Centro Universitário de Lisboa
Escola de Psicologia e Ciências da Vida
Mestrado em Embriologia e Reprodução Humana

IMPLEMENTATION OF AN AUTOMATED WITNESS SYSTEM IN AN ASSISTED REPRODUCTION CENTER

Dissertação apresentada a provas públicas para a obtenção do grau de Mestre em Embriologia e Reprodução Humana, orientada pela Dr.ª Miriam Iglesias Núñez.

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2023/2024

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VERSÃO FINAL

Dissertação defendida em provas públicas na Universidade Lusófona, Centro Universitário de Lisboa no dia 31/07/2024, perante o júri nomeado pelo Despacho de Nomeação n.º: 876 de 2024, com a seguinte composição:
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Resumo

O número de pessoas com problemas de infertilidade ronda cerca de 17% da população mundial. Dessa percentagem, apenas uma parte tem a possibilidade de aceder às tecnologias disponíveis em clínicas de fertilidade e hospitais para poder ultrapassar esta dificuldade. Quem decide avançar com o processo espera que tudo corra como planeado, ou seja, que os gâmetas utilizados e o embrião escolhido são colocados na paciente correta sem que ocorram erros pelo caminho. Para ajudar a impedir que possíveis erros ocorram, a tecnologia tem tido um papel cada vez mais importante nos laboratórios de fertilidade com o intuito de registar e confirmar todos os procedimentos. Atualmente existem vários sistemas de testemunha eletrónicos, cada um com as suas particularidades, mas todos com o mesmo propósito principal de impedir a ocorrência de erros e eliminar a necessidade de ter uma segunda testemunha na execução dos procedimentos principais. Neste caso, vamos focar a nossa atenção no sistema escolhido a ser implementado no Hospital Universitário Quirónsalud em Madrid, o RI Witness, mostrando as suas vantagens e desvantagens, bem como alguns contratempos que ocorreram durante o processo.

Abstract

The number of people with infertility issues is around 17% of the entire population. In that percentage, only part has the possibility of taking advantage of the technologies available to surpass this problem with the help of fertility clinics and hospitals. Those who go through with the process expect that everything goes according to plan, meaning the gametes or embryo chosen end up in the right patient without any mistakes being made in the process. To help prevent mix-ups from happening there has been an increasing involvement of technology in the laboratories to register and confirm each procedure. Many different Electronic Witness Systems (EWS) have been developed, each with their slight differences, but all with the same main purpose of preventing mismatches and eliminating the need for a manual double witness. In this case, we will be focusing our attention on the EWS chosen to be implemented in the laboratory at University Hospital Quirón Salud Madrid, the RI Witness system, showing its advantages and disadvantages, as well as some setbacks that occurred in the process.

Key words: RI Witness; EWS; RFID; mismatch; human error.

Abbreviations

WHO – World Health Organization.

HFEA – Human Fertilization and Embryology Authority.

ESHRE – European Society of Human Reproduction and Embryology.

IVF – In vitro Fertilization.

ICSI – Intracytoplasmic Sperm Injection.

Lab – Laboratory.

EWS – Electronic Witnessing System.

RFID – Radio Frequency Identification.

ID – Identity.

UID – Unique Identity.

PGT – Pre-implantation Genetic Testing.

SOP – Standard Operating Procedure.

PC – Personal Computer.

PDF – Portable Document Format.

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1. Introduction

As stated in a report published by the World Health Organization (WHO), approximately 1 in 6 people around the world struggle with infertility, corresponding to 17.5% of the adult population. According to the *Sociedad Española de Fertilidad*, in the Spanish population, this percentage ranges between 15% and 17% (1 in 6 People Globally Affected by Infertility: WHO, 2023; Marchador, 2023).

For those who can access the technologies available to surpass this challenge, it goes without saying that a baby is desired at the end of the journey. Moreover, one that genetically matches the choice made concerning the gametes used, either the couple's gametes or a donor's.

Embryologists are the ones who take care of sample handling from the very first moment of gamete collection, right until the last one, the embryo transfer. In addition, patients' oocytes, sperm and embryos are manipulated by different embryologists in the clinic throughout the whole process (Holmes *et al*., 2021). To ensure that the procedures go smoothly, a witness is required in every key step of IVF (in vitro fertilization) to verify that gametes are being matched correctly and that embryos are placed in the right patient.

Initially, manual double witnessing was suggested both by HFEA (Human Fertilization and Embryology Authority) and ESHRE (European Society of Human Reproduction) to prevent any possible mix-ups in the laboratory. It was expected that having two people carrying out the procedures' verifications would be better than one. Soon after, it was recognized the major flaw of this system, human error (Adams, 2006; Ifenatuoha *et al*., 2023).

It is known that quite a few mistakes have been made in fertility clinics throughout the years concerning sample matching and embryo mix-ups (Bender, 2006). As far as the error grading system goes, this is undoubtedly the one that is most severe, since it may seriously affect patients psychologically, as well as the clinic's credibility (Ifenatuoha *et al*., 2023; Thornhill *et al*., 2013).

Although it is believed that only 1% of errors occur in fertility treatments, this percentage has been rising as years go by. Some say it is due to the increased supervision of the procedures by other colleagues, and this leads to more mistakes being seen and consequently reported (Gupta *et al*., 2020; *Los Errores de La Fecundación in Vitro*, 2009).

To turn this around, it is highly important that a reliable safety system allowing patient identification as well as reproductive cells traceability is implemented during the key steps in every IVF laboratory (Beatriz Amorocho Llanos, 2017; Ifenatuoha *et al*., 2023).

These key steps include initial gamete collection, mixing of gametes by either conventional in vitro fertilization or intracytoplasmic sperm injection (ICSI), gamete or embryo transfer between tubes/dishes, freezing and thawing of gametes and embryos, and finally embryo transfer into patients (Holmes *et al*., 2021).

To prevent errors from ever happening at any of these steps, the need to eliminate the double manual witness arises. Since the world and every field of medicine is evolving every day, in a way where technology plays a bigger role, the introduction of these advances in our IVF labs was only a matter of time.

So, the electronic witnessing systems (EWS) came to take over manual double witnessing. Their main goal is to eliminate the need for a manual double witness and turn the procedures into a more controlled and automatic operation. It makes the process more reliable and less stressful, both for patients and embryologists, and for those reasons its use is recommended in the IVF laboratories (Forte *et al*., 2016).

Nowadays, there are already several different automated systems available to facilitate the clinic's workflow and much more. Their main purposes are the same, despite the different methods used to get there.

In this case we will be focusing our attention on an electronic witnessing system based on RFID (Radio Frequency Identification), designated RI Witness. This system was the one installed in the IVF laboratory at Quirónsalud University Hospital, Madrid, one of the first of the group Quirón to implement this technology.

This was the location in which I did my curricular internship from the 09th of October of 2023 until the 12th of January of 2024. After this period I kept in contact with my supervisor in order to complete my dissertation about the RI Witness installation and its use in their laboratory.

2. Preliminary phase

a) Justification of the need for an electronic witnessing system

Before the introduction of electronic witnessing systems in the laboratory, manual double witness was the method used to guarantee that no mix-ups occurred (Gupta *et al*., 2020).

This meant, every time a crucial procedure was being performed, another colleague would have to step in and verify the samples/embryos being used in order to confirm that everything was in order. The problem comes from the fact that both the embryologist performing the procedure and the witness are human beings, therefore not eliminating the premise that every procedure is prone to human error.

Human errors can be a consequence of stress, conscious and unconscious automaticity (either paying less attention to a procedure due to familiarity or inadvertently reducing the attention a procedure requires, respectively), ambiguous accountability (when both embryologists in charge of a similar task are not clear on their safety check responsibility and do not reinforce safety or reduce the risk of failure) and independent redundancy (the double checking procedure does not happen independently and so, where a mistake could be caught by the second witness, it is not anymore). This can translate into wrong labelling when writing patient's names on tubes, dishes and paperwork; poor dish handling; poor technical abilities and so on (Adams, 2006; Ifenatuoha *et al*., 2023; Thornhill *et al*., 2013).

Either way, these are all natural to human nature and impossible to eliminate with 100% certainty despite extensive training and practice.

These are the main reasons why an EWS is needed. To help prevent mix-ups, to trace samples, record every crucial step along the way, and as an additional advantage, to reduce the time spent doing checks with manual double witnessing. Both for the embryologist doing the procedure, as well as for the second witness, that most times needs to stop their work, creating a poor optimization of time for them both.

Studies have shown that the introduction of an EWS as the main witnessing procedure has major reductions in time wasted with verifications, both for the main embryologist and the second witness, when compared to the manual double witnessing procedure (Holmes *et al*., 2021).

On a day-to-day basis, a reduction, on average, of 14.73 minutes was observed in a study conducted in Boston, United Sates of America. These approximately 15 minutes might

not seem like much when we compare them to the hours spent on a working day. However, when we translate them into 89.66 hours per year, we realize the impact an EWS can have on a clinic's time management.

In this same study, embryologists were questioned whether the EWS gave them more reassurance over the procedures being performed and they stated it gave them more confidence (84.8% of the respondents) and peace of mind (82.6% of the respondents) (Holmes *et al*., 2021).

A case study conducted at a clinic in Nottingham reviewed the differences the installation of the RI Witness system had on the clinic's results. The number of cycles performed grew 27.5% in a 4-year period, comparing the year before the system was introduced in the lab (2016) and two years after doing so (2019).

An increase in productivity of 16% was observed per staff member as the time waiting for a second witness, or being the second witness, was eliminated. Moreover, lower stress levels were reported and a better work environment was created due to the introduction of RI Witness (*RI WitnessTM ART Management System*, n.d.).

An even more recent study from 2022 surveyed an IVF clinic in the United States and their results showed a 92% agreeance from the embryologists that RI Witness is an easy-to-use system, with 97% also finding it to be intuitive, and 87% agreed that the job-related stress was reduced (Di Berardino *et al*., 2022).

These are characteristics and improvements we should all want in whatever field we work in, since it translates into a better work and mental health environment.

When dealing with the introduction of new technologies in the IVF laboratories, we have to take into consideration how this might be perceived by the patients, since it might have a positive or detrimental effect on them and, in the long run, in the clinic.

A study that took place in an IVF clinic in Rome, Italy, showed that 90.4% of patients expressed their concerns with a possible sample mismatching event happening, and 92.1% felt that the electronic witnessing system reduced these concerns. Additionally, 97.1% of the patients also felt comfortable with the introduction of the new technology in the lab (Forte *et al*., 2016).

Going back to the 2022 study previously mentioned, concerning the patients perspective, with the introduction of RI Witness, 100% of the respondents had greater confidence in that clinic, were more likely to select it for their procedures and felt reassured by the reduced risk of mix-ups (Di Berardino *et al*., 2022).

Subsequently, in general, the patients are happy with the introduction and will eventually prefer a clinic with an EWS implemented in their laboratory of choice.

b) Existing legislation/regulation

Even though in some countries double witness is mandatory, in others it is not (Holmes *et al*., 2021).

According to the HFEA Act 1990 (as amended):

> "Centres must have in place robust and effective processes to ensure that no mismatches of gametes or embryos or identification errors occur. Centers must double check the identification of samples and the patients or donors to whom they relate at all critical points of the clinical and laboratory process. These checks must be completed and recorded at the time the relevant clinical or laboratory process/procedure takes place. A record must be kept in each patient's/donor's medical record" (Human fertilization and Embryology Authority, 2009, p. 184).

This statement reinforces the urgency of having a good witnessing protocol present in every laboratory to ensure no mistakes are made but also that everything must be traceable and accessible to everyone in the lab whether or not any mistakes occur in any procedure. All of these parameters are easier to accomplish by having an EWS in our IVF labs.

The European Society of Human Reproduction and Embryology also releases guidelines concerning the good practices in the IVF laboratory. Their recommendations from 2015 state that during the critical steps of IVF (stated in the introduction), manual double witnessing as well as/or electronic witnessing are highly recommended (Revised Guidelines for Good Practice in IVF Laboratories, 2015). These methods help avoid mix-ups from occurring and make it easier to trace the different procedures conducted in the laboratory.

c) Errors in other centers (real cases)

As mentioned formerly, cases of IVF errors occurring have been happening for quite some time now. The first case recorded of a mix-up in assisted reproduction dates to 1987 and from then on multiple other cases have been reported (Bender, 2006; Gupta *et al*., 2020).

For example, in 2021 in Cádiz, Spain, a couple that underwent a fertility treatment found out, only after the birth of their child, that the father was in fact not the biological father but a donor (Marchador, 2023).

Many cases in various countries, such as the United States of America, Thailand, Italy, Germany, Poland, Czech Republic, Israel, Turkey and others have been reported, usually due to patients' initial suspicion that the child is not theirs genetically.

These suspicions usually arise when the phenotypic characteristics of the child do not match the parents' or chosen donors' phenotype (Bender, 2006; Forte *et al*., 2016).

If, for instance, it happens that the child somewhat resembles both parents enough that no suspicions arise, there is no way to know how many patients might have had a newborn partially or completely genetically belonging to someone else.

With an EWS, the likelihood of such mistakes happening would be drastically reduced.

3. RI Witness

a) Different system types and models available on the market

RI Witness is one of many different options available to choose from to replace manual double witness. Such options include systems based on silicon barcodes that are attached directly into eggs' or embryos' surfaces (not sperm), systems based on barcode labels, and systems based on Radio Frequency Identification (RFID) technology (Ifenatuoha *et al*., 2023; *RI WitnessTM ART Management System*, n.d.).

There are many electronic witnessing systems available such as RI Witness, Gidget, Matcher electronic witnessing system and more.

All of them can prevent mismatches from happening, trace samples throughout the whole process and record crucial information about the cycle. The one you end up choosing comes down to preference based on price, the technology used, the software and hardware needed, as well as what model best suits the laboratory in which it will be implemented.

b) Why RI Witness?

With so many EWS options available nowadays, why choose this one in particular?

The decision to install RI Witness at University Hospital Quirónsalud, Madrid, was made at a corporate level.

At the time, when decisions concerning the implementation of this system were being made, Quirónsalud Assisted Reproduction was a part of the EUGIN group, and the latter had RI Witness already set up in their laboratories.

Consequently, RI Witness was the chosen EWS to be installed not only at Quirónsalud University Hospital in Madrid, but also at two other locations (Quirón Malaga and Quirón San Sebastian) that were chosen as a first implementation phase in group Quirón. Later on, other Quirón laboratories would gradually implement this same technology.

Since the beginning of the process, Quirónsalud Assisted Reproduction and EUGIN went separate ways and the plans that previously existed regarding the future of RI Witness in other Quirón centers was discontinued, at least for the time being.

c) Automated witnessing system RI Witness

As human error is impossible to set aside, this system helps diminish it by controlling each step and following every single tube and dish used in the different procedures across the different fields in the laboratory. This electronic witnessing system, that belongs to Cooper Surgical, uses RFID technology to control and register all activity undergoing in the IVF laboratory (*RI WitnessTM ART Management System*, n.d.).

Figure 1 - Some of the RI Witness' materials needed for it to work properly.

d) What is RFID?

Radio Frequency Identification is a way of labelling, transmitting information and automatically identifying objects or people using a technology based on radio waves (*RI WitnessTM ART Management System*, n.d.).

This technology is present in the Healthcare sector and has shown diverse benefits from patient monitoring and safety, reduction of medical errors, medical device's tracking and improved financial controls (Abugabah *et al*., 2023).

In IVF laboratories, this technology is introduced in microchips that are present in the labels attached to all plasticware assigned to each patient, therefore identifying which culture dishes, test tubes and patient identity cards belong to each individual (*RI WitnessTM ART Management System*, n.d.). In this particular case, bracelets with barcodes were used instead of ID cards to better suit the department protocols.

e) Health risks associated with RFID and radio waves

In order to introduce a new technology in the IVF laboratory, certain safety measures need to be verified before its implementation, to guarantee that that technology itself does not, in any way, impact gamete quality and adequate embryo development.

On a day-to-day basis we are surrounded by numerous radio frequency emissions from many technological devices. On Figure 2 we have a graphic comparing the different radio frequency levels various technologies emit. As we can observe, the RI Witness RFID tags emit a radio frequency much lower compared to our cell phones that we carry around with us every day. Besides, these tags are only active when near a reader, since they do not have any internal energy source. Moreover, embryos are not meant to be exposed to them for extended periods of time.

The only occasions in which they are exposed to such radio frequencies is when they are being manipulated in the workstation on top of the RI Witness readers.

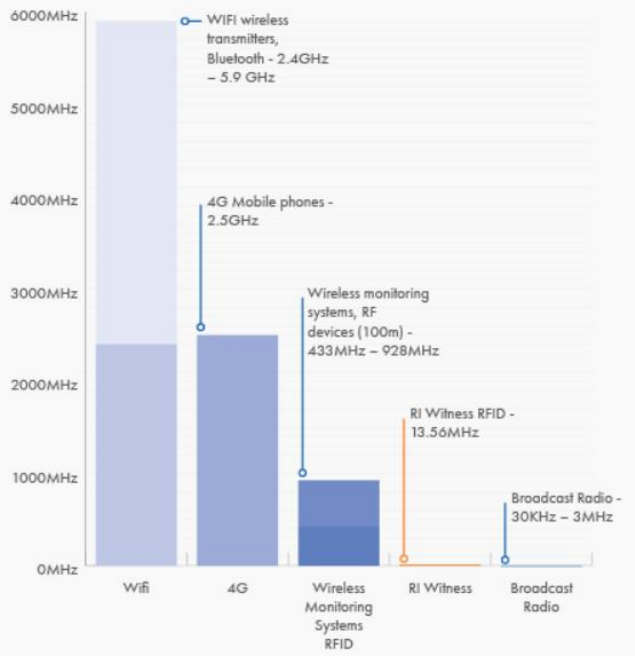

Figure 2 – Comparison of day-to-day technologies' radio frequency emissions to RI Witness'.

To ensure that these radio waves were not detrimental to embryo development in the IVF lab, studies were conducted using a radio frequency 700 times higher than the one used in the actual RI Witness RFID tags and it was shown that it was not harmful to embryo development (*RI WitnessTM ART Management System*, n.d.).

Another study conducted in 2020 (Figure 3) reinforced the previous conclusions, showing there were no significant differences observed in maturation, fertilization, cleavage, and embryo development rates when compared to a control group ($p > 0.005$) (Gupta *et al.*, 2020).

Groups/cases (*n*)	Number. of OCC retrieved	OCC/ patient	Maturation rate (%)	Fertilization rate (%)	Cleavage rate (%)	Day-3 (Grade A) embryo development rate (%)	Day 5, blastocyst good-grade development rate (%)
Control (185)	2263	12.23	86.04	75.60	100	60.73	28.60
Positive control (408)	5309	13.01	75.87	76.32	99.61	59.11	22.17
EWS (56)	695	12.41	83.16	74.39	93.95	64.60	26.48

EWS=Electronic witness system

Figure 3 – Efficacy and safety of the EWS on maturation, fertilization, cleavage rate, and embryo development rate of good-quality day 3 embryos and day 5 blastocysts compared to a control.

f) How does it work and what are the main advantages?

From the moment they enter the clinic, the patients are given a unique identity (UID) card or bracelet containing a personal code that will be presented when starting the treatment (*RI WitnessTM ART Management System*, n.d.).

In this case it was preferred to give bracelets to patients with their identification and a barcode instead of identity cards. Their purpose is exactly the same, but instead of the system reading the card with the RFID tag automatically, there is the need to scan the bracelet of the patient with a manual reader at the beginning of the treatment (*RI WitnessTM ART Management System*, n.d.).

Since the number of unique identities available is so large, a different UID can be attributed to every sample container. This allows for the system to always know which samples have been paired together in which procedure and eliminates human identification errors (*RI WitnessTM ART Management System*, n.d.).

Installed in every workstation are RI Witness plates with incorporated RFID readers working at all times as well as a tablet containing the software that is integrated with the hospital's patient database.

These reader plates have various useful characteristics. They can be integrated at the workstation level, meaning that there is no height differences between the reader and the workstation top, or it can be placed on top of it, leaving a few centimeters between the top part of the reader and the workstation labor area.

Additionally, they have the option of being heated or unheated depending on the procedure that is going to be performed. This change is fairly quick and might be handy on

certain occasions where other RI Witness reader areas with adequate temperatures may not be available to use.

Two key features of these readers reside in the fact that they are able to read more than one microchip at the same time and do not require the handler to scan the tag manually, contrasting with other automated witnessing systems in the market.

These tags are placed on all plasticware before the beginning of the procedure and come in various shapes to best adapt to the diverse models used in the different procedures.

Since the RI Witness readers are available night and day, it ensures that not one single RFID tag is missed and that everything is checked by the system before every sample is handled. Additionally, it also guarantees that the samples being worked on at any time are a match (*RI WitnessTM ART Management System*, n.d.).

After assigning the UIDs to the patients, the tubes and dishes with the samples are handled with the RFID tags. This way we can track when they are moved in each step of the whole process but also record all the important information regarding the cycle process, such as a time stamp of the different procedures, who performed them, and if any mistakes were made in the process (Gupta *et al*., 2020; *RI WitnessTM ART Management System*, n.d.).

Tags are only assigned to final plates or tubes, meaning that every intermediate plate or tube that does not leave the workstation during the procedure does not need an RFID tag. For example, after the oocyte retrieval there is no need to tag every single tube containing the follicular fluid, as well as the plate in which the oocytes are searched for. Only the final plate that goes into the incubator afterwards needs an RFID tag since it is the only one that leaves the workstation.

Moreover, since it is not possible to work on more than one patient's sample at a time, in case of a mismatch detected by the system, it will immediately sound an alarm (*RI WitnessTM ART Management System*, n.d.). This alarm will not stop until one of the incorrect samples is taken away from the RI Witness reader. After doing so, there is also the need to fill in a mismatch report stating clearly and concisely the reason why the mismatch occurred.

Every single procedure conducted, as well as any errors that may occur, are recorded in the patient's history and can be accessed through the computers at any given time.

For cryopreservation of gametes and embryos, as well as for biopsies, there are some specific directives.

For cryotops used to cryopreserve gametes or embryos, barcode labels are printed with a specific printer for that purpose. Each barcode is associated to the patient's RI Witness ID number and can be identified at all times.

In the specific cases where an embryo biopsy is performed, RI Witness is equipped to not only identify each embryo cryotop with a distinct barcode, but also automatically attributes the result of the PGT test performed to each embryo (if desired by the clinic). This means that whenever the transfer time comes, the embryologist is able to see previously to the procedure on the RI Witness system which embryos are approved for transfer and which ones are not.

Moreover, by having to scan the barcode before the transfer procedure, it ensures that the embryo being chosen is suitable for the technique. If by mistake the wrong embryo is chosen, as mentioned previously, an alarm will sound thus preventing the embryologist from progressing with the transfer (*RI WitnessTM ART Management System*, n.d.).

On figure 4 we see illustrated a few of the main steps where RI Witness plays an important role from the beginning of the cycle, gamete collection, fertilization, embryo culture, biopsy (in the cases it is performed) and a mismatch example.

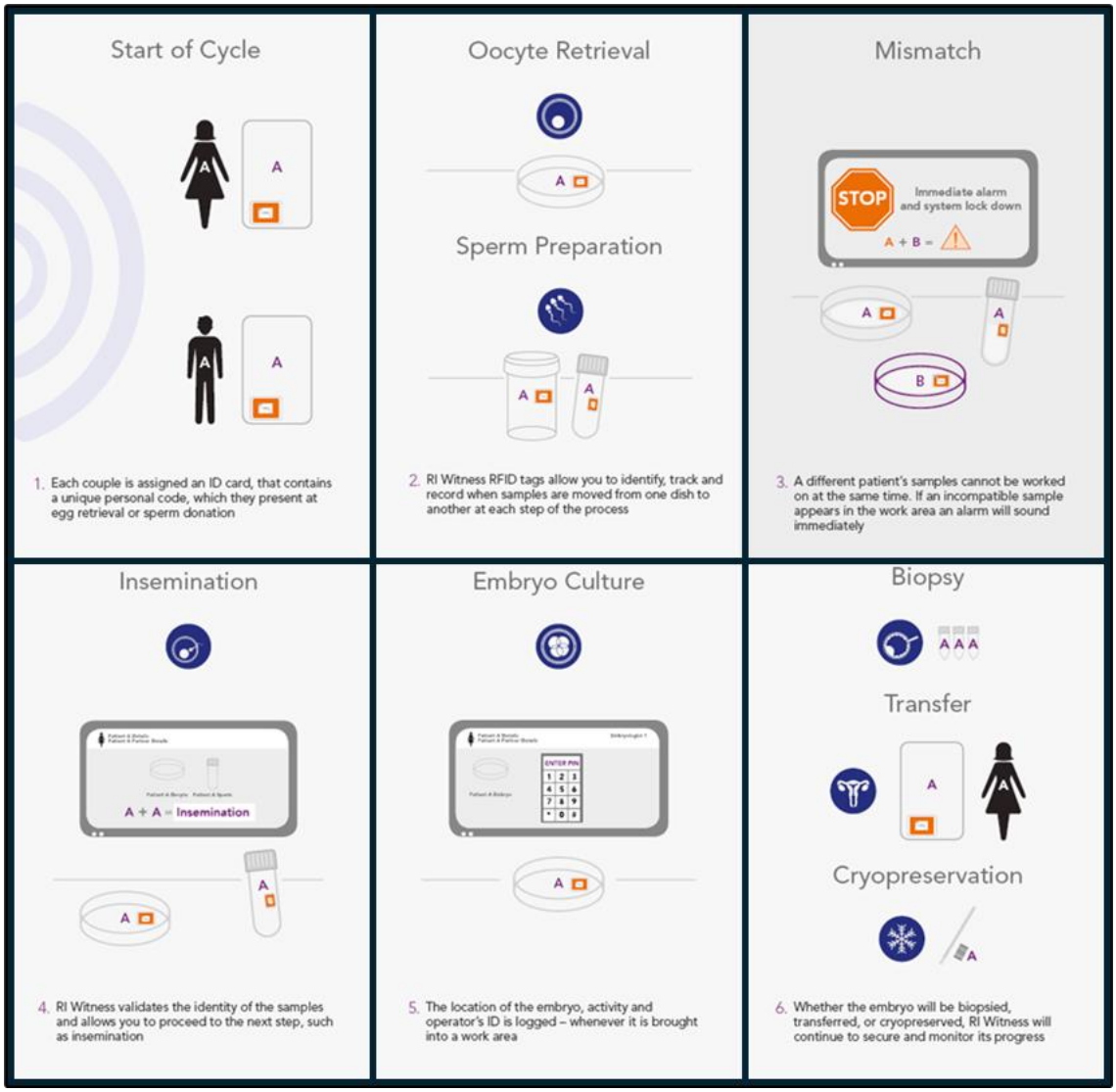

Figure 4 - Key steps of RI Witness intervention and mismatch case.

g) Advantages in general, over double witnessing and over barcoding systems

Since the system is automatic, and working at all times, it is not necessary, as before with manual double witnessing, that another embryologist supervises another's sample handling, to ensure correct matching.

This RI Witness advantage alone allows more time for the embryologists to do other important tasks undergoing in the lab, reduces distractions, frees up the double witness workload, and makes it possible to trace each and every step by any of the staff members (*RI WitnessTM ART Management System*, n.d.).

RI witness ensures that every gamete, embryo, biopsy and cryopreserved sample have their own patient identity attributed to them, therefore decreasing the room for error during handling in every procedure (*RI WitnessTM ART Management System*, n.d.).

Moreover, by warning the embryologist immediately about the sample mismatch, it allows the error to be immediately corrected, ensuring the whole IVF process goes well in that aspect.

Compared to the barcoding system, using an EWS based on RFID technology prevents the embryologists from skipping important steps as it has an inbuilt forcing function preventing them from doing so, as well as the ability to restrain embryologists from handling more than one patient's samples at the same time.

Besides, barcodes use "line-of-sight technology" which means that the embryologist has to orient the barcode towards the reader, further implying it relies entirely on them remembering to do so. If this step fails to be completed, or an human error occurs when doing it, false records are created (*RI WitnessTM ART Management System*, n.d.).

As said previously, RFID tags do not require the handler to approach or orient the samples towards the reader. The tags are read automatically as soon as they enter the reader area and, since it can read multiple samples from the same patient at one time, saves the embryologist time in that aspect as well.

In the case where silicon barcodes are attached to oocyte's and embryo's surfaces, this translates into a labor-intensive task, requiring the embryologists to spend more time doing an additional procedure (*RI WitnessTM ART Management System*, n.d.). This goes against one of the main purposes of the electronic witnessing systems, that is, giving the embryologists more time so they can focus on other important tasks.

Other RI Witness system advantages that have been listed include reduced stress and distractions, increased efficiency among staff members, SOP (standard operating procedures) compliance and auditing (Thornhill *et al*., 2013).

Additionally, this EWS has a special solution that allows laboratories to have access to their data in real time, which allows them to have a greater insight into their clinic's performance as well as comparing it with other clinics of the group that have this same technology. RI Witness IQ solution allows you to access every procedure that has been conducted in the lab, granting you the opportunity to evaluate, for example, the time spent performing a certain procedure by every staff member.

With RI Witness IQ is possible to have constant access to such data, as well as a monthly report to evaluate whether or not some training might be necessary for certain embryologists so that they can achieve their peers' results, consequently improving patient care by standardizing as much as possible every procedure in the lab (*RI WitnessTM ART Management System*, n.d.; Thornhill *et al*., 2013).

RI Witness IQ solution brings four characteristics that play an important advantage in the lab, them being Standardization, Monitoring, Customization and Visualization.

Standardization and Monitoring allows you to reinforce SOP's and improve lab efficiency by being able to track every procedure and operator, making it easier to evaluate where improvements could be made.

Customization and Visualization are key to making the information easy to interpret. It is possible to customize which features and data appear on outputs and reports, according to the needs and interests of your laboratory, and information is showed as flow charts to facilitate its understanding (*RI WitnessTM ART Management System*, n.d.).

The system, apart from the great advantages already mentioned, also has another plus side. Derived from the fact that RI Witness system has an established forcing function that does not allow you to skip procedures, it is a great tool for new embryologists coming into the clinic to practice.

As a new staff member joins the team, there is the need to learn the clinic's protocols, as well as the workflow of the lab that has already been established. With RI Witness's guiding function, it is easier for someone who is starting their activity to get the hang of every sequence of procedures and what is need for each one (*RI WitnessTM ART Management System*, n.d.; Thornhill *et al*., 2013).

4. Implementation phase

a) Equipment installation and workflow chart

Before the RI Witness system was able to be used daily, 3 phases needed to be completed first. The equipment installation, software installation and training phase. Without any of these steps the correct use of such a system is not possible.

The equipment installation inside the laboratory was done by a technician who coordinated with the embryologists to schedule his activity for different times of the day when there would not be any laboratory work being done at that moment, to not interfere with any of the procedures' normal flow.

The different equipment installed consisted of work area readers, controlling software, PC, barcode readers, tablets and a barcode printer for cryotops (*RI WitnessTM ART Management System*, n.d.).

After the equipment was installed, there was the need to coordinate with the hospital's informatics department the connection of every needed device by RI Witness to the hospital's network. This was necessary for the system to be able to obtain the needed information from the patients' database to work properly.

The RI Witness software was installed in every tablet in each important workstation and computers throughout the lab.

After everything was installed, the Cooper Surgical technician created the workflow chart with the lab manager according to the laboratory's order of procedures and names given to each step (figure 5). The system allows this diagram to be modified if any changes are made in the order of which procedures are performed or if new ones are introduced in the lab, making the system very flexible to adapt to different lab workflows depending on the laboratory where it is being installed.

Like every system that has been or might be introduced in the lab, for it to work properly and create the corresponding results, the staff members need to be trained to use these systems correctly.

Even though the RI Witness system is electronic and automated, the ones performing the actual procedures are still the embryologists and so, the required attention that such processes involve must always be present.

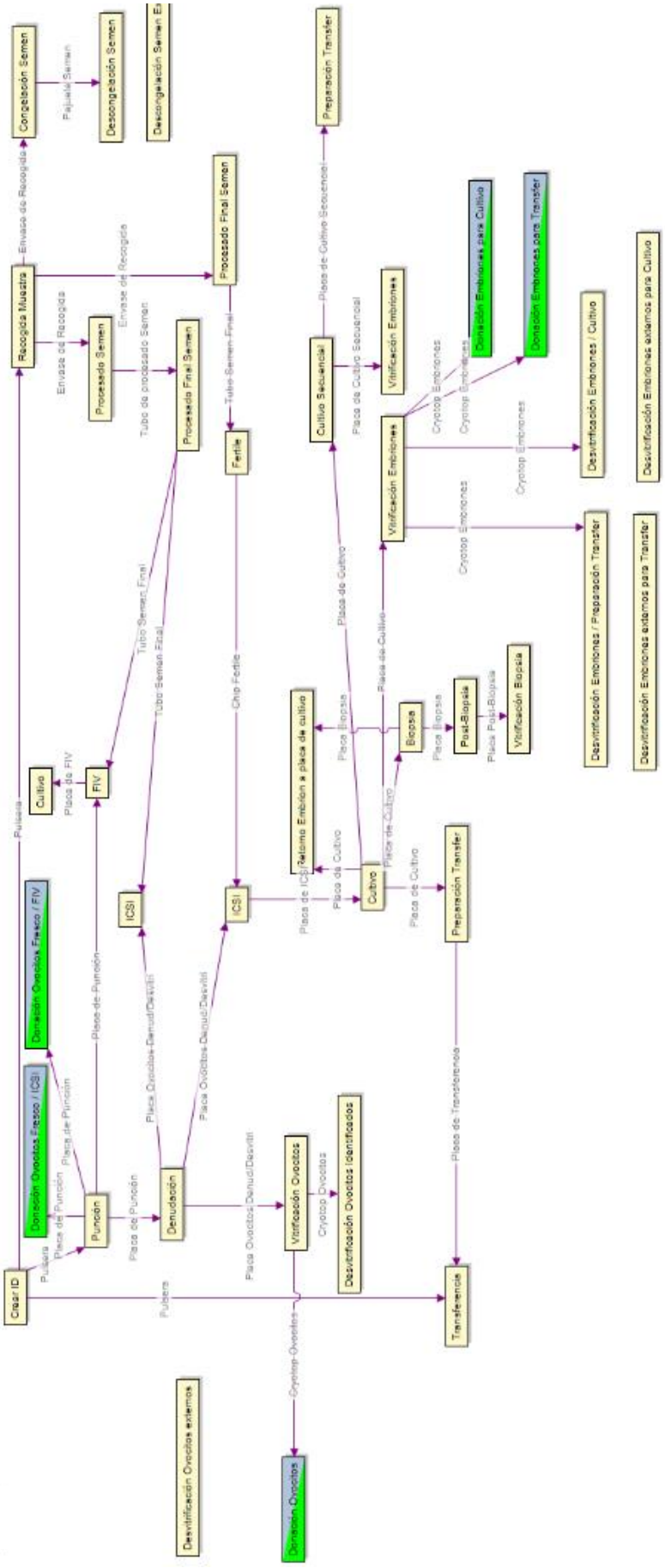

Figure 5 – Workflow diagram established for the laboratory (in Spanish).

It cannot happen that blind witnessing becomes a problem with EWSs similar to those we have discussed previously with manual double witnessing (Sterckx *et al*., 2023). It is not possible to 100% eliminate the human factor, however, we can try to reduce it as much as possible.

After the installation process, a detailed explanation of the main features of RI Witness and how it is supposed to be used daily, was also given to the embryologists by the Cooper Surgical technician. Embryologists were taught how to assign patient IDs/history number to RFID tags, how the diagram works and what key elements are needed on top of the reader for certain options to appear on the tablet, and how certain features are available but optional and it comes down to what the embryologists decide is best and needed for their laboratory. The embryologists were also instructed on how to proceed in case of a mismatch, since this is one of the main purposes of the RI Witness system.

5. Performance

a) Errors detected by the system and correction of incidents

The system's main purpose and one of the reasons why RI Witness is so interesting compared to manual double witness is its ability to automatically detect mismatches. Every IVF lab dreads the possibility of having such errors occurring, due to the potential devastating outcomes such as lawsuits, loss of patient's trust in the clinic but also the psychological effects it might have on them (Thornhill *et al*., 2013).

This system automatically detects errors in sample matching as soon as the RFID tags in dishes and tubes, that do not belong together, are placed on top of the reader. When it happens, it is programmed to sound an alarm and the tablet screen will automatically show a red display, both of which will only go away once one of the mismatched samples is taken outside of the reader area.

After doing so, a new window opens to fill in with the reason why the mismatch occurred. The reasoning must be written in a concise and clear manner to be understood properly and without a doubt in the future, if needed. The embryologist may then proceed with the correct matching of the samples and completion of the procedure.

This mismatch will be registered in the patient's file with time, date and procedure in which it occurred attached to it and independently of the reason of their occurrence, they are not erasable. Moreover, it is possible to print a PDF (Portable Document Format) with the information about the patients' cycle with a description, time and date of every procedure as well as any potential mismatches that might have occurred.

A study going back to 2013 evaluated the true mismatch rate of RI Witness and their duration. It showed that all procedures were recorded accurately and the mismatch rate of 0.11% was comparable to others found in similar laboratory activities (<1%). These mismatches were rectified in under 10 seconds, which was not enough time for any mistakes to be made by the handler after the audible alarm. (Thornhill *et al*., 2013)

b) Disadvantages

Although there are definitely many advantages to the use of RI Witness as examined beforehand, some disadvantages are also worth mentioning.

The space available to manipulate oocytes, semen samples and embryos is very restrictive. Instead of essentially having the entire workstation to use, now, only the space with the RI Witness readers is available, not leaving much room to move dishes, tubes and other necessary materials around, since these need to be on top of the reader during the procedure.

Due to this fact, and additionally that the reader in this particular case is on top of the workstation surface, it may not be as comfortable for someone who is used to the previous display. Until they get used to it, some handling accidents might happen in the beginning. As we mentioned, it is possible to have the RI Witness reader at the same level as the workstation thus preventing such accidents from potentially happening.

Since the workstations are supposed to be, as much as possible, a sterile environment, two concerns arise with the introduction of this EWS.

The airflow that needs to be in place inside the workstation can be compromised due to the amount of new equipment installed. Cleaning is also a harder task. Since there are more surfaces to clean, there is an added difficulty cleaning underneath the new RI Witness surface. Plus, with all the additional cables the system needs, some spots might be left unclean and less sterile, both not wanted in an IVF laboratory.

Even though the RI Witness system frees time from the second embryologist by not having to be present at the most critical procedures, in the beginning, the introduction of RI Witness takes time away from the embryologist realizing the procedure itself.

Previously, since the person responsible for executing the technique only had to do it following the correct steps in the right order, now there is the need to introduce a new variable in the equation. The new actions include selecting in the tablet what procedure is going to be conducted, depending on what items are on the workstation, and confirming the information given by the program about patient ID and procedure.

It might not look like a lot of time in the future with practice, but in the beginning, until you get fully accustomed to working with RI Witness, it is a slight adjustment. For embryos or oocytes, time spent outside of their optimal conditions in the incubator is potentially detrimental for their adequate development. This being said, although RI Witness frees the second embryologist, it may be compromising the patient's embryos and gametes in other aspects.

Moreover, the RFID tags are expected to work properly, but as we know with other technologies, it is only a matter of time until something does not work as well as it should, or at all, and for those reasons the embryologists need to safeguard these situations by manually labelling everything additionally to the RFID tags. By doing so, if an error occurs, they can

proceed with the normal laboratory workflow without it being compromised by a technological malfunction (Sterckx *et al*., 2023). So in this case, the embryologists, besides having the previous task of labelling the plasticware manually, now also need to correctly attach the RFID tags.

Although the RI Witness system might be a valuable tool, the presence of a manual double witness is still recommended in some cases.

This is because the system is not yet able to trace embryos individually during the procedures, meaning it might happen that potential errors related with embryo mix-ups from the same patient can occur. And, if that happens, there is no way to identify these mistakes with the EWS (Sterckx *et al*., 2023).

Moreover, since the tags for cryotops that do not include RFID microchips due to the fact that they cannot sustain the lower temperatures of the liquid nitrogen, it implies that whenever there is the need to do a thawing procedure, either of embryos or oocytes, a barcode reader has to be used for RI Witness to identify them. This means that the operator must remember to proceed with this step, which is a disadvantage since, once again, we rely on the attention of the embryologist to do so.

Additionally, in this Hospital in particular, the function that allows embryos that have been biopsied to have their PGT results connected with each cryotop has not been implemented.

This means that when the barcode of each cryotop is read, there is no information regarding the embryo suitability for transfer. For this reason, at this step, it is necessary that a manual double witness is present to confirm that the right embryo is being taken of the nitrogen tank.

Even though electronic witnessing has excellent advantages, as we have seen here, there are too some disadvantages to consider.

c) Difficulties

With the introduction of a new system in the laboratory, errors were bound to happen and difficulties would come up at some point. I will walk you through some of them in order of occurrence for you to better understand that, in spite of all the advantages, there are also some setbacks that are worth mentioning that happened during the installation process and use of the RI Witness system specific to its implementation at University Hospital Quirónsalud, in Madrid.

During the initial phases of the system adjustments to the lab, a critical problem soon came to light.

To be able to use RI Witness, there is the need to login in Windows as well as in the RI Witness system with the user belonging to each embryologist. The problem deriving from this apparently simple and not harmful step is that, due to hospital cybersecurity measures, the session period for each time any person remains logged in is only 5 minutes.

This, without a doubt, is not acceptable in an IVF laboratory where most procedures, going well, take longer than that. If, by chance, anything goes wrong or there is any difficulty added to the procedure for whatever reason, the time is surpassed, and an error is signaled by the system.

This being said, the embryologist would need to interrupt the procedure and log in once again, both in Windows and RI Witness, having to scan every sample again (and the patient's bracelet if applicable to the procedure being performed).

With all these steps, apart from the obvious that oocytes, embryos and patients cannot just wait for the system to be back on again, the time that was supposed to be saved with the RI Witness system is wasted elsewhere, potentially having worse consequences to the success of the treatment than manual double witnessing.

Therefore, there should be an option to have a general user always logged in both Windows and RI Witness, and when there is a change in the embryologist doing the procedure, it is only necessary to change users inside the RI Witness system itself, without having to log out and back in again. Moreover, the time period that a user can be logged in must be extended.

Further down the line, this problem was solved by the informatics department allowing the tablets to be left without any time limit regarding Windows getting blocked after some inactivity time. By always being active, they only need to log in RI Witness. For this, each embryologists has a chip, that by placing it on top of the reader, automatically logs the person into the system, without the need for them to be introducing any passwords, making it a quicker and easier process.

On the 2nd of February, the system was still not fully ready to be used. Many problems were still to be solved such as access to the patient's bracelet printer, therefore not enabling any of the patients to be introduced in the system; the lack of a computer in the sampling room; one of the computers at the reception did not allow any of the different users to enter the RI Witness system; whenever the tablets found inside the lab got blocked due to inactivity time, logging in Windows was not enough to be able to use RI Witness, there was the need to restart

the tablet just so you could access the system. The informatics department tried to solve these problems on more than one occasion with no luck initially, but eventually resolved all of them.

Despite the problems that kept on arising, by this time, the tags needed to identify dishes and tubes for the RI Witness reader to recognize had finally arrived, and most of the RI Witness users were confirmed to be working, each with their own password.

Nonetheless, more than one month later, on the 15th of March, issues were still preventing the laboratory from using RI Witness to track and witness their procedures. A new problem that had not been seen in any other places where this system had been installed was occurring when patient bracelets were printed.

The bracelets were being printed using RI Witness manager, however, in the work area, where it should show the names of the patients, a black/blue opaque rectangle appeared instead, preventing the names from being seen. To try to solve this issue, the lab manager was asked by Cooper Surgical personnel to try to change the screen resolution to see if it would solve the problem, as they had never encountered this situation before.

It turned out that the operating system the computers in the laboratory were using was not compatible with the RI Witness version needed to run appropriately. Once again, the informatics department had to be called in to make the necessary adjustments. After doing so, the situation was resolved.

By this time, it was also established that once the technical part of the RI Witness system was 100% working, there would be a new training session with someone from Cooper Surgical.

This was necessary due to the 3-month period that had gone by since the previous training session had occurred. With all the setbacks and the staff members not being able put their acquired knowledge into practice, the information that had been given at that time needed to be refreshed.

RI Witness started to be used in the lab firstly with random procedures and later on with randomized patients before using it on every single patient.

By this time, working spaces were already established with, as an example, the right side of the workstation at the embryology area being strictly for oocyte search as well as transfers, due to the proximity to the patients' bracelet reader and consequently, the left side would be available for every other procedure.

On the 23rd of April a biopsy of an embryo on the 6th day of development was conducted using RI Witness. There was more than one embryo ready to be biopsied which became a problem when trying to use the EWS. The system did not allow for there to be more than one

biopsy associated with the sequential media plate and without this step it was not possible to proceed with the next phases to reach the embryo vitrification stage.

The same procedure had already been done previously with an embryo on the 5th day of development and everything went according to plan since there was only one embryo being biopsied and then vitrified. In the cases where more than one embryo was ready to be biopsied, there was the need to force the system into creating new biopsy plates, all due to the fact that the system in this case does not assume that a sequential media plate might have more than one embryo ready for biopsy.

The same does not occur when contemplating the GERI plate. In this case, RI Witness allows you to create more than one biopsy plate not revealing any problems when going through with the next steps to achieve the vitrification process.

With this incident, a new post biopsy dish was created for the embryologists to be able to continue with the next step, embryo vitrification.

As of the 6th of May, every patient's case was supervised fully with RI Witness, despite some incidents still occurring.

Such incidents include manual scanners that do not always work, and computers in the sample collection room that, in the beginning of the day, exhibit signs of poor internet connection. This is perhaps due to internet saturation and consequently not allowing the staff members to log in with their RI Witness users. For this reason, it has been requested that a cable connecting the computer directly to the internet connection is installed so that the computer does not need to be connected to the hospital's Wi-Fi.

At the present time, the cable has not been installed yet. Unexpectedly, the system has been working properly even at the beginning of the day, which was the period that caused more issues previously.

Additionally, when proceeding with the vitrification step, no problems came to light when printing the tags needed to identify each cryotop, however, after doing so, it was not possible to select the option vitrification in RI Witness.

All incidents were reported to the Cooper Surgical technician and the informatics department began their tests to evaluate the situation. Regarding the vitrification process, at this stage, the technician did not have a solution or answer as to why that step was not working.

It was thought at some point that an additional step had to be introduced in the RI Witness workflow diagram, the embryo re-biopsy. In some cases, the first biopsy is inconclusive and there is the need to re-do it and RI Witness needs to be equipped with this step in order for it to be performed.

Later on, they concluded that this step was actually not needed and that what happened was that it had been an error from one of the embryologists that prevented the option of doing another biopsy from appearing in the RI Witness system. By forgetting to attach a tag to a new dish, the system was not able to recognize it as a biopsy dish and consequently present the correct course of action in that case.

This shows the importance of practice with such a system, since the laboratory staff is not used to the presence of those technologies during the procedures, making them take longer than usual. This is consistent with the adaptability process expected after introducing a new work methodology.

Regarding the vitrification issue (mentioned previously), on another occasion, they realized a barcode reader had to be moved to a different location due to its malfunction. It used to be connected to the exterior part of the workstation but, due to a possible problem related to its use in tests performed by the informatics department, the connecting cable of the reader had a slight rupture and therefore it was not working properly.

This was the reason why the vitrification step was not appearing on the tablet screen to be selected. After connecting the manual reader directly to the tablet inside the workstation, no additional problems have been encountered.

6. Conclusions

Due to the long period of time it took for the system and every needed material to be in place and ready to use, I was not able to see the system working on a day-to-day basis in the laboratory. By the time that I wrote this dissertation, the laboratory had only been using RI Witness at its full capacities for approximately 1 month. The only time I was able to see the system working was during the first explanation given by the Cooper Surgical technician to the embryologists in the lab on how to use it. Therefore, I am not able to make specific conclusions regarding its ability to prevent true mismatches in this laboratory due to the short period of time that it was running in the lab.

Despite the roughly eight months it took for the RI Witness to start being used, plus some potential disadvantages, there are many advantages to the use of this system, as stated previously. The main one being preventing mismatches from occurring in the lab.

The prospect of having an automated system able to prevent mismatches and document fully the activity undergoing in the lab seems very appealing to be in place in every IVF laboratory.

Moreover, the other advantages it brings to the table surpass the potential disadvantages and difficulties that arose in the beginning, as it is normal when introducing a new system in the pre-existing workflow of the lab.

Furthermore, many of the difficulties that were encountered during the initial phase can be partially attributed to the fact that the laboratory is inserted into a larger net of patient's database that are part of a hospital with many different specialties.

This means safety measures are stricter than in an usual clinic, and the number of steps that had to be taken to ensure informatic safety concerning the tablets' and computers' were much greater. Therefore, the process should run more smoothly and quickly when trying to install it in a clinic rather than a hospital.

As a final conclusion, the implementation of an EWS should be considered in every laboratory as a way of preventing the wrong pairing of gametes and wrong embryo transfers, keeping digital records of every patient's treatment as well as improving patient care.

Technology has come to stay in our laboratories, and we should embrace it as the helpful tool it is to get us to achieve our best results possible every day.

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Figure 3 - Gupta, S., Fauzdar, A., Singh, V., Srivastava, A., Sharma, K., & Singh, S. (2020). A Preliminary Experience of Integration of an Electronic Witness System, its Validation, Efficacy on Lab Performance, and Staff Satisfaction Assessment in a Busy Indian in vitro Fertilization Laboratory. *Journal of Human Reproductive Sciences*, *13*(4), 333–339. https://doi.org/10.4103/jhrs.JHRS_66_20

Figure 5 - Retrieved from the RI Witness program from the University Hospital Quirónsalud, Madrid laboratory.