embryo freezing : % of total embryo(cleavage stage, blastocyst) freezing rates in surplus embryo(after embryos transfer)

[c] % of bla. freezing rates[a] : % of bla. freezing rates in surplus embryo (after embryos transfer and cleavage freezing)

Sometimes, the QR code label becomes partly folded, but there is no problem in reading it, because the image-based scanner has advanced algorithms to overcome the problem of code damage that causes laser scanners the most trouble.

The handling and culturing of reproductive cells require the use of a variety of organic solvents. These organic solvents include mineral oil, various culture media, cryoprotectants, etc. The contamination of QR codes by these solvents or mechanical scratches on the surface of the QR code label can make them difficult to read. According to the label company's (Brother International Corporation, Japan) reports, the P touch labels are laminated for maximum strength and durability and their extraordinary adhesive properties are up to twice as strong as standard laminated labels. Because of the characteristics of the label, we have not encountered any problems reading the QR code caused by mechanical scratches or contamination by an organic solvent in the process of developing the system and clinical practice.

Articles about the QR code label not affecting embryo development could not be obtained directly from Brother International Corporation. However, on the basis of the material they presented, it can be seen that in the process of making the adhesive attempts are made to reduce the chemical substances as much as possible, in an effort to make environmentally friendly products. The label printer cassette (P touch recyclable cassette) has acquired various environmental certifications, including the Eco Mark and Brother green label in Japan. According to the material safety data sheet (MSDS) of the P touch label, the amount of chemicals used is not greater than the reference values. Even though the reference values are not for the cell biological level, it is observed that there is no influence on embryonic development.

IG systems have been added not only as visual prompts using a monitor, but also audible effects involving sounds that include alarms and human voices. Patients are often nervous during the procedure, but the use of sound effects, especially human voices, assists in the work by guiding both the nurses and patients.

In addition to the mandatory verification process, IG provides some additional features, for example, a verification process between the swim-up tube and new tube which collects the motile sperm at the final stage of sperm preparation. After 1 h of swim-up, we added the verification process before and after sperm preparation. Also, fingerprint recognition systems that can identify individuals will be upgraded to hand vascular pattern recognition systems. Some patients have difficulty detecting their fingerprints because of hazy prints and have resistance to fingerprint recognition systems. Hand vascular pattern recognition systems, which recognize the pattern of blood vessels on the back of the hand, encounter almost no resistance on the part of the patient and avoid the detection problems of the fingerprint system.

There is a disadvantage in that each treatment step became more complicated. However, the increased confidence of the medical staff in ART offsets this disadvantage. The patients also gained further confidence over the course of treatment. More than nine out of ten patients who received treatment using the IG system expressed the opinion that it is generally satisfactory. A satisfaction survey will be conducted on the IG system in the future.

Using a security system, we have been able to reduce the possibility of mismatching or mix-ups. Therefore, the installation of verification systems, such as IG, Matcher or IVF Witness™, should be encouraged in medical institutions that perform ART. Of course, it is not intended that the verification system guarantee the safety of the whole ART process. However, the possibility of ART mix-ups could be considerably reduced if upgrades and continuous complementary technical verification devices are introduced. Currently, IG is in the early development phase and its upgrade to a more stable version is needed.

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