

TECNOLOGIE WITNESS E CRIOCONSERVAZIONE

TECNOLOGIE WITNESS E CRIOCONSERVAZIONE



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Roma, Marostica, Napoli, Umbertide

**Optimizing
Human Gamete
and Embryo Freezing**

13 giugno 2014



Human Fertilisation and Embryology (HFE) Act 1990 (as amended)

2 Other terms

(1) “traceability” means the ability–

(a) to identify and locate gametes and embryos during any step from procurement to use for human application or disposal,

(b) identify the donor and recipient of particular gametes or embryos,

(c) to identify any person who has carried out any activity in relation to particular gametes or embryos, and

(d) to identify and locate all relevant data relating to products and materials coming into contact with particular gametes or embryos and which can affect their quality or safety.



Witnessing clinical and laboratory procedures



Mandatory requirements

Licence conditions

- T71 Centres must have in place robust and effective processes to ensure that no mismatches of gametes or embryos or identification errors occur. Centres 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.



Witnessing clinical and laboratory procedures

- 18.1** Witnessing protocols should ensure that every sample of gametes or embryos can be identified at all stages of the laboratory and treatment process to prevent any mismatches of gametes or embryos.
- 18.2** Centres are responsible for ensuring that witnessing protocols are relevant to their local systems and conditions, based on HFEA model protocols. Where appropriate, clinics may adapt HFEA model protocols to take into account their local systems.

See also:

- **Relevant HFEA model protocols at:**
www.hfea.gov.uk/docs/witnessing-protocols.pdf

- 18.3** Electronic systems such as barcoding and radio frequency identification (RFID) for assisted conception are appropriate, subject to a risk assessment as set out at 18.34–18.43.

ELECTRONIC WITNESSING: OUR EXPERIENCE

- **Significant increase in the number of IVF cycles performed at our centre**
- **Need to improve our lab efficiency**
 Double manual witnessing is time consuming and distracting
 Concept of “Involuntary automaticity” → the second witness may see what he “expected to see”

	RI Witness™	Barcoding systems such as Matcher™ and Human double-witnessing
Sample Checking / Forcing Function	The system scans and detects all labware <u>automatically</u> where procedures are performed. Therefore, users cannot skip a check or perform a procedure without being checked.	The labware must be presented by the user for identification (either to a barcode reader, or a human witness). The safety of the lab therefore <u>relies on people remembering</u> to perform the checks.
Prevention of mistakes	If incompatible labware is brought into the working area then the user is immediately alerted visually and audibly before any work can be carried out. A potential mistake is therefore avoided.	For a potential mistake to be avoided, the user must remember to initiate a check prior to commencing work. When using multiple dishes and tubes, great care must be taken to ensure that all the labware has been correctly checked.

OUR EXPERIENCE: ELECTRONIC WITNESSING

Electronic witnessing

RFID Tags

RFID Tag Reader



Square RFID Tag



Test Tube with RFID Tag



Circular RFID Tag



RFID Patient Card

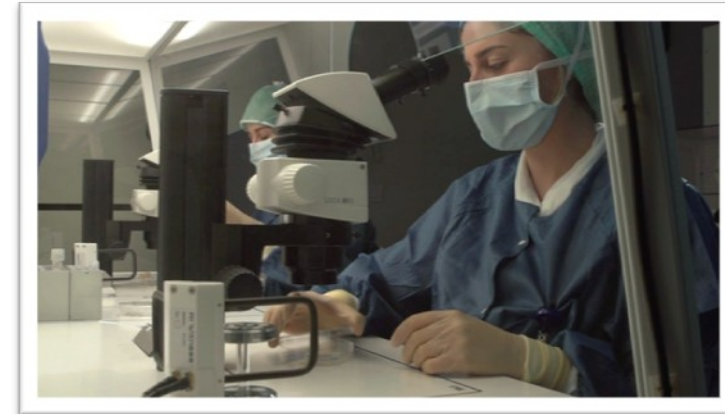


Controlling software

OBSERVATIONAL STUDY – OBSERVED OUTCOMES

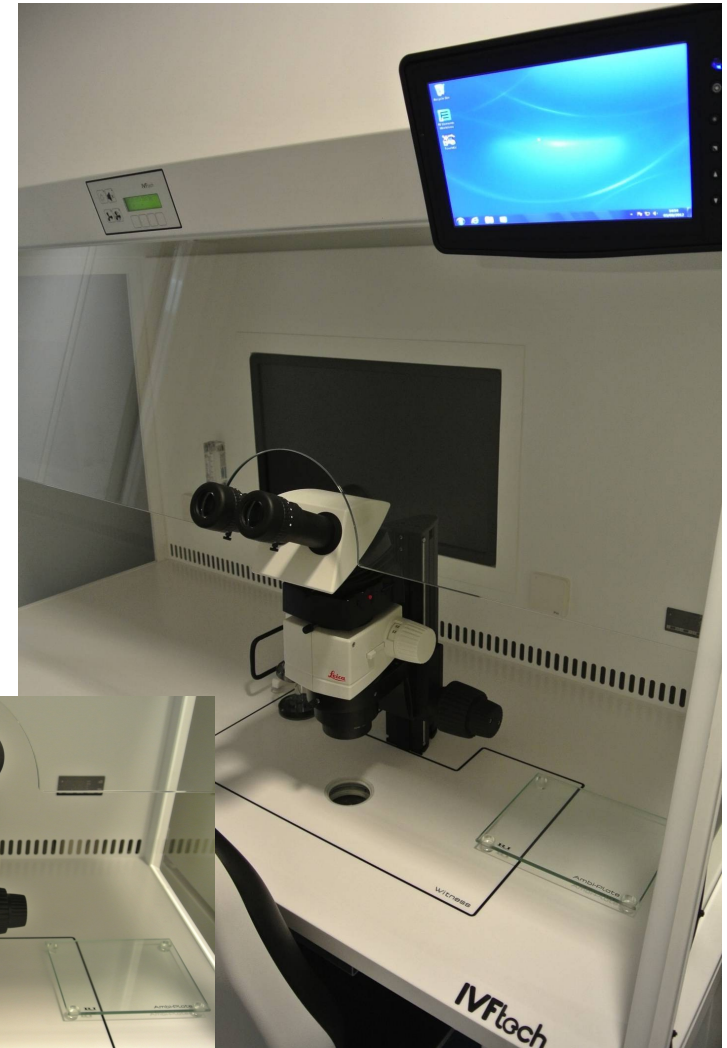
Timing required for an *ex-novo* installation of an electronic witnessing system (RI Witness™) into a busy IVF clinic:

- to integrate and install the system in the working area
- for the setting and configuration of the workflow-chart
- Patient Satisfaction
- for the training of all the clinical embryologists



INTEGRATION OF THE SYSTEM

- Work Area Readers
 - Controlling Software
- ⇒ 4 working days
- PC Ad Monitor
 - Barcode Reader
- Training of Laboratory Staff
- ⇒ 7 working days

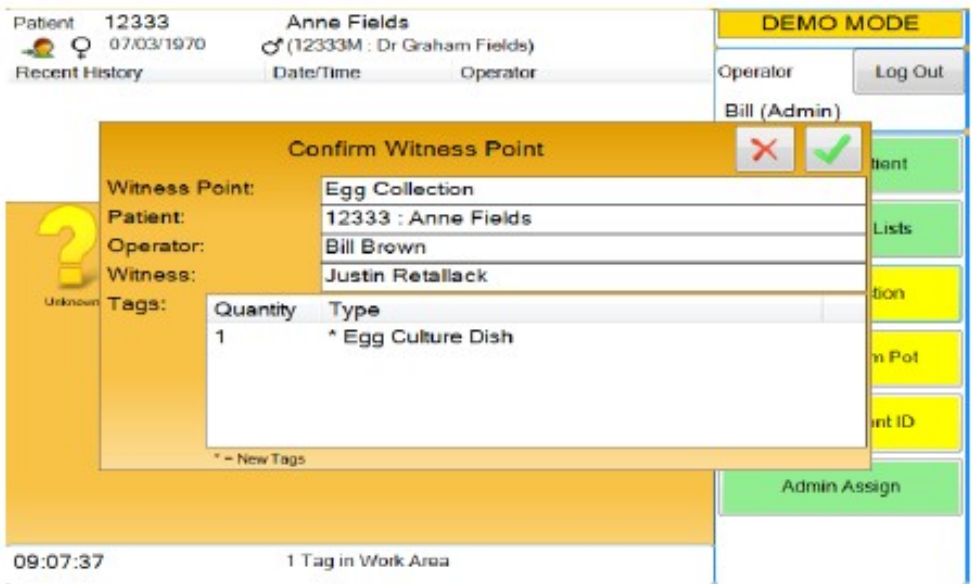


VALIDATION PERIOD - SEPTEMBER 2012

- Adjustment of the system workflow according to our laboratory's existing protocols
- Reduction of the system users errors to less than 1%
- Double manual witnessing simultaneously performed



- “True mismatches”= mismatches derived from a simultaneous presence of two different patient samples in the working area
- “Secondary mismatches” = mismatches derived from acceptable common errors (i.e. pre-allocated tags within the frequency range of the reader, but outside of the workstation)



Patient 12333 Anne Fields
 07/03/1970 (12333M : Dr Graham Fields)
 Recent History Date/Time Operator

DEMO MODE
 Operator Log Out
 Bill (Admin)

Confirm Witness Point

Witness Point: Egg Collection
 Patient: 12333 : Anne Fields
 Operator: Bill Brown
 Witness: Justin Retallack

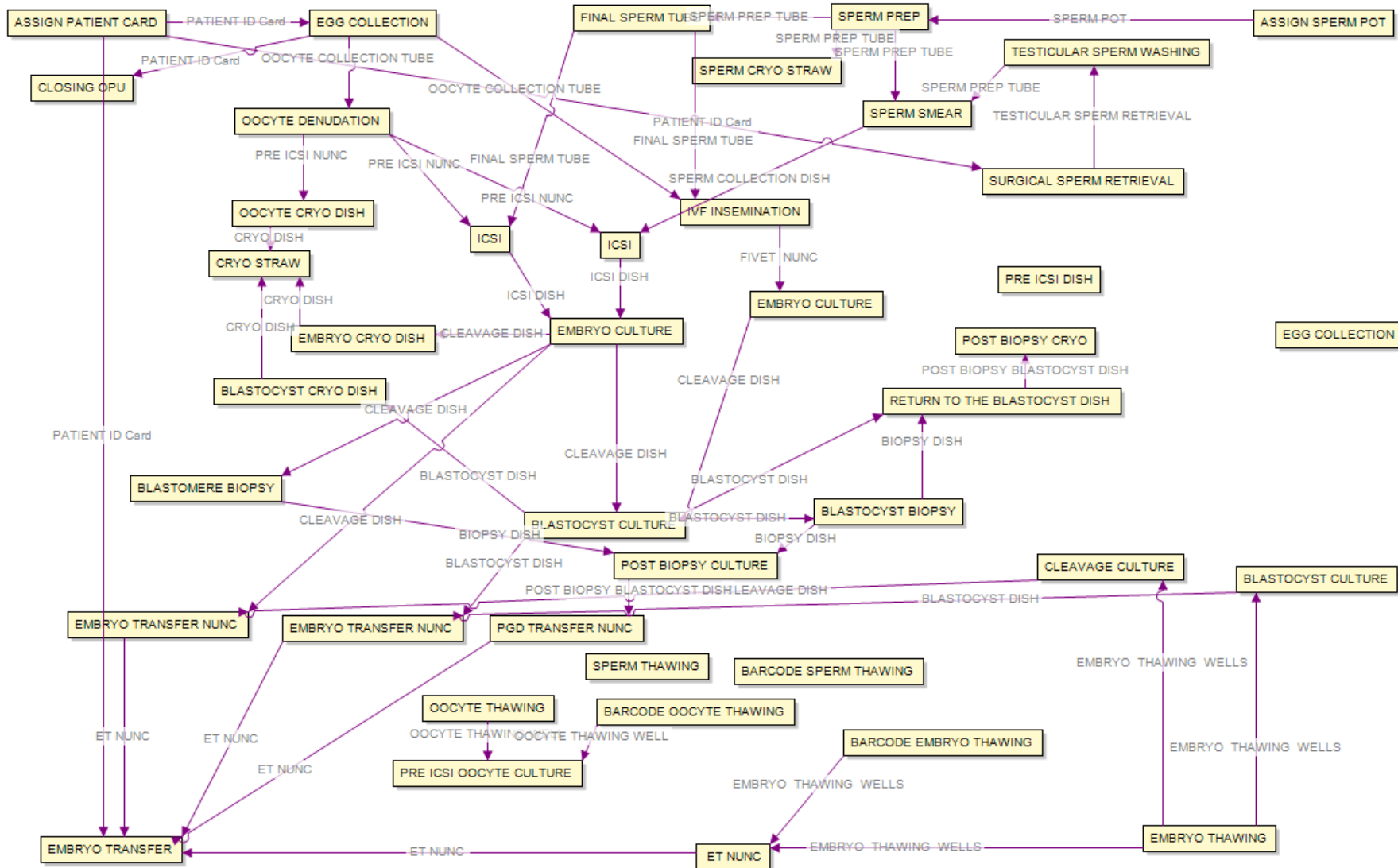
Quantity	Type
1	* Egg Culture Dish

* - New Tags

09:07:37 1 Tag in Work Area

Admin Assign

CONFIGURATION OF THE WORKING FLOW CHART



RESULTS



	Validation period	Post-validation period
Patients (N)	302	852
Witnessing steps (N)	2099	5921
Mismatch rate (%)	0.80% (17/2099)	0.66% (39/5921)
“True mismatch” rate (%)	0.09% (2/2099)	0.10% (6/5921)
“Secondary mismatch” rate (%)	0.71% (15/2099)	0.56% (33/5921)

0.1% mismatch/step x 7 steps/cycle = ~0.7% mismatch/cycle
x 0.25 pregnancy/cycle = ~0.17% mismatch/pregnancy



*Center for Reproductive Medicine
presents:*

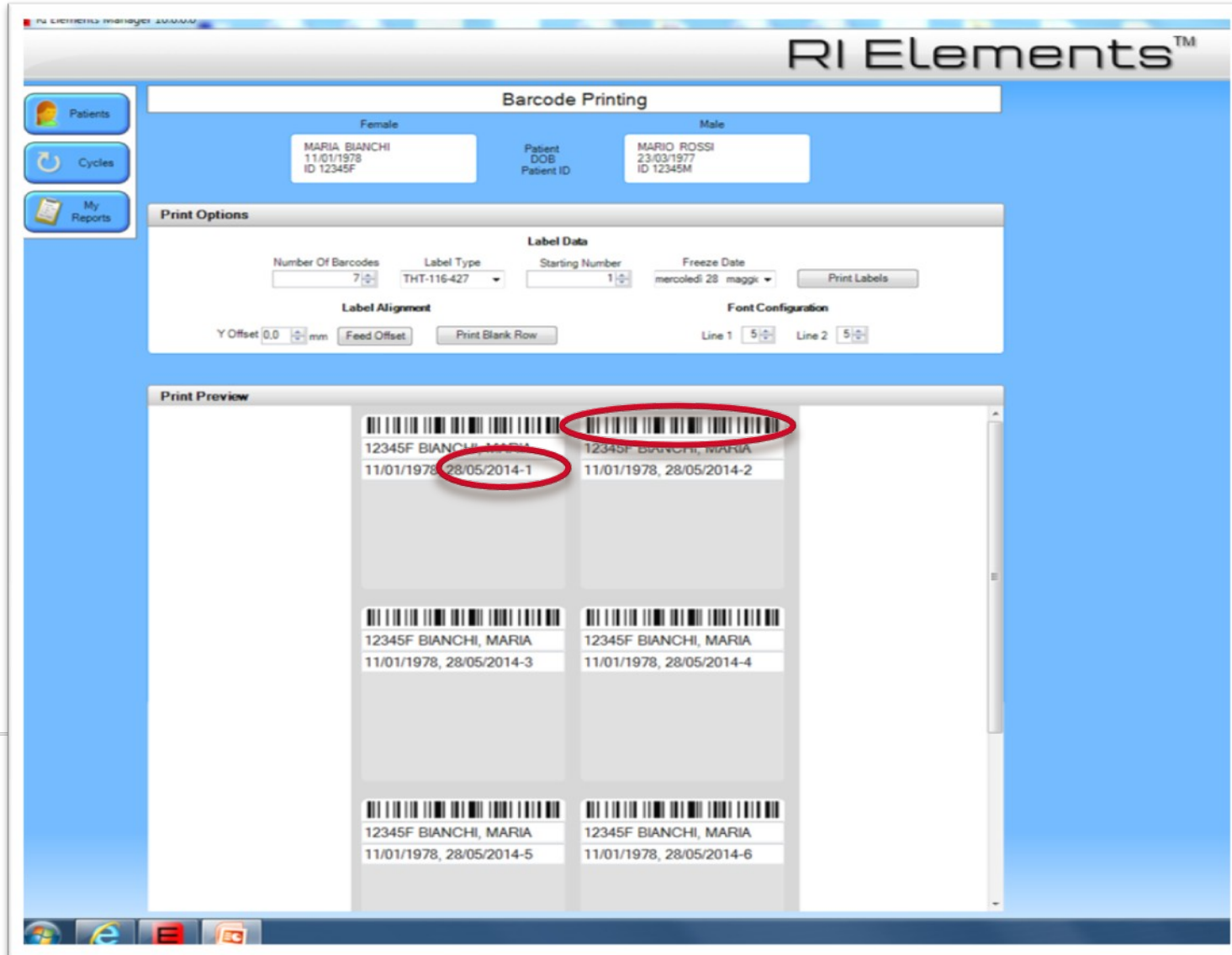
**Implementing
An Electronic Witnessing System
Into A Busy IVF Clinic**

ELECTRONIC WITNESSING: CRYO ELEMENTS



- A secure system providing exit and entry point management between the Lab & cryopreservation using Brady® barcode labels.

ELECTRONIC WITNESSING: CRYO ELEMENTS



The screenshot displays the RI Elements software interface for barcode printing. The main window is titled "Barcode Printing" and features a navigation sidebar on the left with buttons for "Patients", "Cycles", and "My Reports".

At the top, there are two patient selection boxes: "Female" (selected) and "Male". The "Female" box contains the name "MARIA BIANCHI", DOB "11/01/1978", and ID "12345F". The "Male" box contains the name "MARIO ROSSI", DOB "23/03/1977", and ID "12345M".

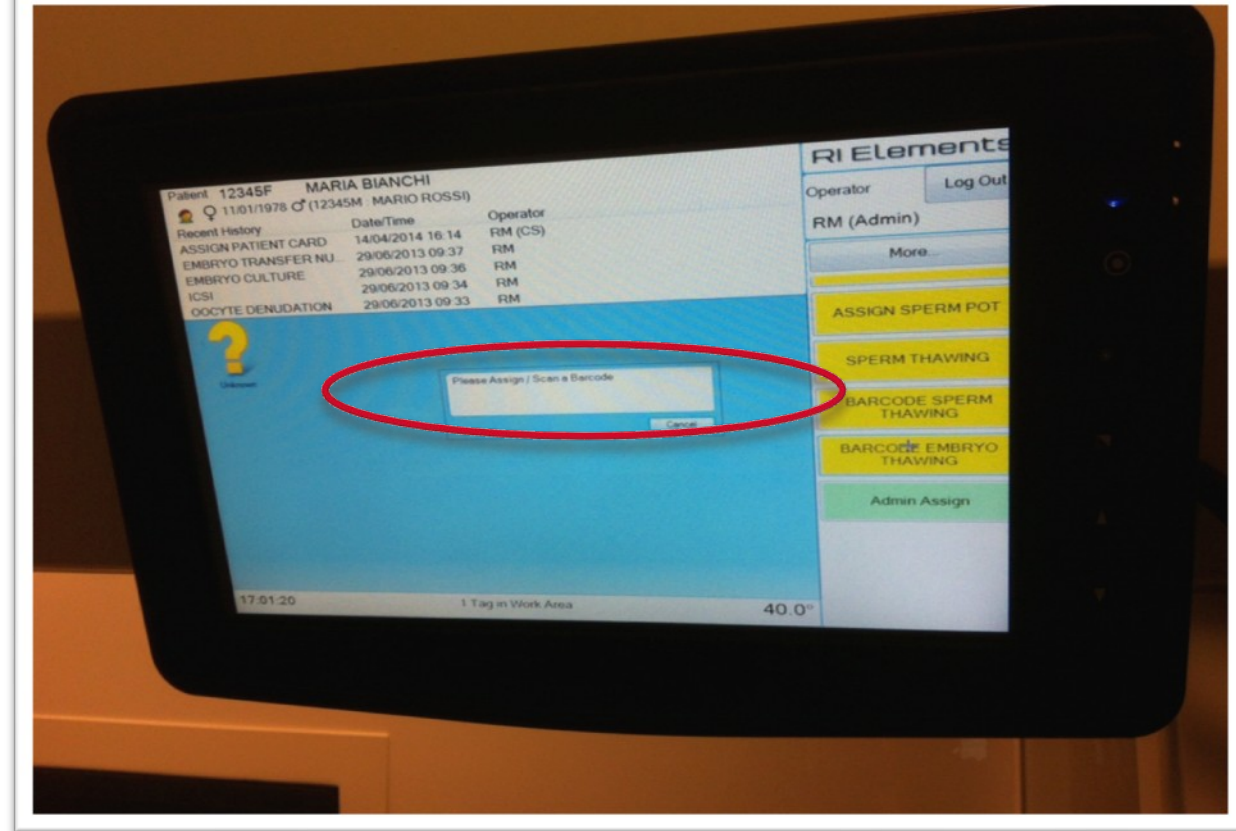
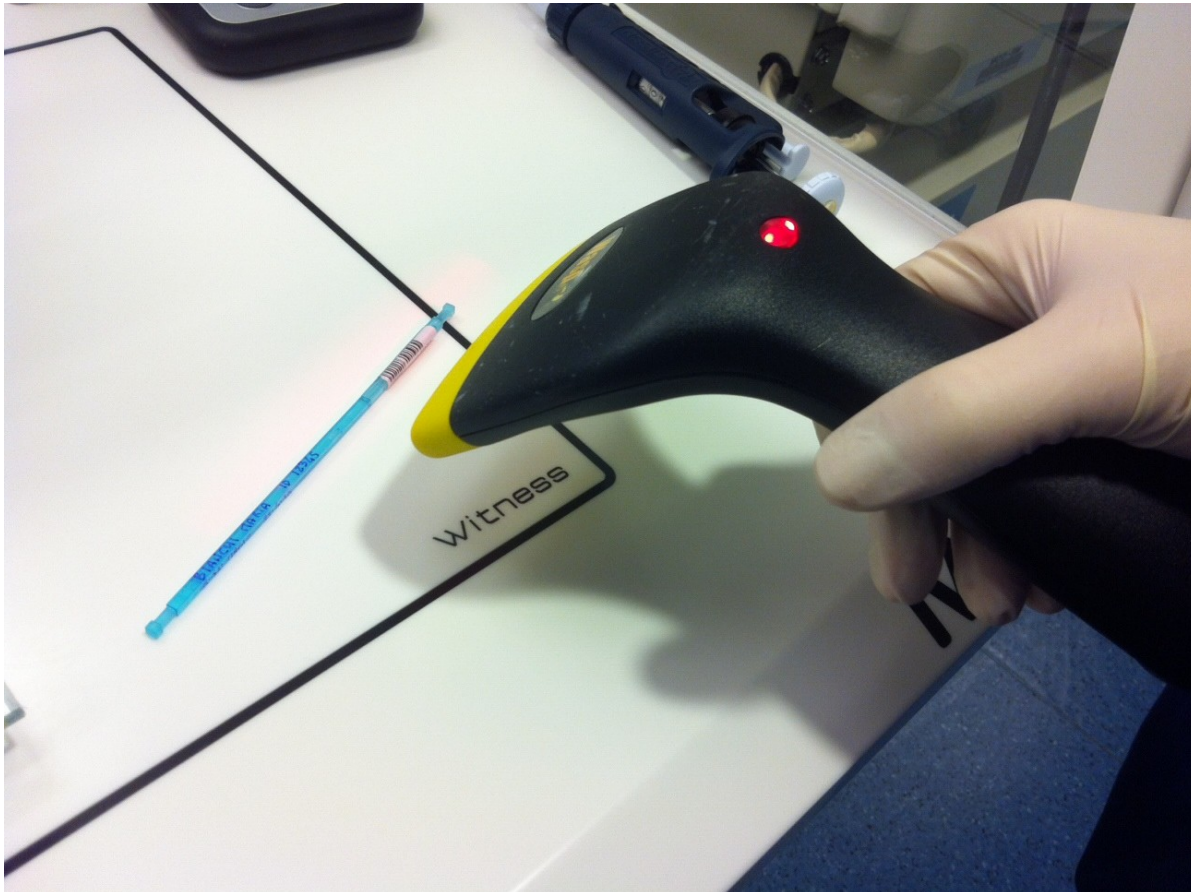
The "Print Options" section includes:

- Label Data:** Number Of Barcodes (7), Label Type (THT-116-427), Starting Number (1), and Freeze Date (mercoledì 28 maggio).
- Label Alignment:** Y Offset (0.0 mm), Feed Offset, and Print Blank Row.
- Font Configuration:** Line 1 (5) and Line 2 (5).

A "Print Labels" button is located to the right of the Label Data section.

The "Print Preview" section shows a grid of six labels. The first two labels are circled in red. The first label is for "12345F BIANCHI, MARIA" with DOB "11/01/1978" and a date "28/05/2014-1". The second label is for "12345F BIANCHI, MARIA" with DOB "11/01/1978" and a date "28/05/2014-2". The remaining four labels are for "12345F BIANCHI, MARIA" with DOB "11/01/1978" and dates "28/05/2014-3", "28/05/2014-4", "28/05/2014-5", and "28/05/2014-6".

ELECTRONIC WITNESSING: CRYO ELEMENTS



ELECTRONIC WITNESSING: WEAKNESS

Scongelo di Embri per uso nel trattamento 09035014911
PAZIENTE (0025)

Data scong.
Oper. scong.
Testim. scong.
Tecnica scong.

Collocazione dispositivi: C
Crioprot. usato: KITAZAT

Embr.
<input type="checkbox"/> 1
<input type="checkbox"/> 5
<input checked="" type="checkbox"/> 6
<input type="checkbox"/> 7
<input type="checkbox"/> 8
<input type="checkbox"/> 10

Collocazione dispositivi: C
Crioprot. usato: KITAZAT

Embr.
<input checked="" type="checkbox"/> 6

Collocazione dispositivi: C
Crioprot. usato: KITAZAT

Embr.
<input type="checkbox"/> 7
<input type="checkbox"/> 11

PGS Cycles

gr1; C13.
gr1; C12.
gr1; C12.
gr1; C12.
C23; C23.
gr1; C22.

Aneuploid

Euploid

KEEP CALM AND DOUBLE CHECK

12345F BIANCHI, MARIA
11/01/1978, 28/05/2014-4

12345F BIANCHI, MARIA
11/01/1978, 28/05/2014-4

Andretto | scongelo selezionati

DIRECT LABELING SYSTEM: SILICONE-BASED BARCODES

To provide a proof of concept for a direct oocyte/embryo labeling system

Human Reproduction, Vol.26, No.1 pp. 96–105, 2011

Advanced Access publication on November 18, 2010 doi:10.1093/humrep/deq309

human
reproduction

ORIGINAL ARTICLE *Embryology*

A novel embryo identification system by direct tagging of mouse embryos using silicon-based barcodes

Sergi Novo¹, Leonardo Barrios¹, Josep Santaló¹,
Rodrigo Gómez-Martínez², Marta Duch², Jaume Esteve²,
José Antonio Plaza², Carme Nogués¹, and Elena Ibáñez¹

¹Departament de Biologia Cel·lular, Fisiologia i Immunologia, Facultat de Biociències, Universitat Autònoma de Barcelona, Spain ²Instituto de Microelectrónica de Barcelona, IMB-CNM (CSIC), Campus Universitat Autònoma de Barcelona

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Hum. Reprod. Advance Access published November 13, 2013

Human Reproduction, Vol.0, No.0 pp. 1–11, 2013

doi:10.1093/humrep/det409

human
reproduction

ORIGINAL ARTICLE *Embryology*

Barcode tagging of human oocytes and embryos to prevent mix-ups in assisted reproduction technologies

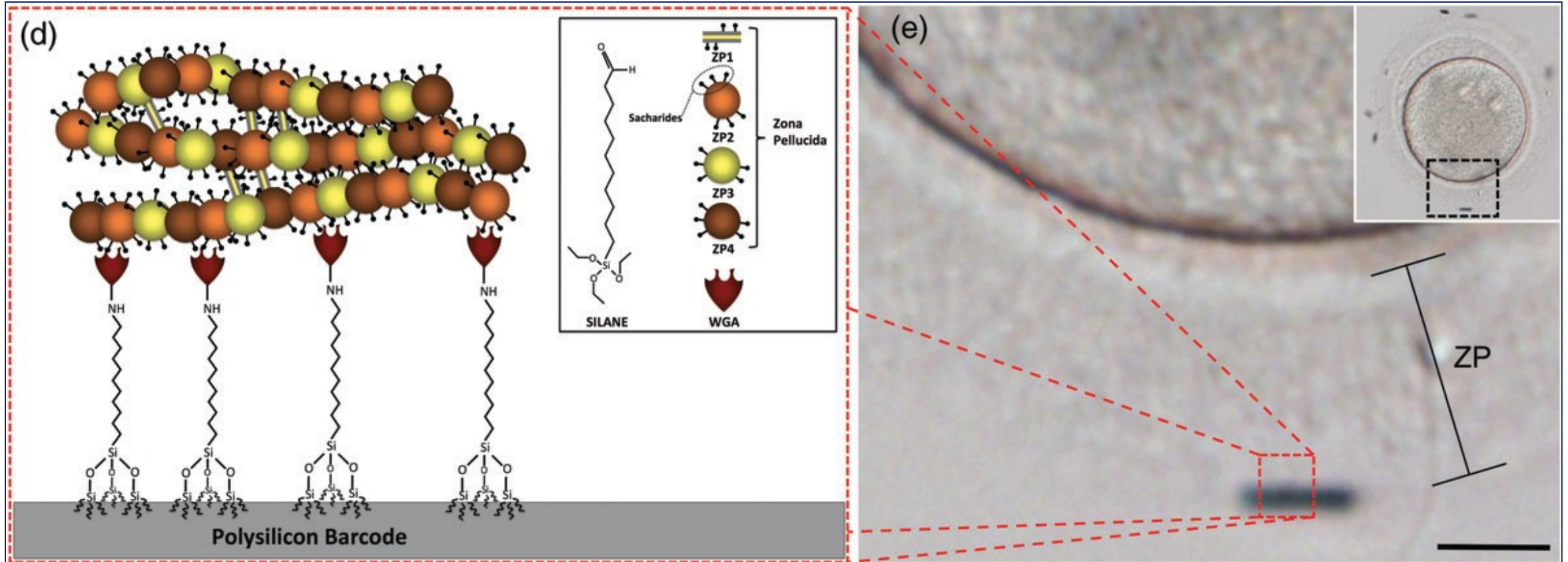
Sergi Novo¹, Carme Nogués¹, Oriol Penon², Leonardo Barrios¹,
Josep Santaló¹, Rodrigo Gómez-Martínez³, Jaume Esteve³,
Abdelhamid Errachid⁴, José Antonio Plaza³, Lluïsa Pérez-García²,
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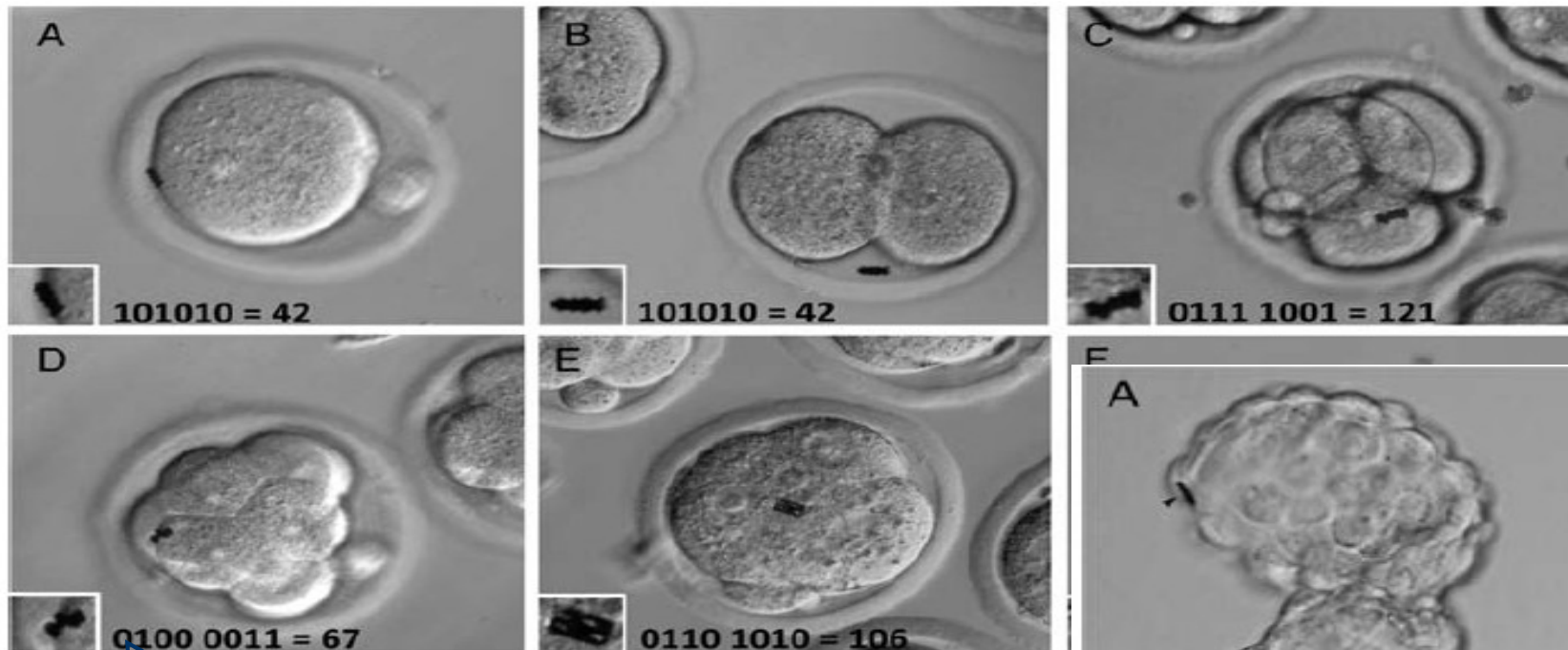
SILICONE-BASED BARCODES



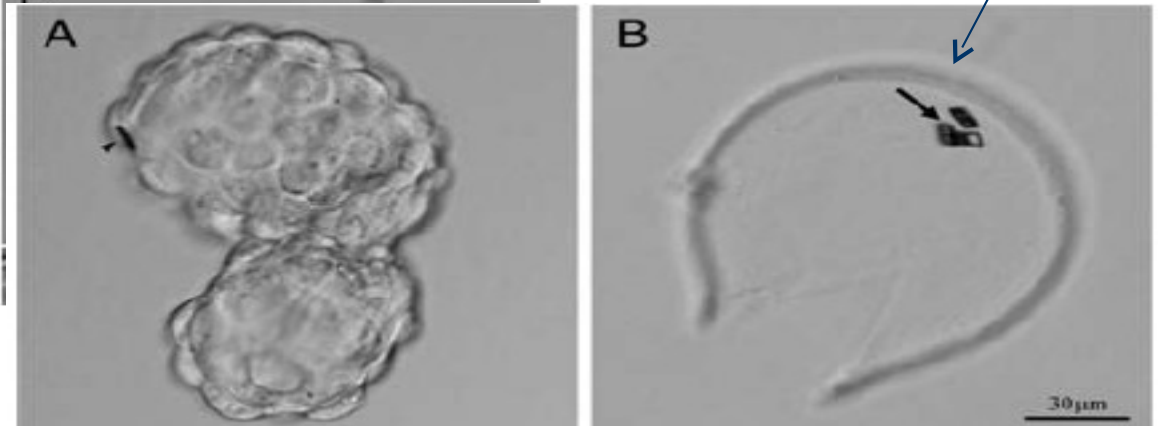
DIRECT LABELING SYSTEM: SILICONE-BASED BARCODES

In vitro development of embryos microinjected with different types of polysilicon barcodes into their perivitelline space.

MOUSE MODEL



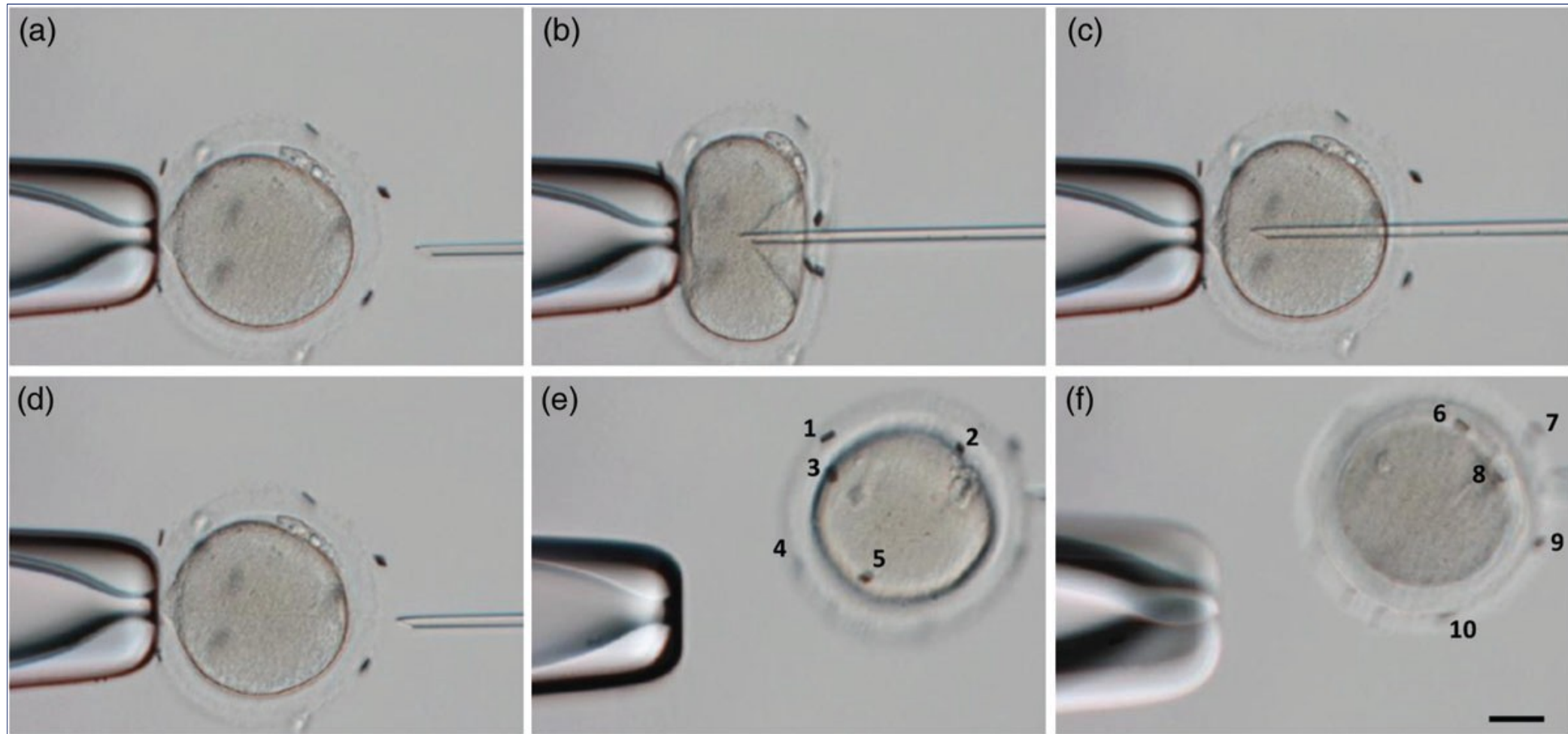
Remaining barcodes



Magnified images of the barcodes

DIRECT LABELING SYSTEM: SILICONE-BASED BARCODES

HUMAN OOCYTES



DIRECT LABELING SYSTEM: SILICONE-BASED BARCODES

Table V Morphokinetic parameters of control and tagged embryos developed up to full blastocyst stage.

Parameter analyzed	Time (h \pm SEM (n))	
	Control	Tagged
Disappearance of pronuclei time-point	9.1 \pm 0.6 (16)	8.2 \pm 0.7 (19)
1st cytokinesis duration	0.45 \pm 0.03 (19)	0.47 \pm 0.05 (21)
2-Cell stage time-point	13.9 \pm 1.8 (19)	11.9 \pm 0.8 (21)
Reappearance of nuclei after first cleavage time-point	15.2 \pm 0.9 (10)	16.1 \pm 1.5 (13)
Reappearance of nuclei after first cleavage duration	3.0 \pm 0.4 (10)	3.3 \pm 0.5 (13)
3-Cell stage time-point ^a	26.5 \pm 2.8 (17)	24.6 \pm 1.3 (18)
2-Cell stage duration ^a	12.6 \pm 0.6 (17)	12.7 \pm 0.7 (18)
4-Cell stage time-point	27.4 \pm 2.4 (19)	26.2 \pm 1.2 (21)
3-Cell stage duration ^a	1.0 \pm 0.2 (17)	1.3 \pm 0.3 (18)
5-Cell stage time-point	39.2 \pm 2.6 (19)	41.8 \pm 2.2 (21)
Compaction time-point	77.2 \pm 1.9 (19)	75.2 \pm 1.4 (21)
Morula time-point	85.4 \pm 2.0 (19)	84.0 \pm 1.7 (21)
Blastocyst time-point	94.8 \pm 2.0 (19)	92.0 \pm 1.9 (21)
Full Blastocyst time-point	104.1 \pm 2.4 (19)	101.2 \pm 2.3 (21)

SEM, standard error of the mean. No significant differences were detected for any parameter analyzed between control and tagged embryos ($P > 0.05$; Mann-Whitney and Student's *t*-test).

^aData for two control and three tagged embryos that divided directly from 1 to 3 cells are missing.

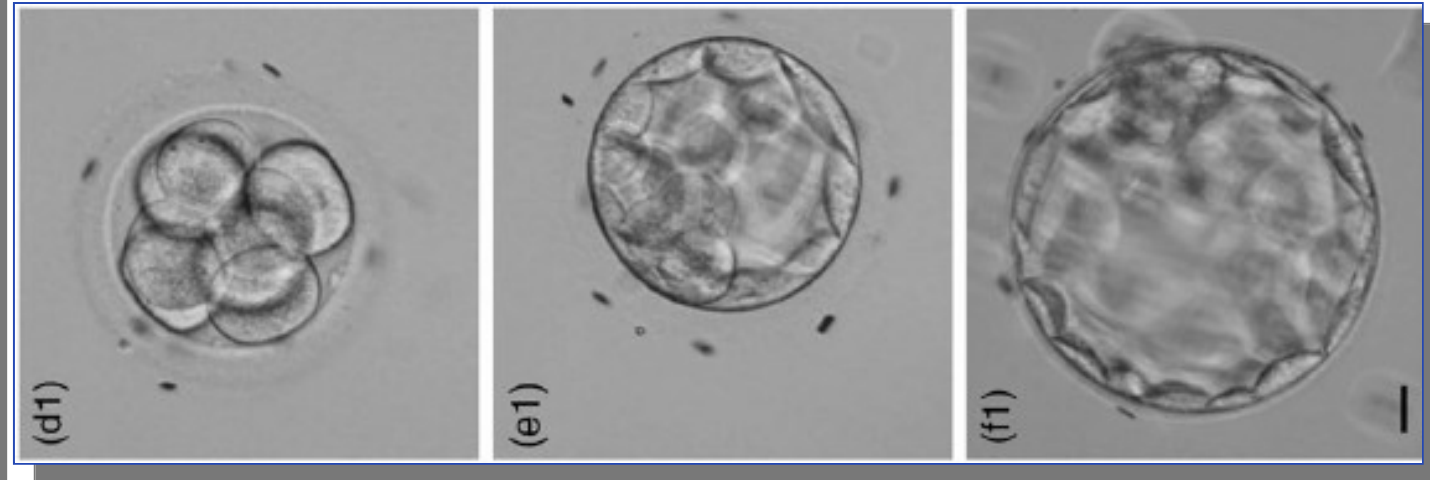


Table IV Cell counts in Day 6 blastocysts after differential staining.

Group	No. of blastocysts	Mean number of cells/blastocyst \pm SEM			Mean of ICM/TCN ratios \pm SEM
		TCN	ICM	TE	
Control	24	100.9 \pm 11.2	22.3 \pm 1.9	78.5 \pm 9.4	0.24 \pm 0.01
Tagged	25	111.9 \pm 13.6	24.7 \pm 2.5	87.2 \pm 11.3	0.23 \pm 0.01

No significant differences were detected for any of the parameters analyzed between control and tagged blastocysts ($P > 0.05$; Mann-Whitney and Student's *t*-test). SEM, standard error of the mean; TCN, total cell number; ICM, inner cell mass; TE, trophectoderm.

ELECTRONIC WITNESSING: PATIENT SATISFACTION

Does the introduction of an electronic witnessing system in the IVF lab hold the potential to reduce patients anxiety about mismatching errors and to enhance couple satisfaction?



ELECTRONIC WITNESSING: PATIENT SATISFACTION

A questionnaire consisting of 8 items was developed on the basis of patients forum and literature analysis on the topic.



Sociodemographic variables:

- Age
- Gender
- Education
- Previous IVF treatments

g.en.e.r.a. Studio ID | 022013

Sesso compilatore: M F

ANALISI DI GRADIMENTO DEL NUOVO TESTIMONE ELETTRONICO PER L'IDENTIFICAZIONE DEI CAMPIONI BIOLOGICI

In collaborazione con la Psicologa, Dott.ssa Marina Forte e lo Statista Dott. Alessio Farcomeni, Università La Sapienza di Roma.

Con questo questionario vi chiediamo gentilmente di esprimere il vostro prospetto su questa nuova tecnologia di identificazione dei campioni biologici (ovociti, spermatozoi, embrioni) recentemente introdotta nei nostri laboratori. Vi informiamo che i dati personali saranno trattati in conformità ai sensi dell'articolo 23 del D.Lgs. 30 giugno 2003, n. 196 sulla privacy e utilizzati in forma anonima a fini di pubblicazioni scientifiche. Vi ringraziamo sentitamente per la vostra collaborazione nel miglioramento del nostro servizio.

1. In merito alla procedura di identificazione dei campioni biologici, l'uso di un sistema elettronico (IVF Witness) rispetto al sistema tradizionale (IVF Standard) è:

1= molto più sicuro; 2= un po' più sicuro; 3= abbastanza sicuro; 4= molto sicuro; 5= moltissimo sicuro; 6= nessuna opinione

2. L'uso di un sistema elettronico (IVF Witness) rispetto al sistema tradizionale (IVF Standard) è:

1= molto più preciso; 2= un po' più preciso; 3= abbastanza preciso; 4= molto preciso; 5= moltissimo preciso; 6= nessuna opinione

3. L'uso di un sistema elettronico (IVF Witness) rispetto al sistema tradizionale (IVF Standard) è:

1= molto più affidabile; 2= un po' più affidabile; 3= abbastanza affidabile; 4= molto affidabile; 5= moltissimo affidabile; 6= nessuna opinione

4. L'uso di un sistema elettronico (IVF Witness) rispetto al sistema tradizionale (IVF Standard) è:

1= molto più sicuro; 2= un po' più sicuro; 3= abbastanza sicuro; 4= molto sicuro; 5= moltissimo sicuro; 6= nessuna opinione

5. L'uso di un sistema elettronico (IVF Witness) rispetto al sistema tradizionale (IVF Standard) è:

1= molto più preciso; 2= un po' più preciso; 3= abbastanza preciso; 4= molto preciso; 5= moltissimo preciso; 6= nessuna opinione

6. L'uso di un sistema elettronico (IVF Witness) rispetto al sistema tradizionale (IVF Standard) è:

1= molto più affidabile; 2= un po' più affidabile; 3= abbastanza affidabile; 4= molto affidabile; 5= moltissimo affidabile; 6= nessuna opinione

7. L'uso di un sistema elettronico (IVF Witness) rispetto al sistema tradizionale (IVF Standard) è:

1= molto più sicuro; 2= un po' più sicuro; 3= abbastanza sicuro; 4= molto sicuro; 5= moltissimo sicuro; 6= nessuna opinione

8. L'uso di un sistema elettronico (IVF Witness) rispetto al sistema tradizionale (IVF Standard) è:

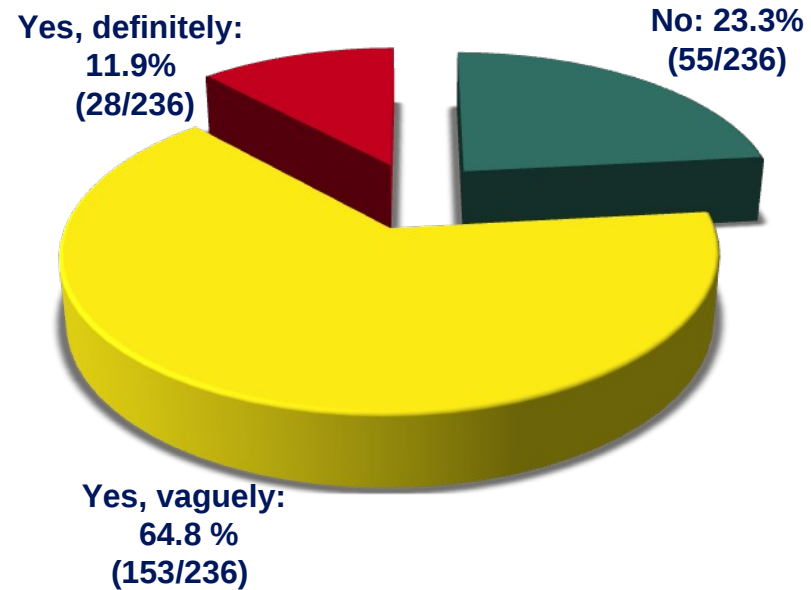
1= molto più preciso; 2= un po' più preciso; 3= abbastanza preciso; 4= molto preciso; 5= moltissimo preciso; 6= nessuna opinione

A likert scale of values ranging from 0 to 6 has been assigned to each answer

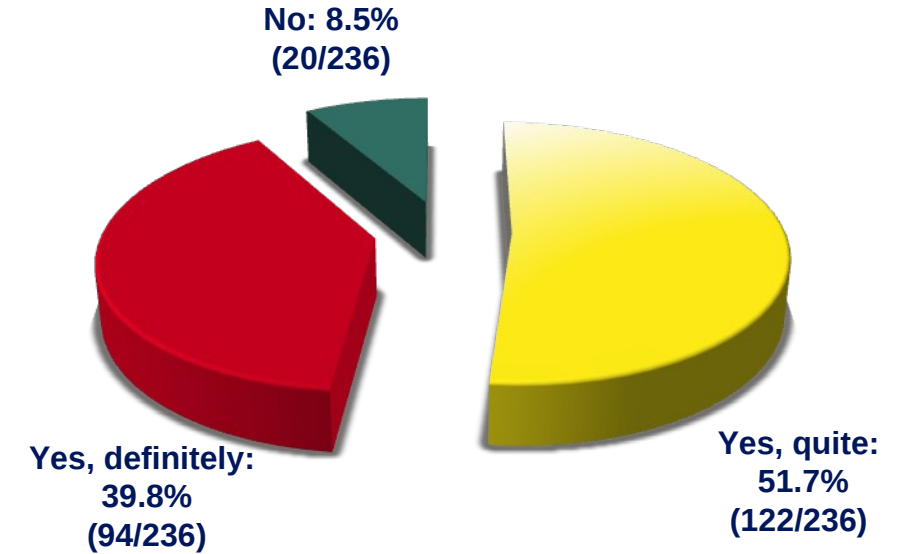
ELECTRONIC WITNESSING: PATIENT SATISFACTION



Awareed of IVF “mix-up” risk?



Concerned about IVF “mix-up”?

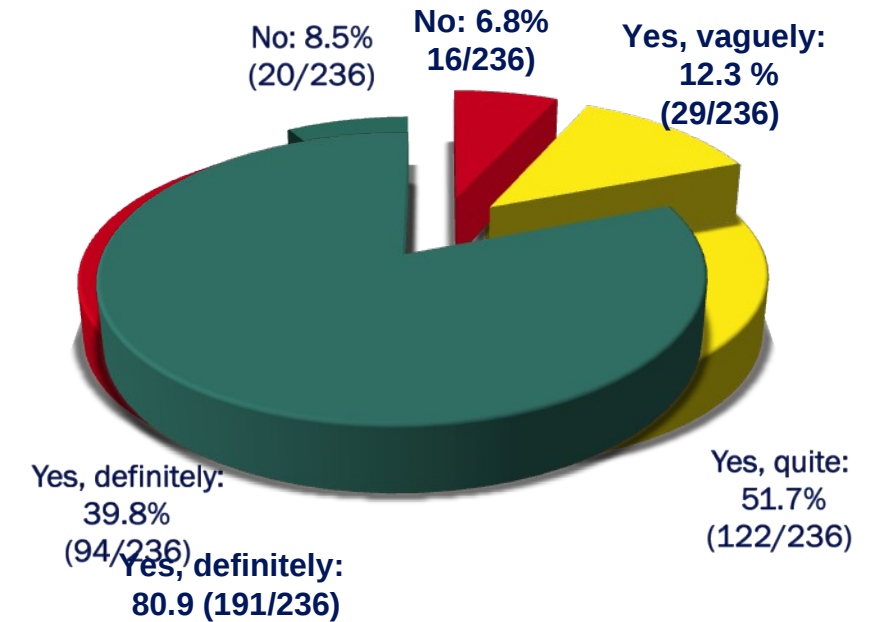


ELECTRONIC WITNESSING: PATIENT SATISFACTION

Anxiety reduction with EW?



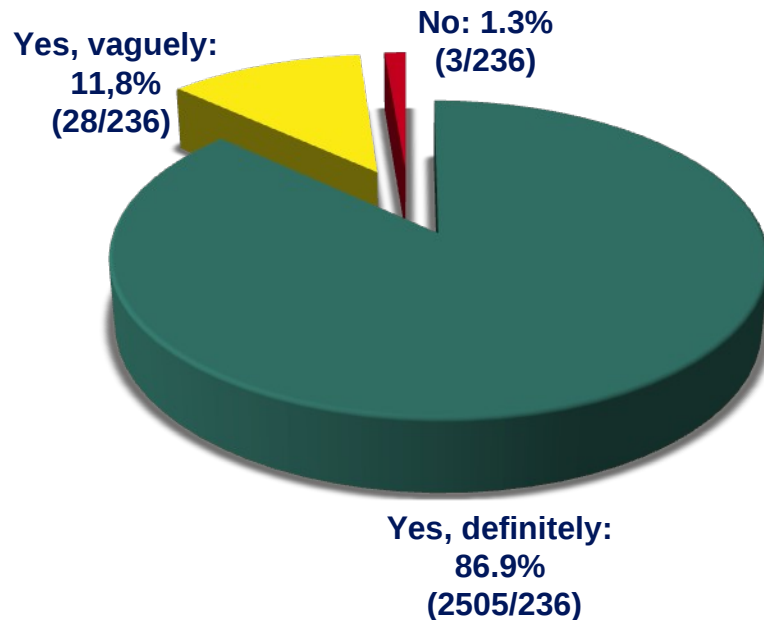
ELECTRONIC WITNESSING



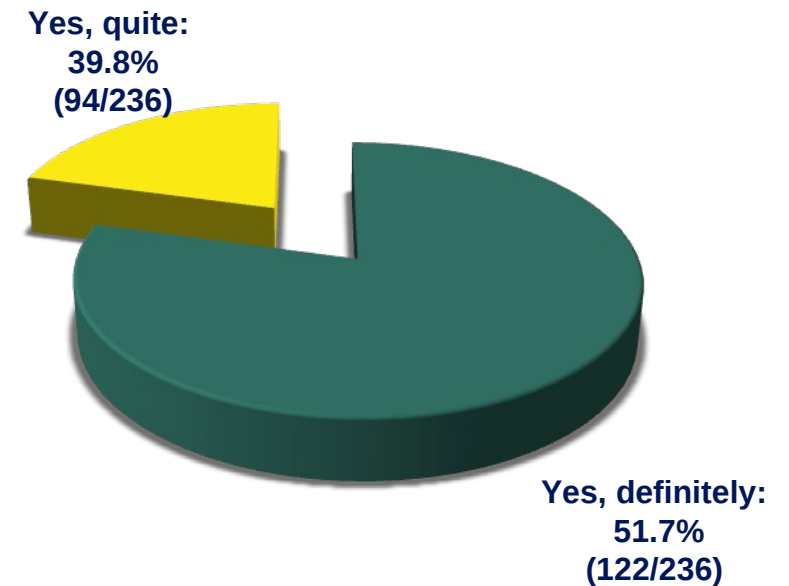
ELECTRONIC WITNESSING: PATIENT SATISFACTION



Traceability



Patients reassurance



Multiple logistic regression analysis did not revealed any influence of socio-demographic variables on patient's attitudes toward IVF electronic witness system.

BENEFITS

- Easy to implement
- Safeguards the reliability of the entire IVF process
- Traceability of each step performed
- Reduction of staff workload and distractions
- Patients reassurance

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