GIỚI HẠN VÀ HƯỚNG TỐI ƯU CHO CÔNG NGHỆ TTTON TẠI VIỆT NAM

ThS. Mai Công Minh Tâm

Bệnh viện Âu Cơ, Biên Hoà – Đồng Nai.

Mục tiêu

1. Cung cấp các thông tin liên quan công nghệ Labo TTTON

2. Cung cấp các chứng cứ Y học liên quan đến Labo TTTON

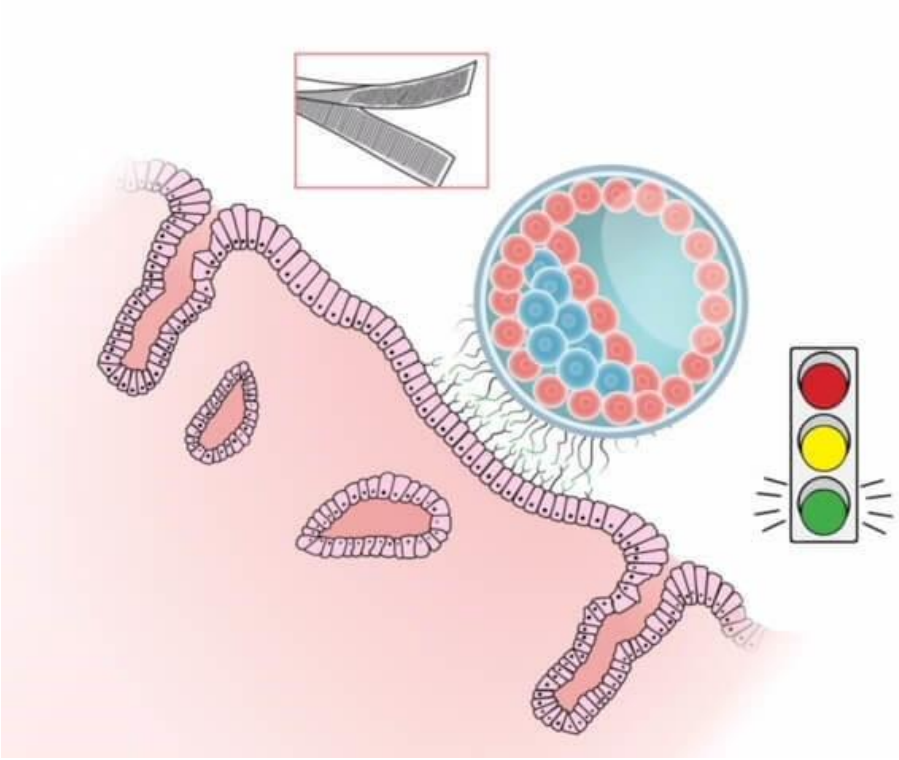
3. Cung cấp các hướng giải pháp giúp tối ưu hoá kết quả Labo TTTON tại Việt Nam.

Nội dung

1. Cấu trúc cơ bản của một Labo TTTON hiệu quả
2. Các công nghệ của Labo TTTON giúp tối ưu hoá kết quả điều trị
3. Các vấn đề còn đang tranh cãi
4. Các thông tin cần thiết để tư vấn TTTON

Để một chu kỳ TTTON thành công ?

(EI = EQ x ER x TE)

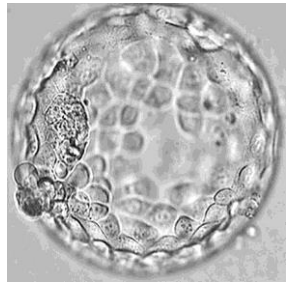


1. Chất lượng phôi (EQ = Embryo quality)
2. Chuyển phôi (TE=Transfer efficiency)
3. Tiếp nhận của Tử cung (ER=Endometrial receptivity)

Paulson et al, AJOG 1990;163:2020


EMBRYOSCOPE

Labo TTTON – Nuôi cấy phôi



Phòng sạch (Vô trùng)

ISO 5/6/7/8 (ISO 14644-1)

Class A/B/C/D (EU GMP 2008)

Tủ cấy hiện đại

Tủ cấy lớn (large incubator)

Tủ cấy thế hệ mới (bench-top)

Tủ cấy time-lapse (TL incubator)

Sàng lọc và chọn lựa phôi

Hình thái phôi (Morphology)

Động học phôi (Time-lapse monitoring)

Di truyền phôi (PGT A/SR/M)

Labo TTTON – Trữ rã phôi

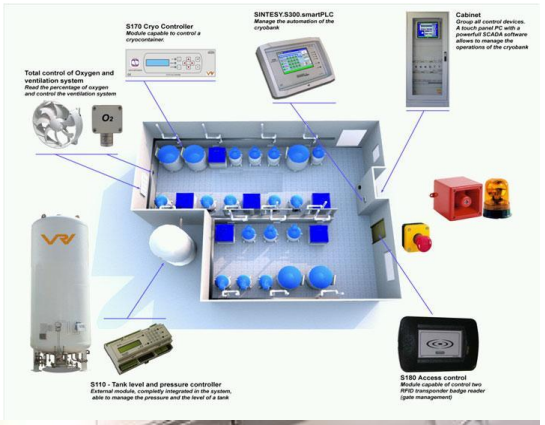
Trữ-rã phôi/noãn

Trữ-rã phôi thuỷ tinh hóa theo phương pháp truyền thống

Tự động hoá (Hệ thống GAVI)

Labo TTTON – Lưu trữ phôi

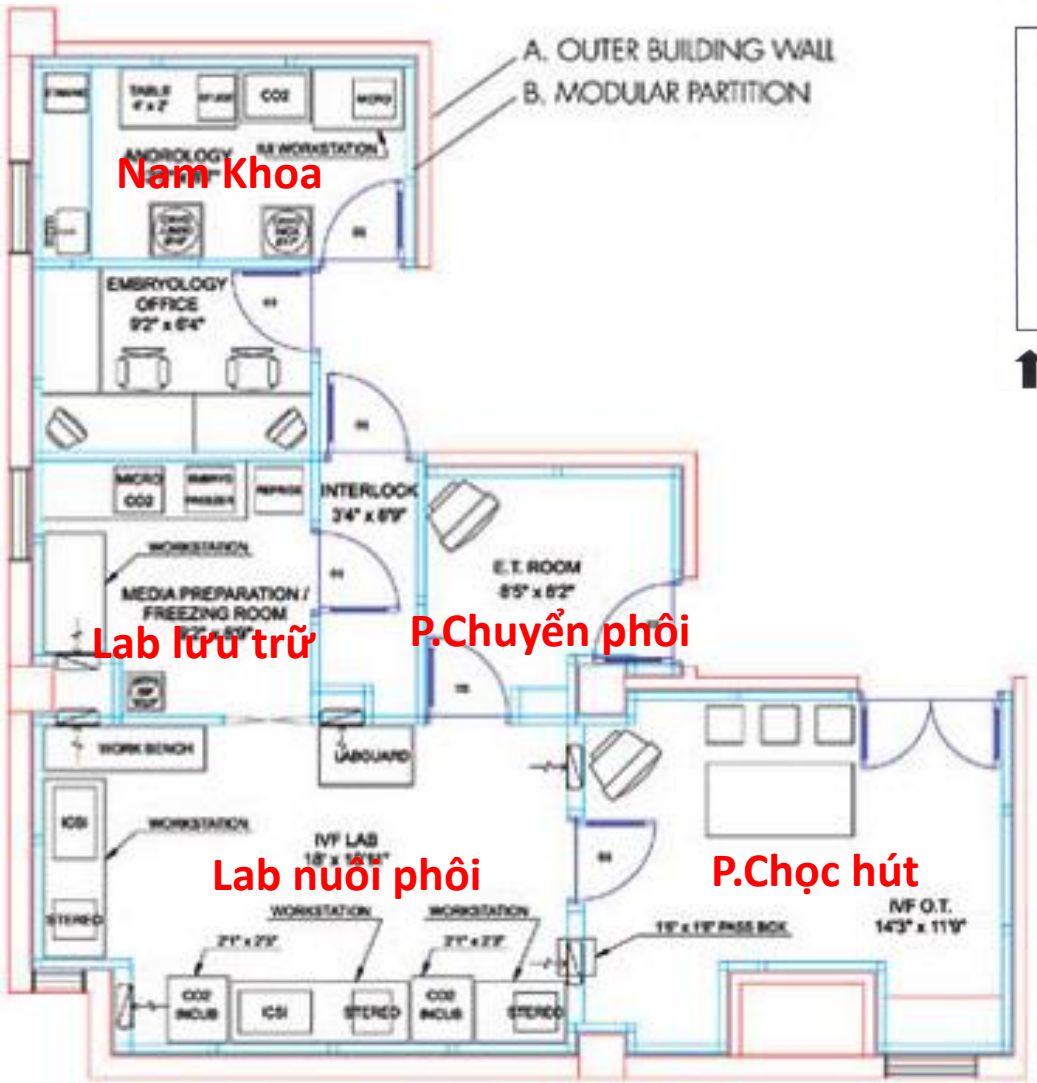
Lưu trữ quy mô lớn

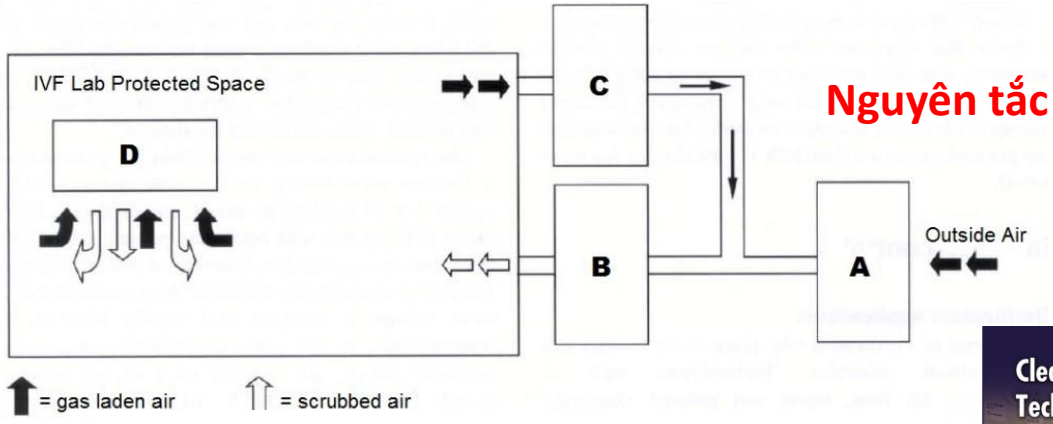


Source: https://nature.ca

Lưu trữ quy mô nhỏ

Cấu trúc của Labo TTTON





Nguyên tắc lọc không khí.

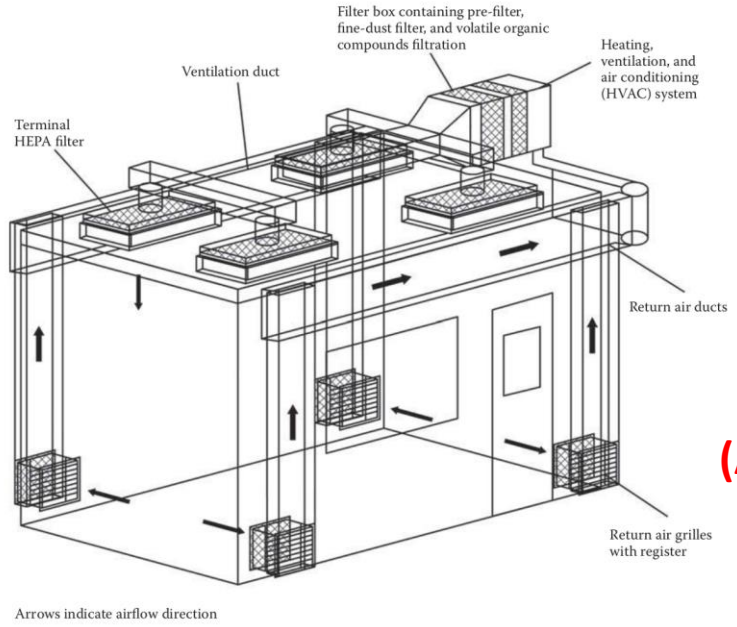
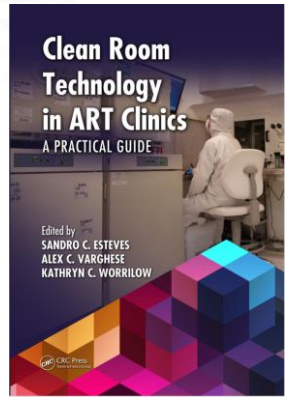


Figure 2.1 Illustration depicting a classic example of centralized air filtration system.

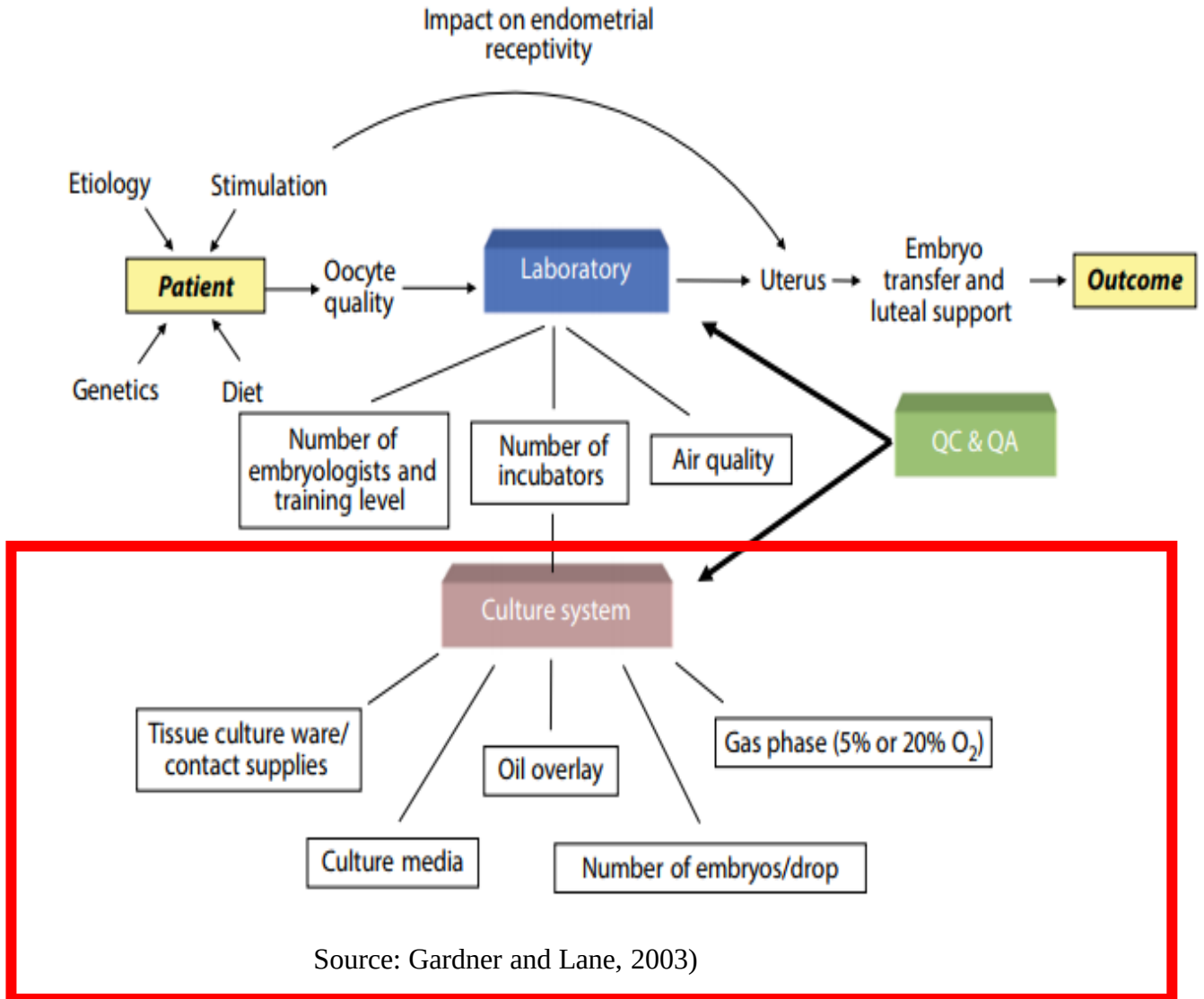


Hệ thống lọc không khí trung tâm
(AHU – Air Handling unit)

Source: http://www.nascentivf.com

Sandro C.E. và cs., 2017. Clean Room Technology in ART Clinics A Practical Guide.

Hệ thống nuôi cấy phôi



Source: Gardner and Lane, 2003)

<u>Các vấn đề cần quan tâm:</u>

- Hệ thống tủ cấy: số lượng, loại tủ.
- Môi trường nuôi cấy: đơn bước hay chuyển tiếp
- Khí sử dụng để ổn định pH: %CO2, có/không O2%, khí trộn sẵn?
- Vật tư tiêu hao dùng trong nuôi cấy phôi.
- HT phủ dầu hay cấy hở.
- Vấn đề khác.

Các loại tủ cấy phôi

Table 1 Incubator technology variables that should be considered when evaluating and selecting a unit for the laboratory.

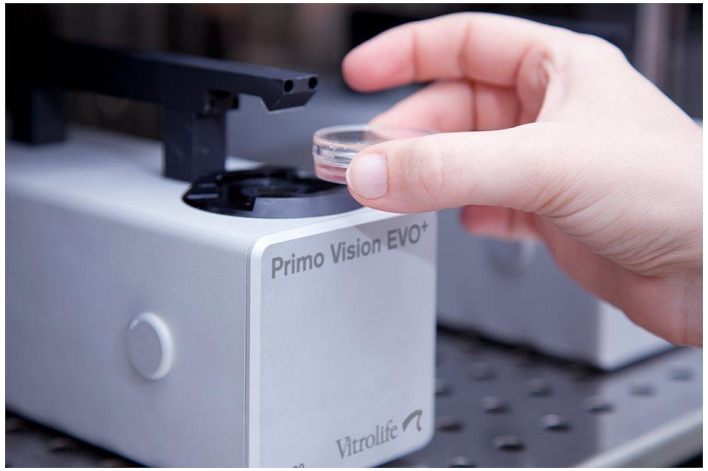
Gas type	*CO_2 sensor*	*O_2 sensor*	*Temperature control*[a]	*Design*[b]	*Humidity control*	*Contamination control*[a,c]	*Other*
CO_2-only	Infrared	Zirconium	Air jacket	Benchtop	Yes[d]	Heat	Data logging
Low O_2 — mixer	Thermal conductivity	Galvanic (fuel-cell)	Water jacket	Two-chamber	No	UV	Cost
Low O_2 — premixed cylinder			Direct heat	Multichamber		H_2O_2	Patient capacity
				Other (i.e. time lapse imaging)		Copper alloy	Service
				Small box		External HEPA	Technology integration
				Large box			

HEPA = high-efficiency particulate absorption.
[a]May be influenced by presence/absence of an internal fan.
[b]Other novel designs exist, but these are general terms to refer to the most commonly used incubators in the IVF laboratory; actual volumes will vary from unit to unit.
[c]Ease of removing inner parts and/or wiping interior is also important to consider.
[d]Some units bubble gas through a water pan to expedite rehumidification.

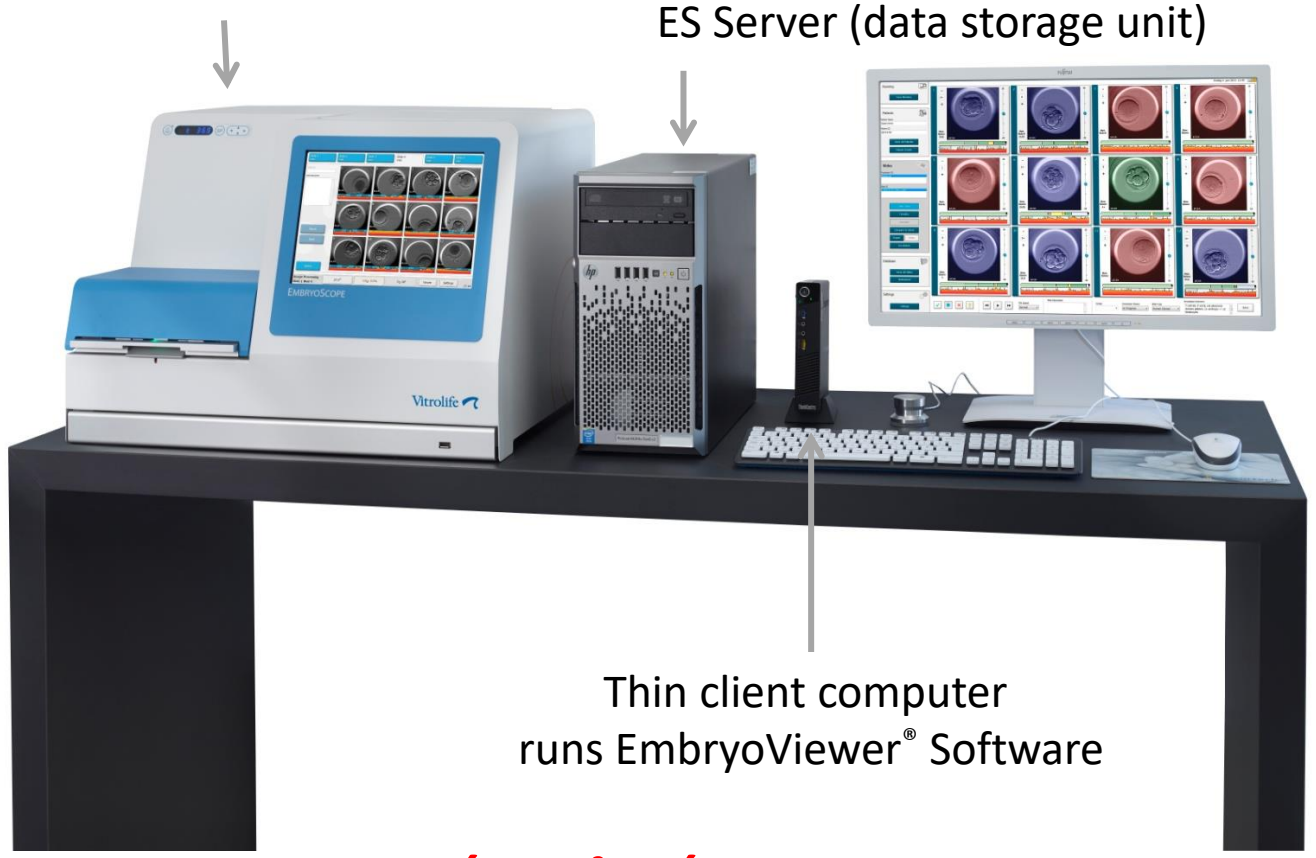
Jason E Swain. Decisions for the IVF laboratory: comparative analysis of embryo culture incubators.Reproductive BioMedicine Online (2014) 28, 535– 547

Tủ cấy lớn

Tủ cấy phôi thế hệ mới
(Bench-top + multi-chamber)



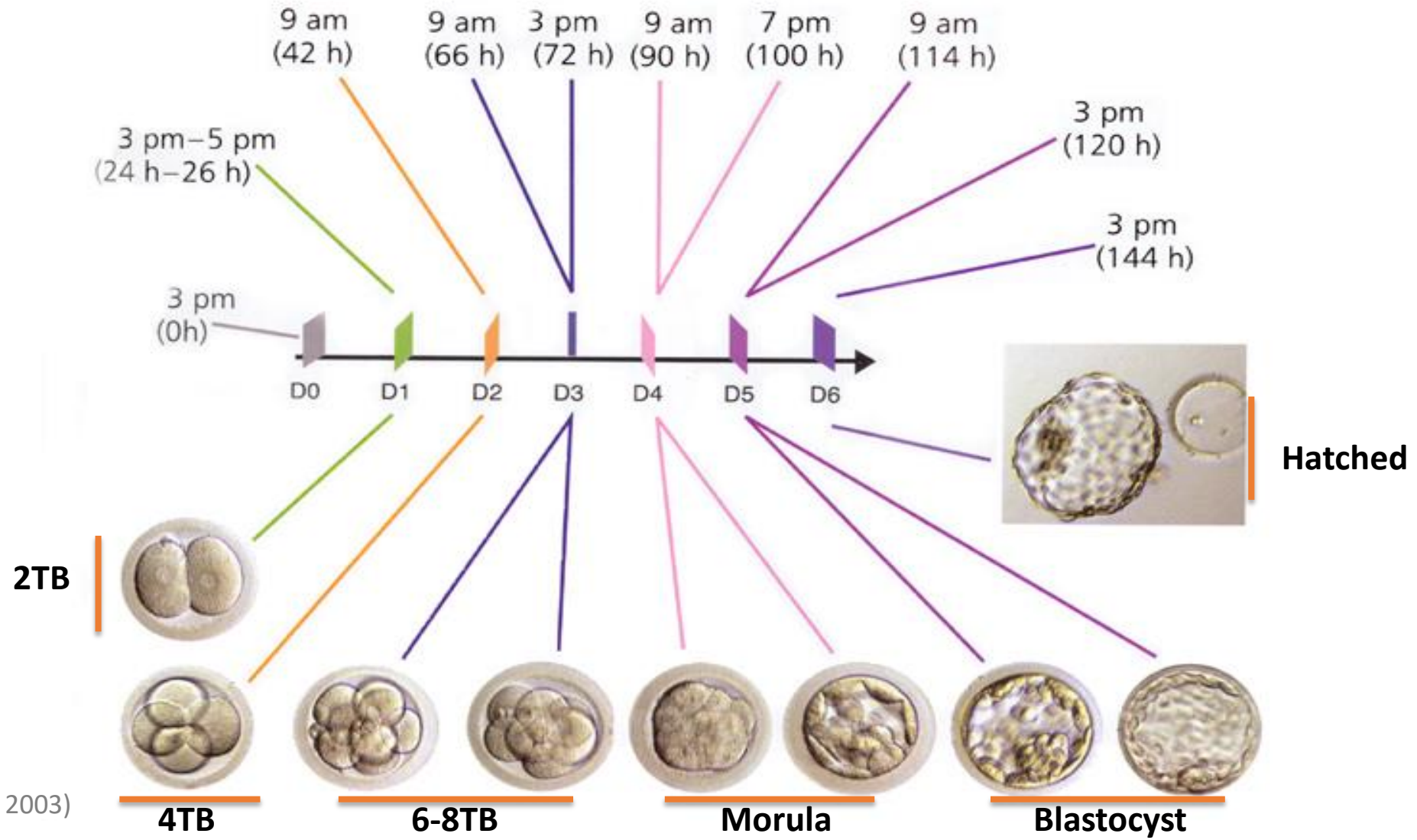
Time-lapse camera



Hệ thống tủ cấy Time-lapse

Đánh giá và chọn lựa phôi – Hình thái phôi

Các giai đoạn phát triển của phôi



(Veeck and Zaninovic´, 2003)

Đánh giá và chọn lựa phôi – Timelapse

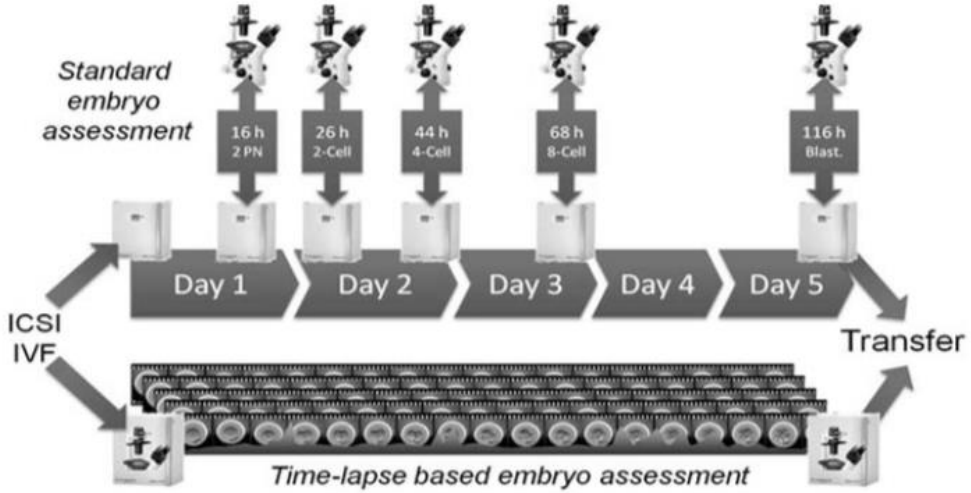
- Hệ thống thiết bị (camera, kính quang học, tủ cấy, phần mềm xử lý) giúp quan sát phôi liên tục và không xâm lấn *(Peter Kovacs, 2014)*
- Phương pháp đánh giá khách quan, cung cấp nhiều thông tin hơn về hình thái, động học của phôi.
- **Tiểu sử:**

  - Trong các nghiên cứu *(Cole, 1967; Massip và Mulnard, 1980; Wale và Gardner, 2010),*
  - Xuất hiện 2nd PB và hiện diện PN *(Payne và cs., 1997),*
  - Động học phôi từ thụ tinh đến phôi nang thoát màng *(Mio và Maeda, 2008).*
  - Trường hợp sinh sống đầu tiên dùng đánh giá phôi bằng Time-lapse *(Pribenszky và cs.,2010)*
  - **Sau đó, phát triển thành một trường phái và một xu hướng mới.**

Nguyên tắc của Timelapse

Superior amount of information with time-lapse

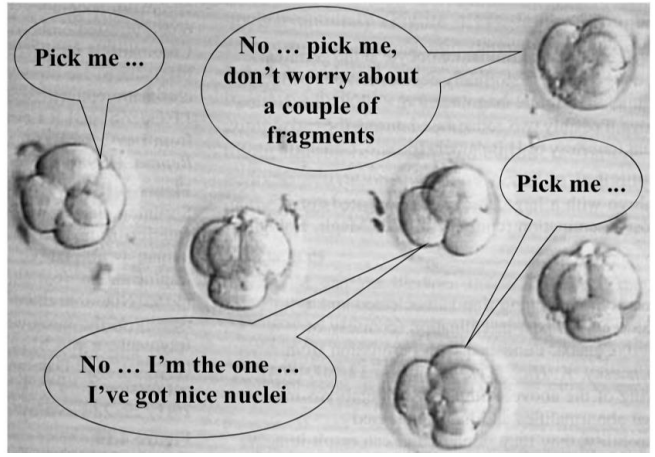
- The difference is not only "quantity"



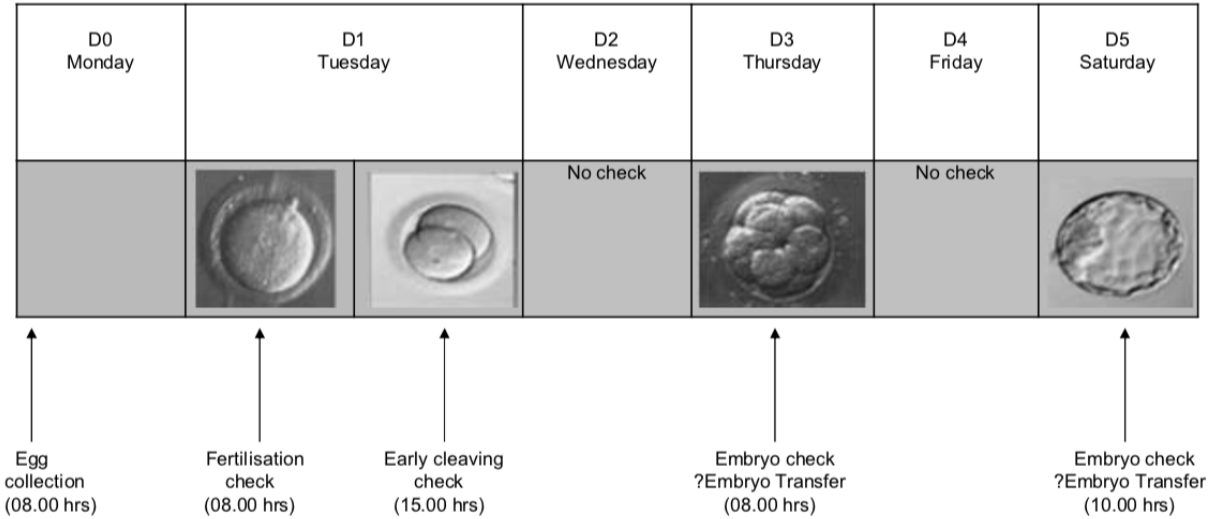
Over 5 days per embryo: approx. 5000 images (700 time values / 7 focal planes)

Zsolt Peter NAGY, 2014

↑ ↑ embryological responsibility ...



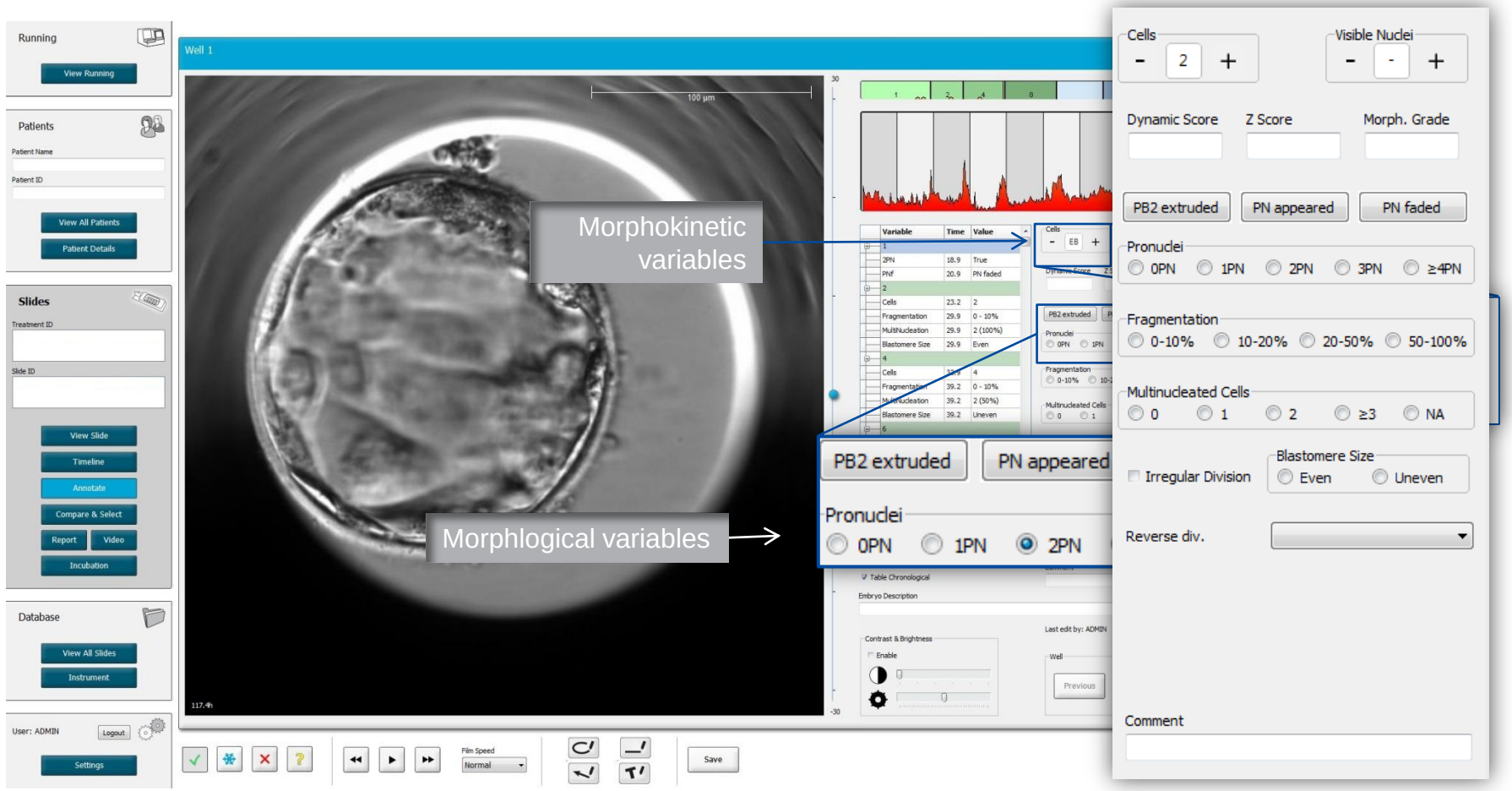
Conventional embryo observations ...



Charles Kingsland, 2014

FEATURES OF EMBRYOVIEWER SOFTWARE

Intuitive embryo evaluation interface (Annotation tool) developed using input from leading embryologists worldwide



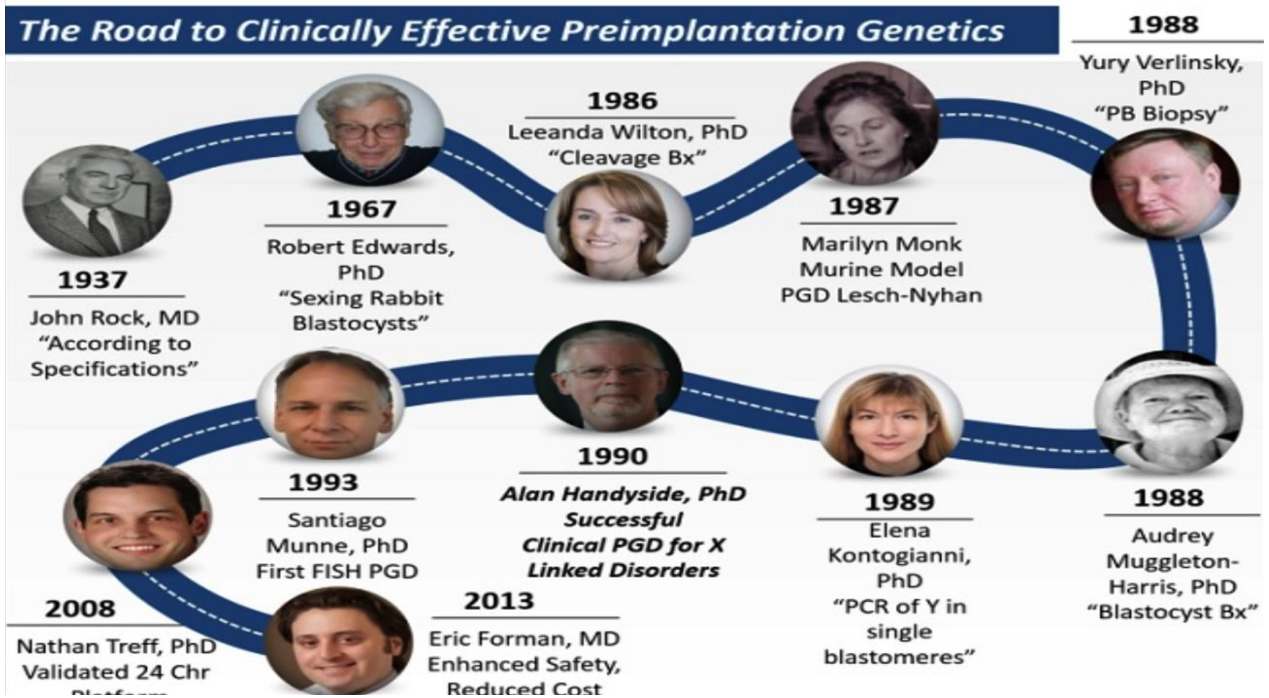
main

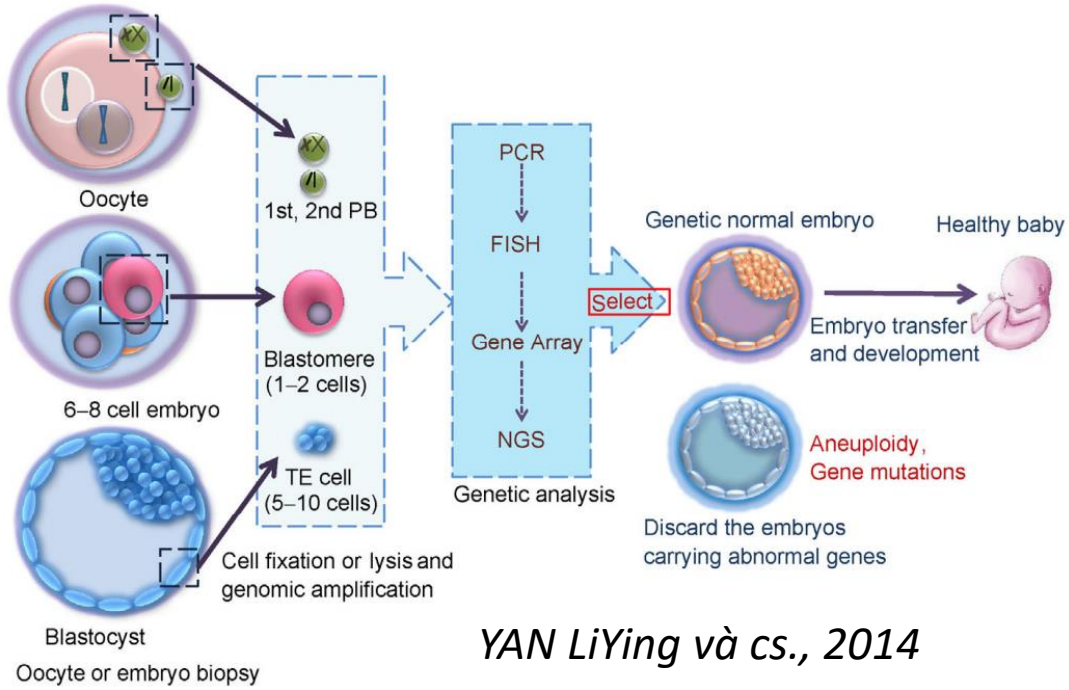
Các loại hệ thống Timelapse hiện nay

TECHNICAL CHARACTERISTICS	PRIMO VISION EVO+	EMBRYOSCOPE D	EEVA	GERI	MIRI TL	EMBRYOSCOPE+
						
OPTICS	Bright field	Bright field	Dark field	Bright field/ Dark field	Bright field	Bright field
INTEGRATED INCUBATOR	No	Yes-Hybrid	No	Yes-Benchtop	Yes-Benchtop	Yes
FOCAL PLANES	3-11	7	1	1	4	11
EMBRYO IMAGING	Pictures by user (10'/60')	Picture every 10'	Picture every 5'	Pictures every 10'	Pictures every 5'	Picture every 10'
CAPACITY-PATIENTS	1/microscope	6/system	1/camera	6/system	6/system	15
EMBRYOS/PT & CULTURE	9-16 individual culture	12 individual culture	12 group culture	16 individual culture	14 individual culture	16 individual culture
DATA ANALYSES	Manual	Manual	Real-time automated	Manual/ semi automated	Semi automated	Manual

Pennetta F[1], Lagalla C, Borini A (2018). **Embryo morphokinetic characteristics and euploidy.** Curr Opin Obstet Gynecol. 2018 Jun;30(3):185-196.

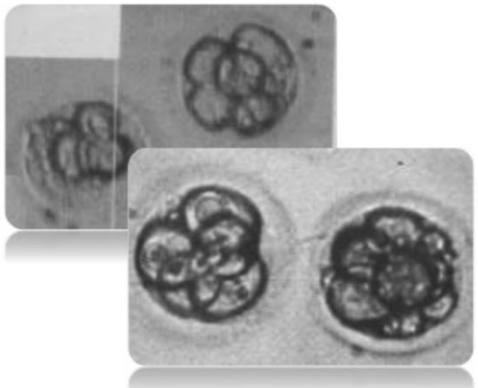
Sàng lọc/chẩn đoán di truyền phôi
(PGT – Preimplantation genetic testing)





YAN LiYing và cs., 2014

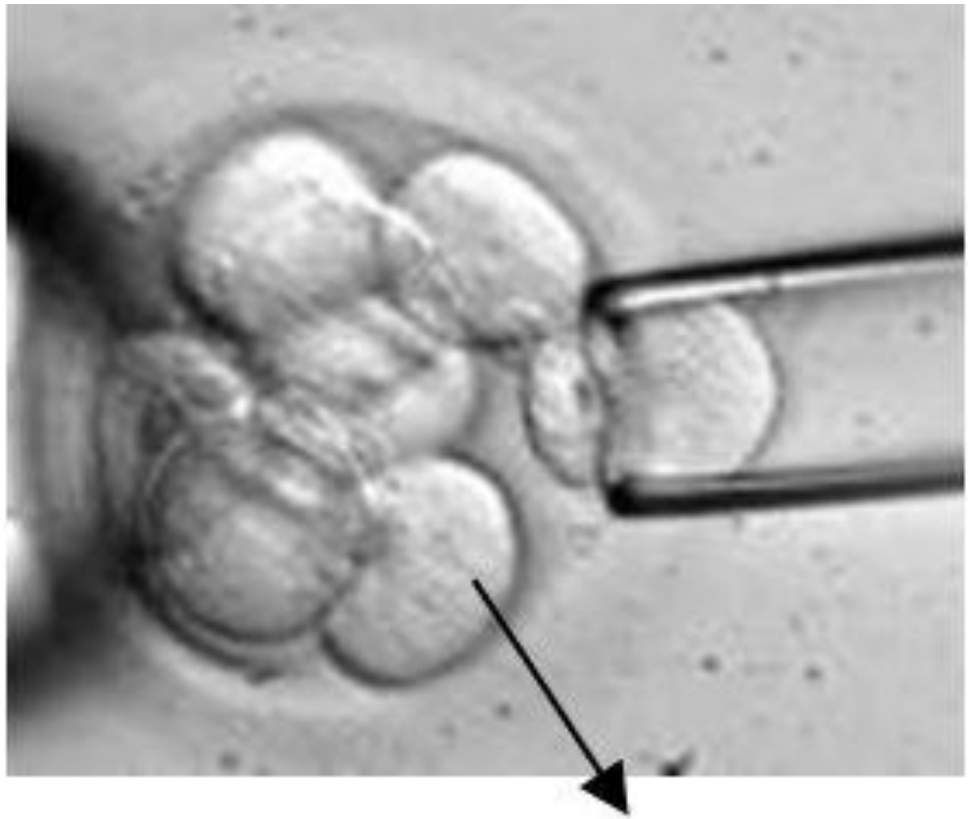
Born July 1990



Handyside và cs., Nature (1990)

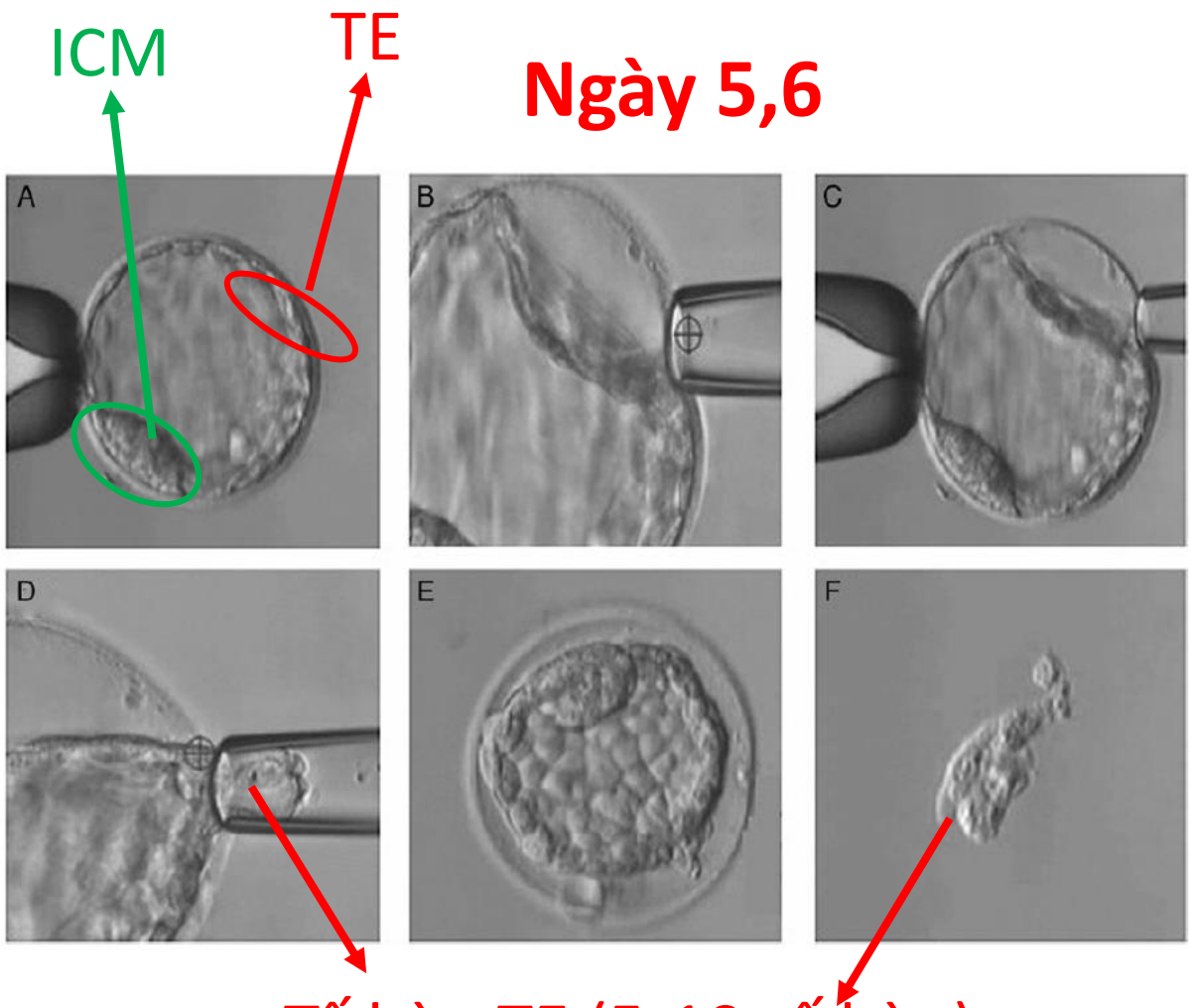
Sinh thiết phôi (Embryo biopsy)

Ngày 3



Phôi bào

Ngày 5,6



Tế bào TE (5-10 tế bào)

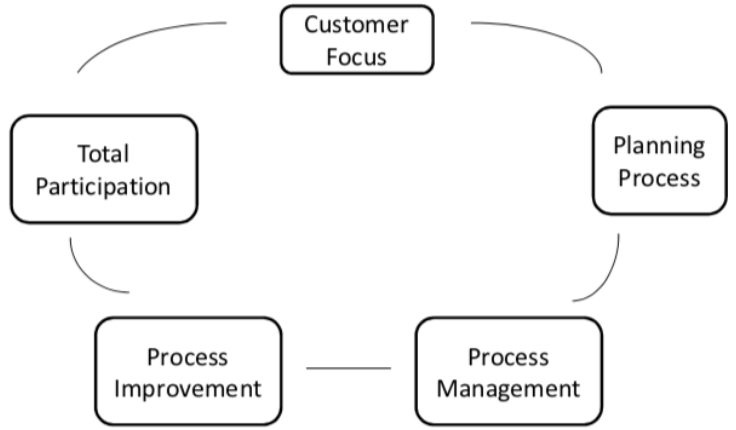
Hệ thống quản trị chất lượng toàn diện
(TQM – Total quality management)

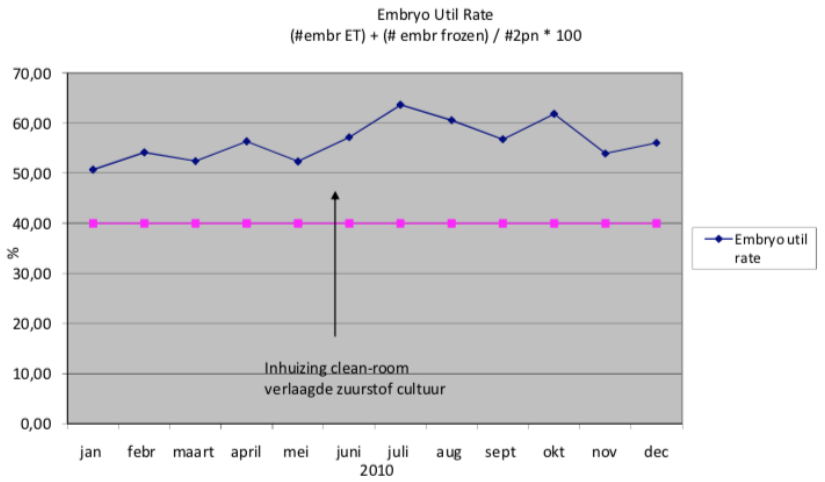
TQM = management philosophy and company practices that aim to harness the human and material resources of an organization in the most effective way to achieve the objectives of the organization and to pursue customer satisfaction

TQM in Healthcare = rigorous set of processes and techniques to measure, improve, and control the quality of care and service based on what is important to the patient

QUALITY OF ORGANIZATION
=
QUALITY OF CARE
(Patients satisfaction + better outcome)

A simple model of TQM





Embryo Utilization Rate (EUR)

$$EUR = \frac{\text{N of embryos transferred (A)} + \text{N of embryos cryopreserved (B)}}{\text{N of 2 PNs (C)}}$$

A = indicator of ET policy (clinical)
B = indicator of cleanroom quality (laboratory)
C = indicator of fertilization efficacy (laboratory)

Chứng cứ liên quan phòng sạch

- Phòng sạch

Reproductive BioMedicine Online (2016) 32, 9–11

www.sciencedirect.com
www.rbmonline.com

COMMENTARY

Implementation of cleanroom technology in reproductive laboratories: the question is not why but how

Sandro C Esteves *, Fabiola C Bento

Abstract Two articles recently published in *Reproductive BioMedicine Online* described how fertility centres in the USA and Brazil implemented air quality control to newly designed facilities. In both case scenarios, a highly efficient air filtration was achieved by installing a centred system supplying filtered air to the IVF laboratory and other critical areas, combining air particulate and volatile organic compound (VOC) filtration. Evaluating retrospective data of over 3000 cycles from both centres, live birth rates were increased by improvements in air quality and laboratory environment. This commentary discusses some of the key aspects of air contamination in the IVF settings, and highlights the fact that a risk management analysis taking into consideration all variables that play a role in air contamination is paramount for the reduction of the risk of poor IVF outcomes due to improper air quality conditions.

J Assist Reprod Genet
DOI 10.1007/s10815-015-0535-x

REVIEW

Air quality in the assisted reproduction laboratory: a mini-review

Dean E. Morbeck[1]

Received: 22 June 2015 / Accepted: 1 July 2015

Abstract Quality of air in the clinical embryology laboratory is considered critical for high in vitro fertilization (IVF) success rates, yet evidence for best practices is lacking. Predominantly anecdotal reports on relationships between air quality and IVF success rates have resulted in minimal authentic clinical laboratory guidelines or in recommendations that are based on industrial cleanroom particulate standards with little attention to chemical air filtration. As a result, a nascent industry of costly, specialized air handling equipment for IVF laboratories has emerged to provide air quality solutions that have not been clearly assessed or verified. Clinics are embracing such technology because their embryology laboratories have become epicenters of assisted reproductive technology as the practice of IVF has moved to blastocyst transfers and utilization of trophectoderm biopsy for preimplantation genetic testing (PGT). Thus, a laboratory's ability to culture, biopsy, and freeze blastocysts is a rate-limiting step that depends on technical proficiency and a supportive and stable culture environment based on a foundation of high-quality ambient air.

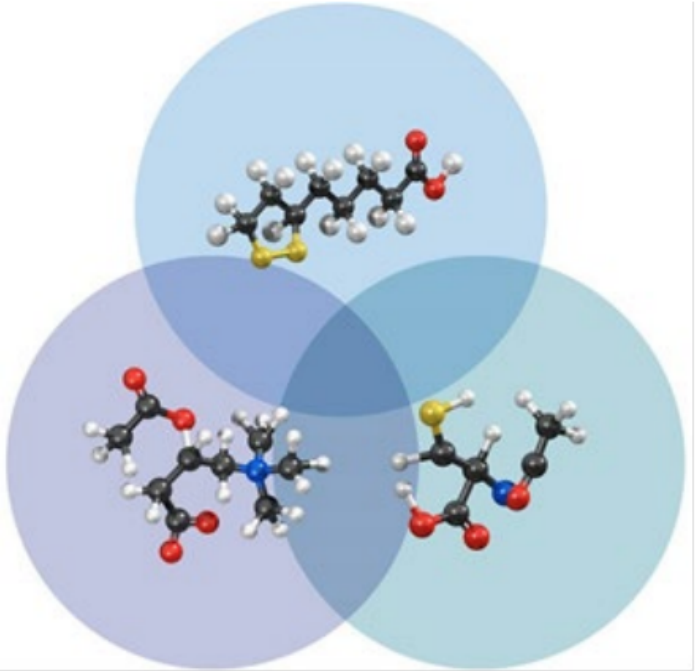
Các công nghệ giúp tối ưu hoá kết quả điều trị

Nâng chuẩn phòng sạch

Total VOC levels <2 $\mu g/m^3$ (~0.5 ppb) of air.
Aldehyde levels below detectable limit of 1 $\mu g/m^3$.

ANDROFERT | Esteves, 39

IVF MEDIA WITH 3 ANTIOXIDANTS



Human Reproduction, Vol.31, No.7 pp. 1445–1454, 2016
Advanced Access publication on May 10, 2016 doi:10.1093/humrep/dew098

human reproduction ORIGINAL ARTICLE *Embryology*

Antioxidants improve mouse preimplantation embryo development and viability

Thi T. Truong, Yu May Soh, and David K. Gardner*
School of BioSciences, University of Melbourne, Parkville, Victoria, Australia

Human Reproduction, Vol.32, No.12 pp. 2404–2413, 2017
Advanced Access publication on November 10, 2017 doi:10.1093/humrep/dex330

human reproduction ORIGINAL ARTICLE *Embryology*

Antioxidants improve IVF outcome and subsequent embryo development in the mouse

T. Truong and D.K. Gardner*
School of BioSciences, University of Melbourne, Parkville, Victoria, Australia

Hệ thống timelapse hiện đại nhất hiện nay.

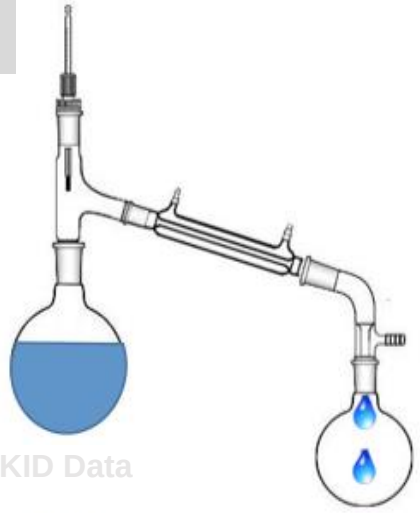
Timelapse – Artificial Inteligence

KIDScore™ D3 Basic Decision Support Tool

PURPOSE

To support the process of **avoiding** embryos with clearly reduced implantation potential

Based on morphokinetic information from a large dataset comprising of known implantation data from day 3 transfers (>3000 KID* embryos)

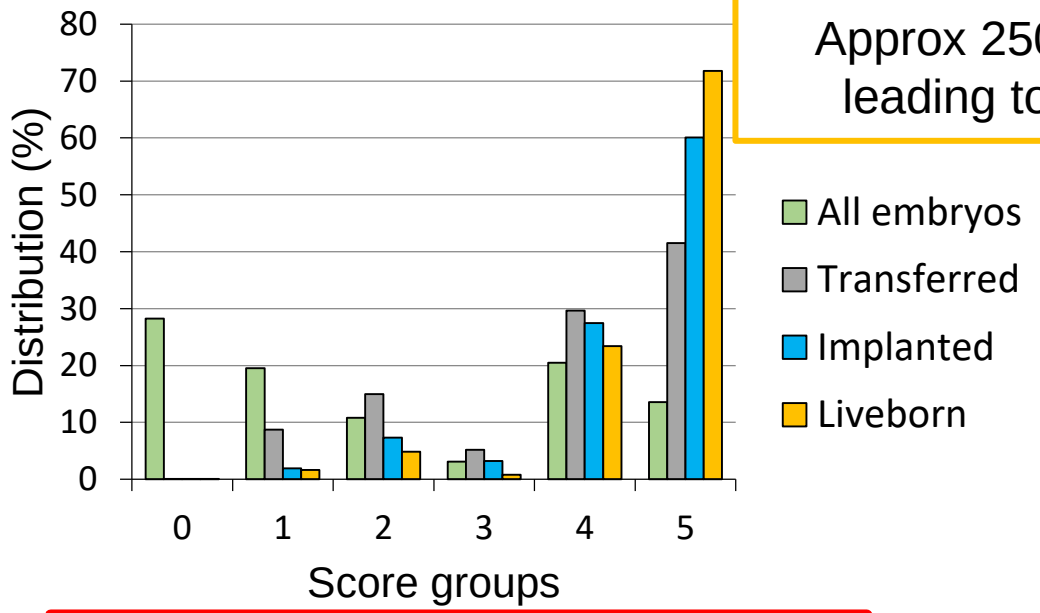


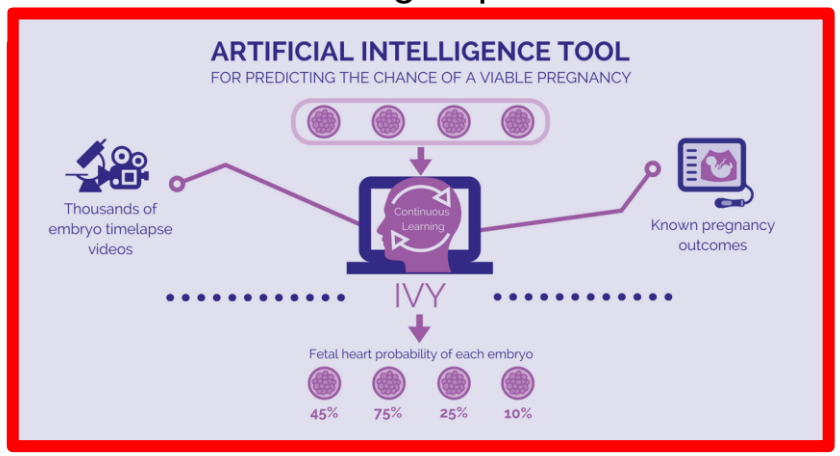
KIDScore™ D3 Basic

*KID (Known implantation data) describes whether or not a specific transferred embryo has implanted

”Liveborn” group

Approx 250 embryos leading to livebirth





https://www.ivf.com.au/success-rates/leading-technology/artificial-intelligence-in-ivf

Automation - Vitrification

O-136 Tuesday, October 31, 2017 11:45 AM

AUTOMATIC VS MANUAL VITRIFICATION OF HUMAN OOCYTES. PRELIMINARY RESULTS OF THE FIRST RANDOMISED CONTROLLED TRIAL USING SIBLING OOCYTES. M. Sole,[a] N. Polyzos,[b] C. Gonzalez Llagostera,[a] B. Carrasco,[a] B. Coroleu,[a] A. Veiga,[c] M. Boada.[a] [a]Hospital Universitario Dexeus, Barcelona, Spain; [b]Reproductive Medicine, Dexeus University Hospital, Barcelona, Spain; [c]Dexeus Salud de la Mujer 08028, Barcelona, Spain.

	Cryotop vitrification	GAVI vitrification	Total
Oocyte donation Cycles (n)	11	11	11
Number of Mii oocytes	68	70	138
Warming Cycles	7	7	7
Warming oocytes	38	42	80
Survival rate	76,3	78,6	77,5
Fertilization rate	65,5	75,8	71,0
Good quality embryos on D3 (%)	15,8	32,0	25,0
Multinucleated embryos D2-D3 (%)	47,4	32,0	38,6
Ongoing embryos (%)	57,9	64,0	61,4

Sole M, Polyzos N, Gonzalez Llagostera C, Carrasco B, Coroleu B, Veiga A, et al. Automatic vs manual vitrification of human oocytes. Preliminary results of the first randomised controlled trial using sibling oocytes. Fertil Steril. 2017;108(3 Supplement):e57.

Roy, T. K., Brandi, S., & Peura, T. T. (2017). Chapter 20 Gavi-Automated Vitrification Instrument. Cryopreservation of Mammalian Gametes and Embryos, 261–277.doi:10.1007/978-1-4939-6828-2_20

QMS –Quality management systems

Quality management systems for your in vitro fertilization clinic's laboratory: Why bother?

Article *in* Journal of Human Reproductive Sciences · March 2013
DOI: 10.4103/0974-1208.112368 · Source: PubMed

CITATIONS
4

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Karolinska University Hospital
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Manish Banker
Nova IVI Fertility- Ahmedabad
51 PUBLICATIONS **423** CITATIONS
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Quality management systems for your *in vitro* fertilization clinic's laboratory: Why bother?

Jan I Olofsson, Manish R Banker[1], Late Peter Sjoblom[2]
Department of Obstetrics and Gynecology, Fertility Unit, Karolinska University Hospital, 141 86 Stockholm, Sweden, [1]Director, Nova IVI Fertility, Pulse Women's Hospital, 108 Swastik Society, Navrangpura, Ahmedabad, India, [2]Queen's Medical Centre, Nottingham, NG7 2UH, United Kingdom

Address for correspondence:
Dr. Manish R. Banker, Director, Nova IVI Fertility, Pulse Women's Hospital, 108 Swastik Society, Navrangpura, Ahmedabad - 380 009, India.
E-mail: manish.banker@novaivifertility.com

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ABSTRACT

Several countries have in recent years introduced prescribed requirements for treatment and monitoring of outcomes, as well as a licensing or accreditation requirement for *in vitro* fertilization (IVF) clinics and their laboratories. It is commonplace for Assisted Reproductive Technology (ART) laboratories to be required to have a quality control system. However, more effective Total Quality Management systems are now being implemented by an increasing number of ART clinics. In India, it is now a requirement to have a quality management system in order to be accredited and to help meet customer demand for improved delivery of ART services. This review contains the proceedings a quality management session at the Indian Fertility Experts Meet (IFEM) 2010 and focuses on the creation of a patient-oriented best-in-class IVF laboratory.

KEY WORDS: Assisted reproduction technique, *in vitro* fertilization, Total Quality Management

INTRODUCTION

In reproductive medicine, a new frontier was opened up and new hope was given to infertile couples when the first baby conceived *in vitro* was born in 1978.[1] According to the World

The growth of the ART industry and the potential health risks to patients and offspring have driven attempts to monitor and regulate the services provided although there are still differences of opinion with regard to what constitutes valid efficacy

Table 3: Requirements of the quality management systems for accreditation of assisted reproductive technology facilities in Australia and New Zealand

The quality management system include documented policies and procedures that have regard to

- Quality management policy, personnel and resources, documents requirements, patient focus, compliance with legislation and guidelines, research and technology design and development, purchasing policy, control of technical components, quality assurance and monitoring systems, and management review of the quality system

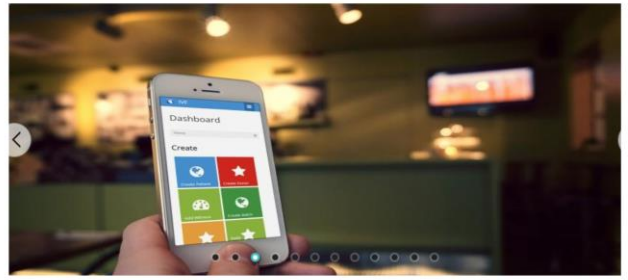
There shall be written policies and protocols for

- Access to treatment
- All procedures undertaken
- Identification and witnessing protocols (patient/gamete/embryo/confidentiality)
- Storage conditions for gametes and embryos and storage timeframes

IMT International
IVF Management Technologies

http://www.imtinternational.com/ivf-electronic-witnessing/

IVF: ART Fertility Clinic Management System



http://techdynamics.org/home/ivf.php

Fertility EHR
FERTILITY CLINIC MANAGEMENT SOFTWARE

https://www.fertilityehr.com/modules.php

Customer experience

Gonen *Fertility Research and Practice* (2016) 2:6
DOI 10.1186/s40738-016-0019-4

Fertility Research and Practice

RESEARCH ARTICLE Open Access

Satisfaction with in vitro fertilization treatment: patients' experiences and professionals' perceptions

Limor Dina Gonen

Abstract

Background: This paper investigates patients' satisfaction with various aspects of fertility care and seeks to determine to what extent fertility specialists are able to assess patient satisfaction. Patients' experiences with in-vitro fertilization (IVF) services and facilities have been compiled and examined in order to discover whether patients' satisfaction is correlated to psychological factors and demographic, socio-economic, and health characteristics, and whether patients' satisfaction has an influence on the willingness to pay (WTP) for IVF treatment.

Methods: The study was carried out on 204 patients and 19 fertility professionals from 8 public IVF units in Israel.

Results: The study found that, overall, infertile patients are satisfied with the care they received. Several demographic variables (age; education; income; number of fertility treatments) and psychological factors ('Pessimism' and 'Activeness'), were found to be significantly correlated with patient satisfaction with IVF. The results yielded a negative correlation between the WTP for IVF treatment and the satisfaction with access to care and physical conditions.

Conclusions: Patient satisfaction is an important component in the evaluation of fertility treatments as well as other medical interventions. Insights into the quality of care as seen from the patients' perspective may help healthcare staff better meet patients' needs, wishes, and priorities.

MedicalExpress

REVIEW

Establishing a quality management system in a fertility center: experience with ISO 9001

Fabiola C. Bento, Sandro C. Esteves

ANDROFERT, Andrology and Human Reproduction Clinic; Referral Center for Male Reproduction, Campinas, SP, Brazil.

In Fertility Centers, quality should be measured by how well the organization complies with pre-defined requirements, and by how quality policies are implemented and quality objectives achieved. Having a quality management system (QMS) is a mandatory requirement for IVF centers established in most countries with regulatory guidelines, including Brazil. Nevertheless, none of the regulatory directives specify what a QMS must have in detail or how it should be implemented and/or maintained. ISO 9001 is the most important and widespread international requirement for quality management. ISO 9001 standards are generic and applicable to all organizations in any economic sector, including IVF centers. In this review, we discuss how we implemented QMS according to ISO 9001 and what we achieved 5 years later. In brief, with ISO we defined our structure, policies, procedures, processes and resources needed to implement quality management. In addition, we determined the quality orientation of our center and the quality objectives and indicators used to guarantee that a high-quality service is provided. Once measuring progress became part of our daily routine, quantifying and evaluating the organization's success and how much improvement has been achieved was an inevitable result of our well-established QMS. Several lessons were learned throughout our quality journey, but foremost among them was the creation of an internal environment with unity of purpose and direction; this has in fact been the key to achieving the organization's goals.

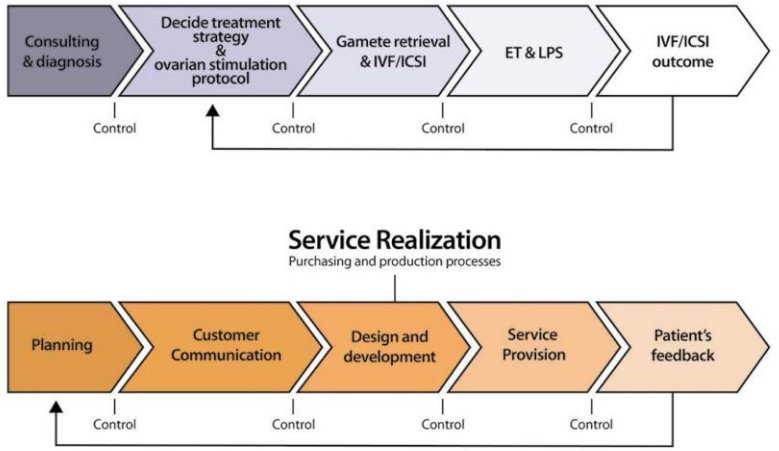


Figure 1 - Flowchart of mapping procedure applied to the in vitro fertilization (IVF) treatment cycle (ICSI: intracytoplasmic sperm injection; ET: embryo transfer; LPS: luteal phase support).

Bento FC, Esteves SC. Establishing a Quality Management System in a Fertility Center: Experience with ISO 9001. MedicalExpress. 2016;3(3):M160302

Non- invasive PGT

SCIENTIFIC REPORTS

OPEN

Preimplantation Genetic Screening with Spent Culture Medium/ Blastocoel Fluid for in Vitro Fertilization

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Penghao Li[1], Zhe Song[2], Yaxin Yao[3], Tianhua Huang[1], Rurong Mao[1], Jun Huang[1], Yongyi Ma[1], Xin Dong[1], Wenlong Huang[2], Jihua Huang[1], Tianjian Chen[5], Ting Qu[1], Lingxiao Li[1], Ying Zhong[1] & Jiang Gu[1,2,4]

Preimplantation genetic screening (PGS) detects chromosomal aneuploidy from DNA extracted from trophectodermal biopsy of the embryos before implantation. Although a controlled study showed no difference in pregnancy rates between this invasive cell biopsy technique and a non-biopsied control group, the potential long-term damage by the current PGS method has not be completely ruled out. We therefore tested a less-invasive protocol which utilizes spent culture medium combining with blastocoel fluid (ECB) to assess chromosomal aneuploidy. We compared the new protocol with the currently employed trophectodermal biopsy method against chromosomal information obtained from the remaining embryo. We found that the new technique generated information about aneuploidy that was not entirely identical to obtained from the biopsied trophectoderm or the remaining embryo. As the origins of the DNA extracted from the three sample types were not the same, the significance and interpretation of each result would have its own meaning. The possible implications derived from the ECB results as well as those from cell biopsy were discussed. The effectiveness of this new approach in selecting the best embryo for uterine implantation awaits further long term evaluation.

Human Reproduction, pp. 1–6, 2018
doi:10.1093/humrep/dey314

human reproduction **MINI-REVIEW** ***Developments in Reproductive Biology and Medicine***

Non-invasive pre-implantation genetic testing of human embryos: an emerging concept

C. Farra[1], F. Choucair[2], and J. Awwad[2,*]

PLOS ONE

RESEARCH ARTICLE

Evaluation of a novel non-invasive preimplantation genetic screening approach

Valeriy Kuznyetsov[1], Svetlana Madjunkova[1]*, Ran Antes[1], Rina Abramov[1], Gelareh Motamedi[1], Zenon Ibarrientos[1], Clifford Librach[1,2,3,4,5]*

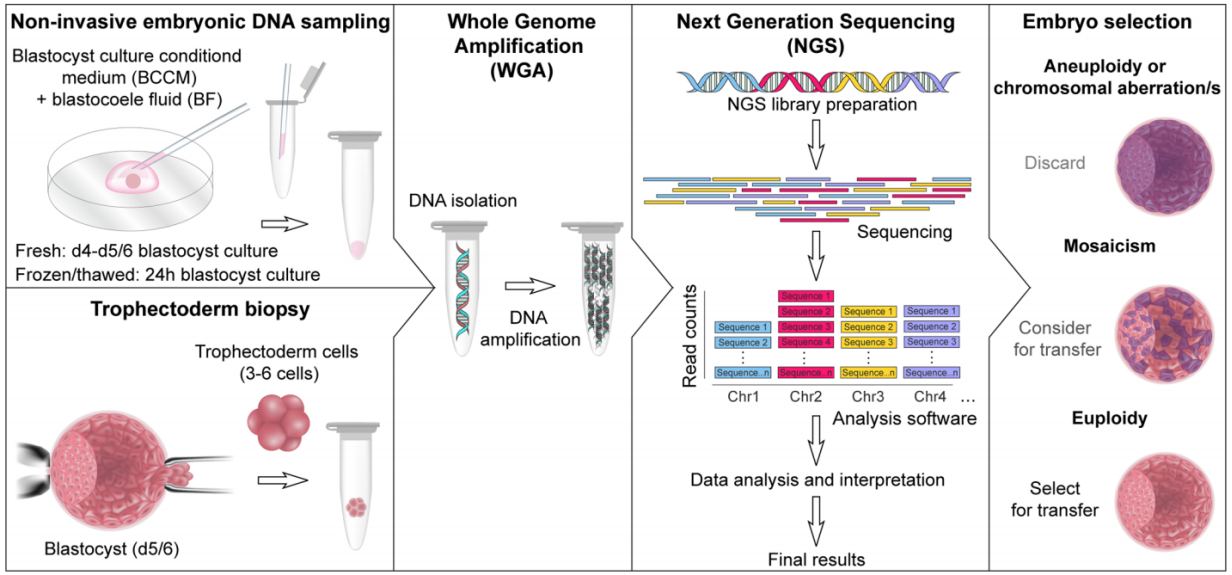
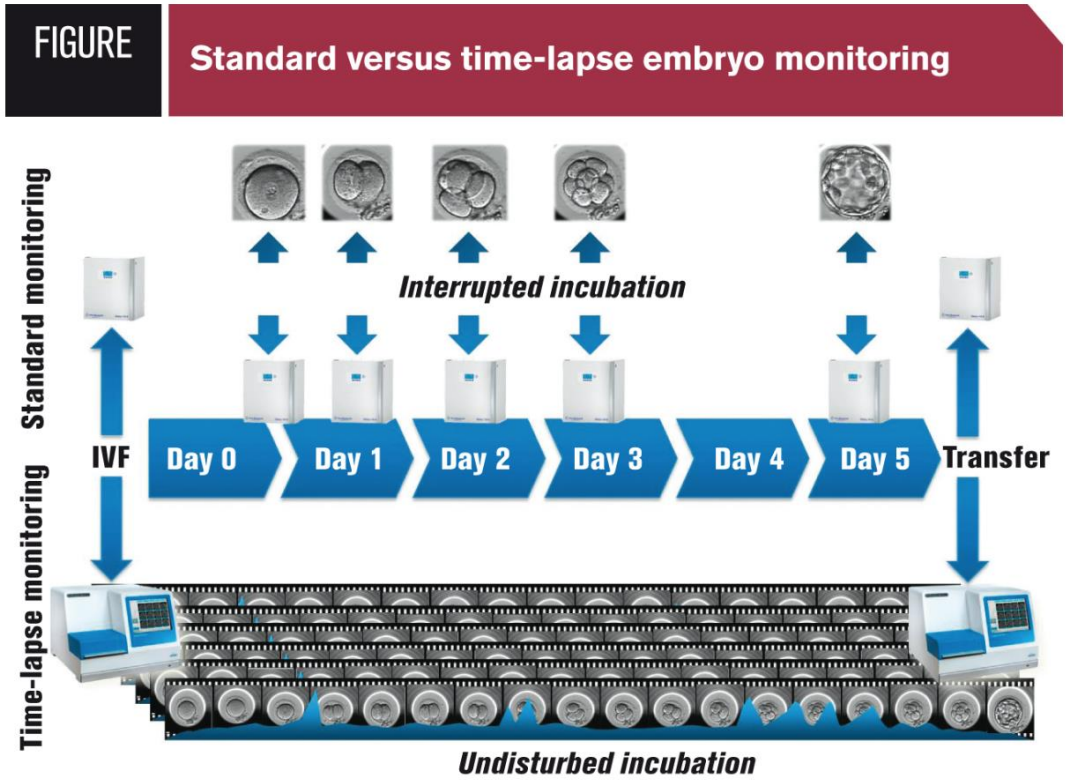


Fig 1. Non-invasive and invasive preimplantation genetic testing workflow.

https://doi.org/10.1371/journal.pone.0197262.g001

Các vấn đề còn đang tranh cãi

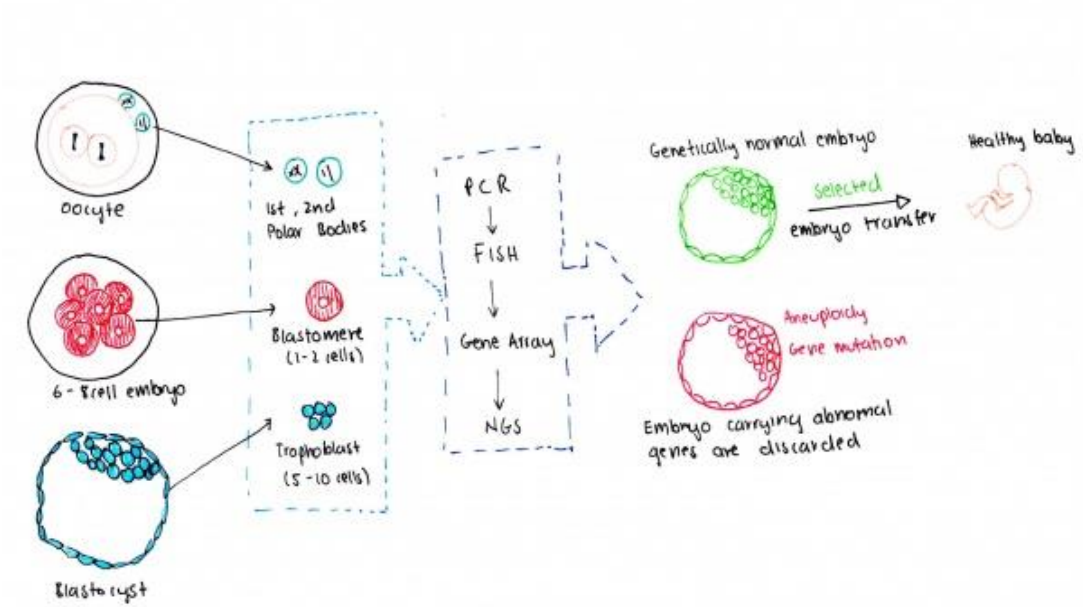
Timelapse monitoring



Source: FertiliTech Inc. Used with permission.

VS

PGT



Phân tích SWOT - Timelapse

HUMAN FERTILITY, 2017
VOL. 20, NO. 2, 74–79
http://dx.doi.org/10.1080/14647273.2017.1283068

Taylor & Francis
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COMMENTARY

Time lapse imaging: is it time to incorporate this technology into routine clinical practice?

Priya Bhide[a], Abha Maheshwari[b], Rachel Cutting[c], Susan Seenan[d], Anita Patel[e], Khalid Khan[e] and Roy Homburg[a]

ABSTRACT

Time-lapse imaging (TLI) systems for embryo incubation, assessment and selection are a novel technology available to *in vitro* fertilization (IVF) clinics. However, there is uncertainty about their clinical and cost-effectiveness and insufficient good quality evidence to warrant their routine use. Despite this, enthusiastic commercial marketing and slipping clinical equipoise have led to the widespread hasty introduction of this technology into practice, often at a considerable expense to the patient. We have reviewed the published literature and aim to summarize the strengths, weaknesses, opportunities and threats of these systems. These specialized incubators provide undisturbed embryo culture conditions and, by almost continuous monitoring of embryo development, generate morphokinetic parameters to aid embryo selection. They are thus hypothesized to improve outcomes following IVF. Although literature reports improved reproductive outcomes, these outcomes are largely surrogate and there is a paucity of studies reporting live births. The use of time lapse systems may reduce early pregnancy loss, increase elective single embryo transfers and limit multiple pregnancies through better embryo selection. However, the quality of the studies and hence the evidence so far, is low to moderate quality. We recommend further research producing robust high-quality evidence for and against the use of these systems.

Conclusions

Time-lapse imaging is a new technology aiming to improve the predictive ability of embryo selection and provide stable culture conditions. If proven to be effective and safe, it has the potential to improve the success rates of IVF treatment and reduce the incidence of multiple births and early pregnancy loss. This would translate into an enormous economic benefit for couples and healthcare providers by reducing time to pregnancy per couple, reduced high-risk obstetric and neonatal care for multiple pregnancies and reduced social and long-term care of children born with the complications of prematurity and cerebral palsy. If proven to be ineffective it would save the considerable expense of the equipment along with the time and training of embryologists. However, at present, there is insufficient high-quality evidence for its safety, efficacy and cost-effectiveness. To further evidence-based medicine, large RCTs to provide this evidence are essential before TLI systems are introduced into routine clinical practice.

Giới hạn của Timelapse

Review

Can time-lapse parameters predict embryo ploidy? A systematic review

Arnaud Reignier [a,b,c], *Jenna Lammers* [a,b], *Paul Barriere* [a,b,c], *Thomas Freour* [a,b,c,*]

A B S T R A C T

Embryo morphology assessment performs relatively poorly in predicting implantation. Embryo aneuploidy screening (PGS) has recently improved, but its clinical value is still debated, and the development of a cheap non-invasive method for the assessment of embryo ploidy status is a highly desirable goal. The growing implementation of time-lapse devices led some teams to test the effectiveness of morphokinetic parameters as predictors of embryo ploidy, with conflicting results. The aim of this study was to conduct a comprehensive review of the literature on the predictive value of morphokinetic parameters for embryo ploidy status. A systematic search on *PubMed* was conducted using the following key words: time-lapse, morphokinetic, aneuploidy, IVF, preimplantation genetic screening, PGS, chromosomal status. A total of 13 studies were included in the analysis. They were heterogeneous in design, patients, day of embryo biopsy, statistical approach and outcome measures. No single or combined morphokinetic parameter was consistently identified as predictive of embryo ploidy status. In conclusion, the available studies are too heterogeneous for firm conclusions to be drawn on the predictive value of time-lapse analysis for embryo aneuploidy screening. Hence, morphokinetic parameters should not be used yet as a surrogate for PGS to determine embryo ploidy *in vitro*.

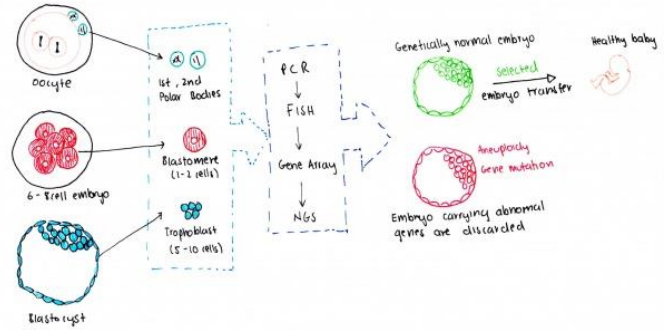
Conclusion

This comprehensive review of the literature demonstrates that morphokinetic parameters should not yet be used as a surrogate for PGS to determine chromosomal status of the preimplantation embryo. More large-scale studies, conducted in homogeneous populations with standard culture and biopsy protocol, using relevant statistical approaches adjusted to patients' characteristics, are needed to gain insight into the putative association between embryo morphokinetic parameters and ploidy, ultimately improving IVF clinical outcome.

Phân tích SWOT - PGT

Assessment of preimplantation genetic testing for embryo aneuploidies: a SWOT analysis

A. Alteri[1], L. Corti[1], A. M. Sanchez[2], E. Rabellotti[1], E. Papaleo[1,2], and P. Viganò[2]



Abstract

The recently re-named preimplantation genetic testing for determining embryo aneuploidies (PGT-A) is presently very popular although its acceptance by the scientific community is controversial. This approach still encounters drawbacks. This paper uses a SWOT (strengths, weaknesses, opportunities and threats) analysis to discuss salient points to be considered when examining the PGT-A strategy in order to gather information from a range of perspectives. One of the strength associated with the procedure is represented by an increase in implantation rate although data from the highest level of evidence do not support an increase in cumulative pregnancy rates. The current difficulty in the management of mosaicisms represents a weakness of PGT-A. The application of the strategy represents an opportunity to favor the single embryo transfer while other advantages such as reduction of time to pregnancy and emotional distress are controversial. Potential important threats, at present still undefined, are represented by the biopsy-related damage to the blastocyst and the impact on neonatal and long term outcomes.

Strengths	Impact/Benefit
increased implantation rate	to be defined
decreased miscarriage rate	reduction of medical treatments reduction of distress

Weaknesses	Impact/Risks
3 RCTs in good prognosis patients 1 RCT in AMA patients	to set up clinical procedures based on poor evidence
cumulative IVF success not improved	overtreatment
spectrum of genetic techniques	misdiagnosis
management of mosaicism	decrease in treatment effectiveness

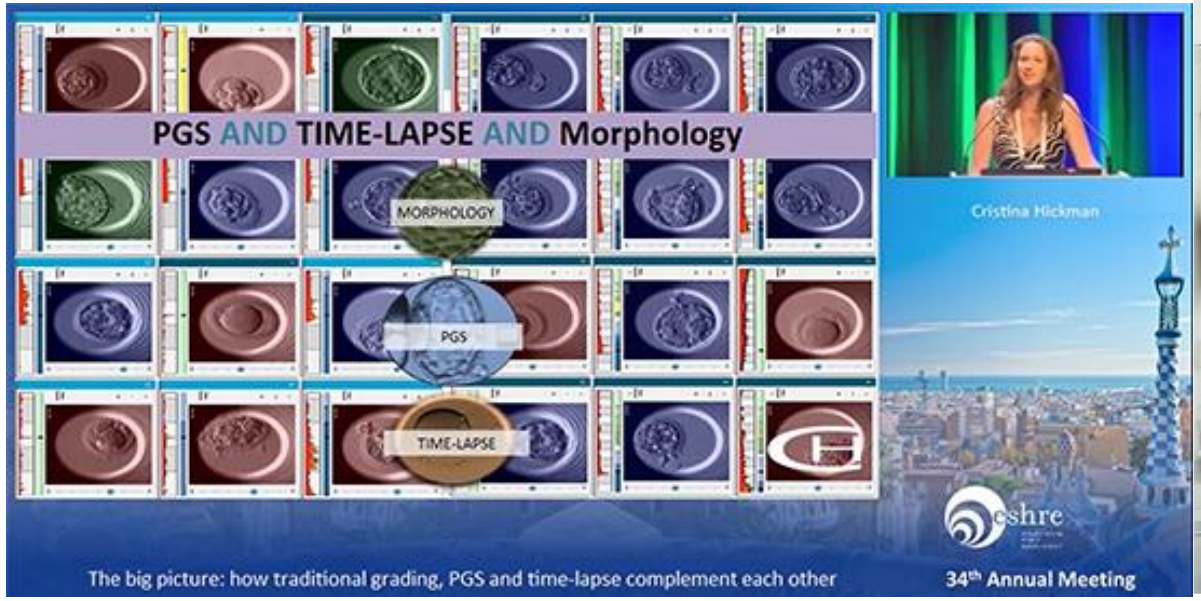
Opportunities	Impact/Benefit
adoption of eSET policy	reduction of multiple pregnancies
reduced time to pregnancy	cost reduction
psychological aspect of healthy care	improvement of patients' management

Threats	Impact/Risks
high cost	patients' dissatisfaction
invasive procedure and not standardized technique	embryo damage
obstetrical and perinatal outcomes: limited data long-term effect: limited data	adverse outcomes

https://doi.org/10.1111/cge.13520 2019

Giải pháp tối ưu

PGT + Timelapse



Các thông tin cần quan tâm khi tư vấn phôi

1. **Chỉ số về tạo phôi và nuôi cấy phôi:** Tỷ lệ thụ tinh 2PN, tỷ lệ phôi phân chia (ngày 3), tỷ lệ phôi phát triển đến ngày 5.
2. **Chỉ số liên quan đến Timelapse:** tỷ lệ phôi phân chia bất thường, tỷ lệ phôi hữu dụng khi nuôi cấy trong Timelapse.
3. **Chỉ số về hiệu quả của chương trình PGT:** tỷ lệ phôi không cho tín hiệu sau sinh thiết phôi, tỷ lệ phôi cho kết quả thể khảm..v.v..
4. **Chỉ số về hiệu quả của chương trình trữ - rã phôi:** tỷ lệ phôi sống sau rã ở ngày 3/ngày 5 (hoàn toàn hay không hoàn toàn).
5. **Chỉ số về hiệu quả của chương trình TTTON:** tỷ lệ có thai lâm sàng, số phôi chuyển trung bình ở ngày 3/ngày 5, tỷ lệ trẻ sinh sống, tỷ lệ biến chứng khác, v.v..

Xu hướng của TTTON trong tương lai

- Nhiều vật tư tiêu hao và thiết bị thiết kế cho TTTON
- Tiếp tục cải tiến hệ thống nuôi cấy phôi và tăng sức sống của phôi
- Đánh giá chất lượng phôi bằng phương pháp khách quan
- Tăng xét nghiệm di truyền phôi
- Cải thiện tỷ lệ làm tổ
- Tăng tỷ lệ trữ rã phôi
- Tăng tỷ lệ chuyển 1 phôi.

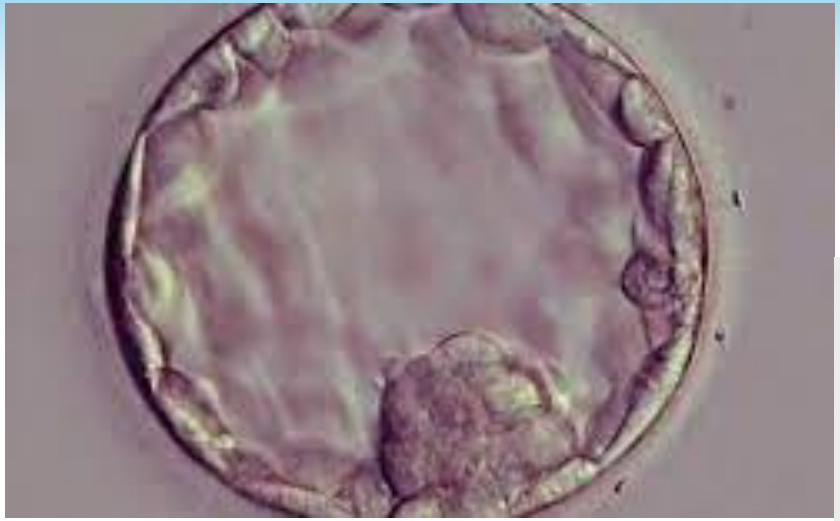
RÚT NGẮN THỜI GIAN CÓ THAI!!!

Thông điệp mang về

- Let the embryo choose ☺ for the IVF Lab.

- "Direct-2-consumers" & "Let the customers choose" tức là "Hãy để cho khách hàng của bạn có quyền chọn lựa."

Thank you!



Our embryologist's responsibilities

Next human generations