
TOGETHER.
ALL THE WAY™
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TIME LAPSE BY VITROLIFE: PRIMO VISION

Brett Glazar, M.S.
Lab Manager/Senior Embryologist

DISCLOSURES

- Employee at Vitrolife
  - MEA Lab Manager
  - R&D team; responsible for U.S. Regulatory Submissions and clinical data management

- Primo Vision and the microwell dish are not yet FDA approved for clinical use in the U.S.
  - Microwell dish is pending FDA approval
  - Primo Vision is approved (CE) for use in Europe, Canada and Mexico

AGENDA

- The Primo Vision concept
- Primo Vision microwell dish
- Computerized embryo monitoring
- Scientific evidence
- Summary

THE PRIMO VISION CONCEPT

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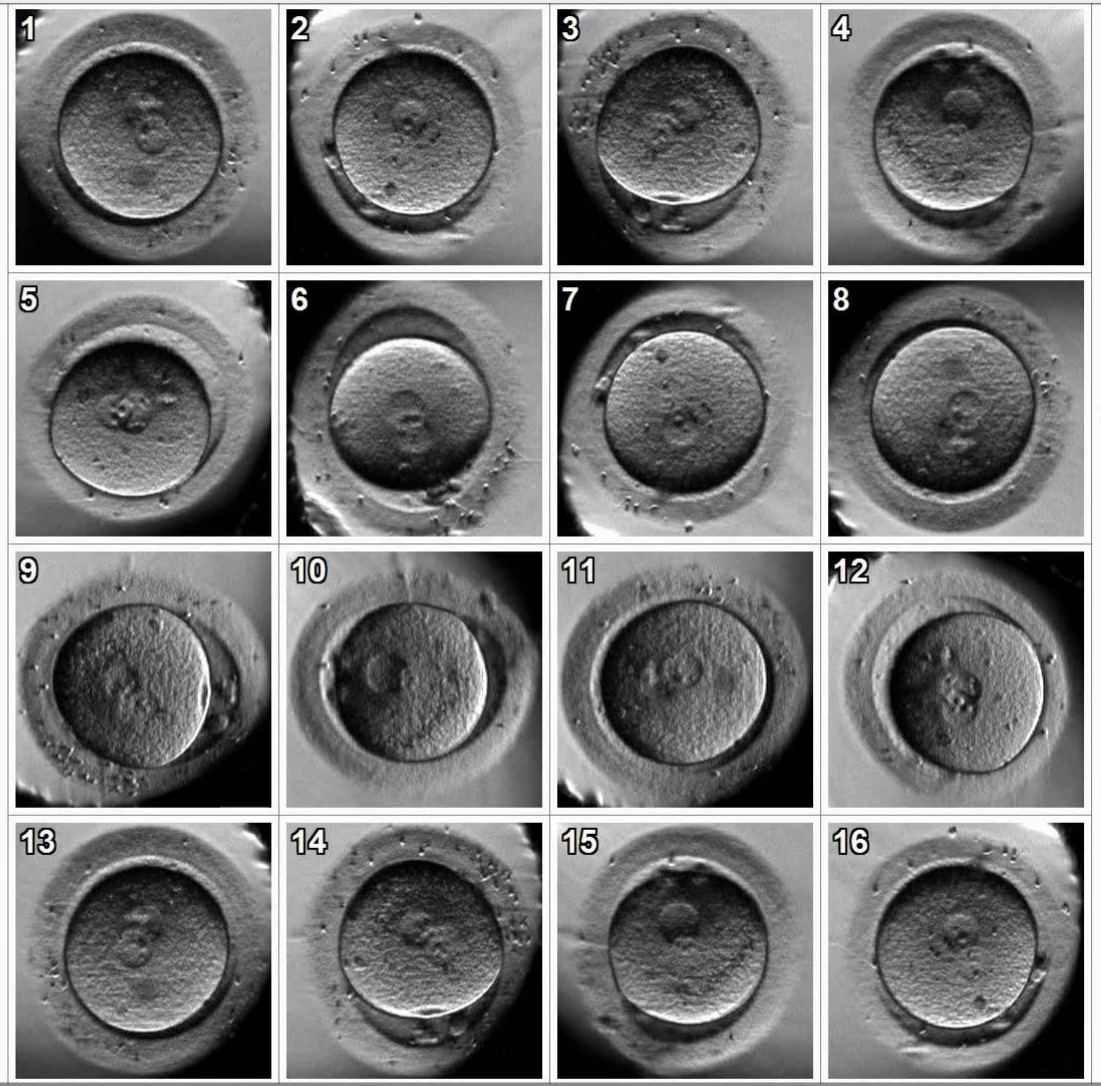
TIME-LAPSE EMBRYO MONITORING

A continuous monitoring brings more to the morphological assessment

Primo Vision EVO

Time Lapse Embryo Monitoring System

Elapsed time: 0 Days,00:00



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PRIMO VISION

A time-lapse system providing safe culture in your incubator

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EMBRYO EVALUATION WITHOUT OPENING THE DOORS OF YOUR INCUBATOR

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OPTICS COMPLETELY SEPARATED FROM CONTROLLING AND ANALYSIS

Culturing environment

Controlling unit

Capture and Analysis

STATE-OF-THE-ART IMAGE QUALITY

Stereo Microscope

- 3D
- Familiar
- Comparable?

Primo Vision Microscope

- Hoffmann contrast optics
- Wide field of view
- 1 micron /pixel
- 5 megapixel CCD chip

MODULAR SYSTEM – SIZE IT AFTER YOUR NEEDS

Let your time-lapse system grow with you

For research

For some patients

For all

GROUP CULTURE ENVIRONMENT

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PRIMO VISION EMBRYO CULTURE DISH

Individually monitored embryos in improved group culture system

- Custom designed and manufactured
- Sterile, disposable
- Group culture in microwells
- 9 or 16-well edition
- CE 93/42 marked and officially one-cell mouse embryo tested (MEA)
- Specially adjusted for in vitro culture in Primo Vision System
- Provides significantly better culture environment than traditional culturing[1,2]

[1] Ergin E. et al., Turkey, ESHRE 2014
[2] Fancsovits P. et al., Hungary, ALPHA 2014)

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OPTIMIZED CULTURE

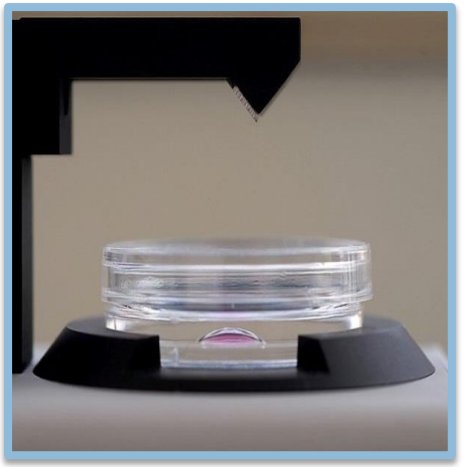
Individually monitored embryos in improved group culture system

Individual Monitoring

- 9-16 embryos
- Rim for stable carrying
- Orientation sign
- Alphanumeric well identification

Improved culture

- Embryos developing:
  - In their own microenvironment
  - Under a common microdroplet




COMPUTERIZED EMBRYO MONITORING

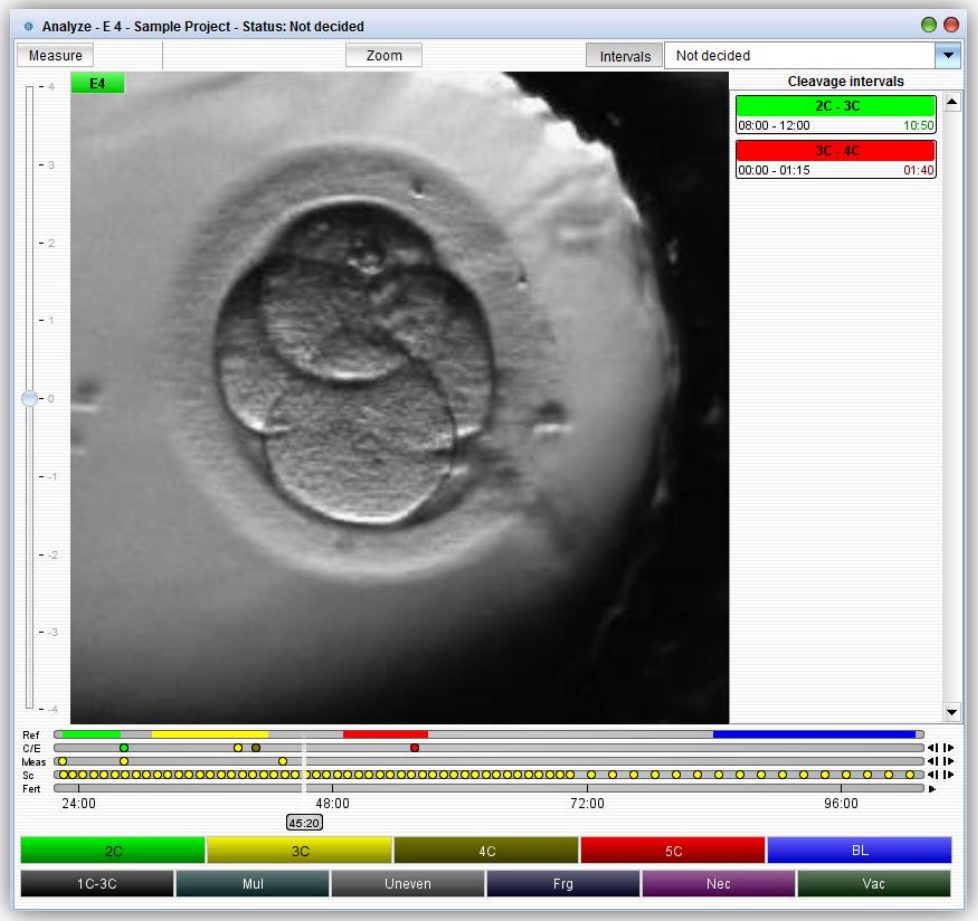
COMPUTERIZED EMBRYO MONITORING

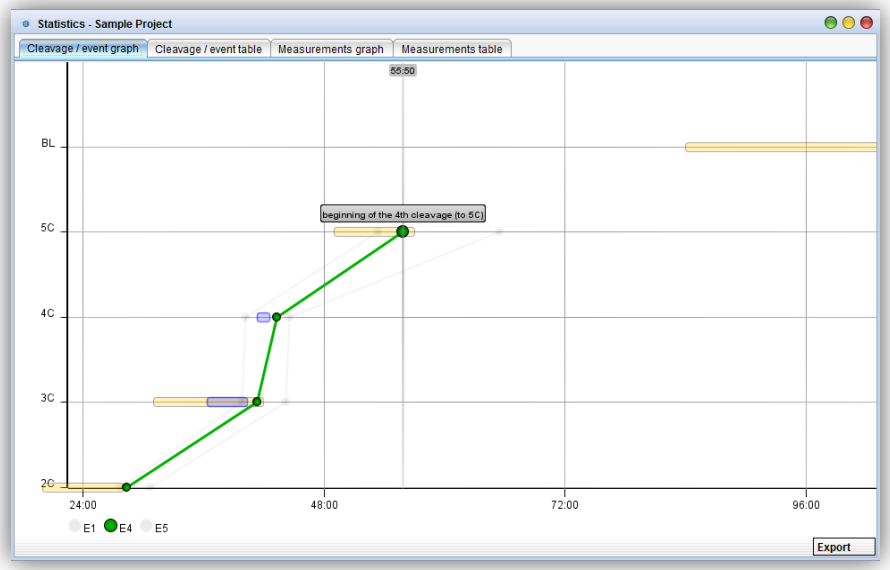
Offers new possibilities

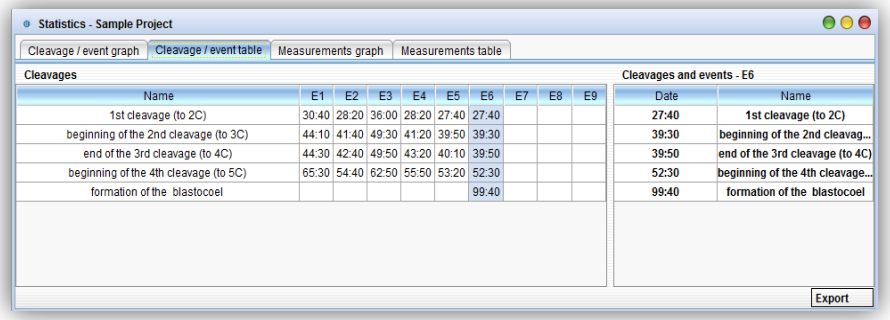
- Automated image capturing: 5-10 minutes capture intervals
- Annotate embryos' development manually
- Compare and rank the embryos by their potential according to latest science
- Create personalized reports
- Follow your embryos remotely from your office or computer
- Share results via video and iPAD
- Create an archive of all your result – a perfect base for research

ANNOTATE IMPORTANT TIMINGS

In an easy ”Play and click”-way







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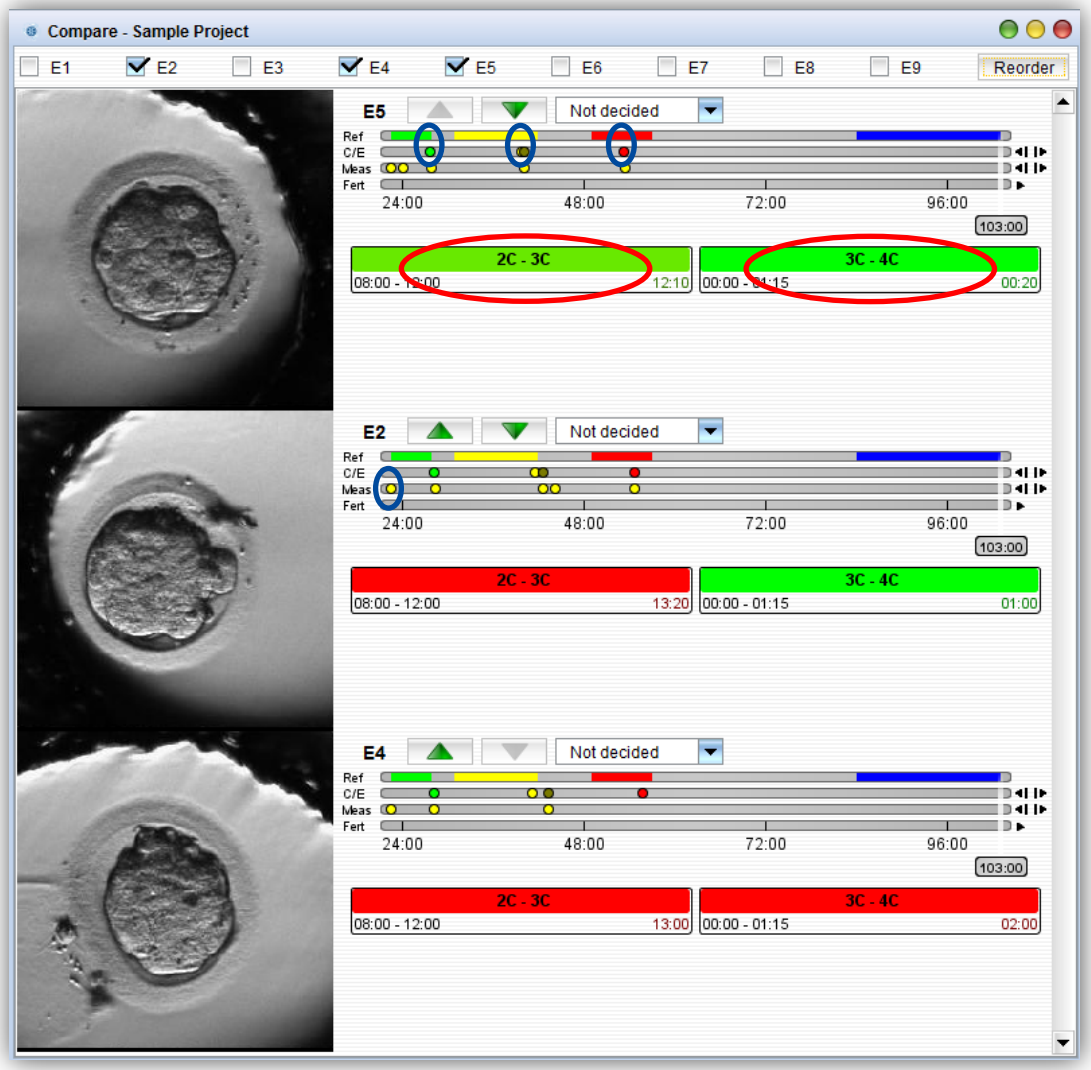
COMPARING IS EASY

Follow your best embryos separately



- Cleavage times
- Interphases between cleavages
- Review events
- Measurements

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REPORTS ARE CREATED AUTOMATICALLY

A simple way of archiving

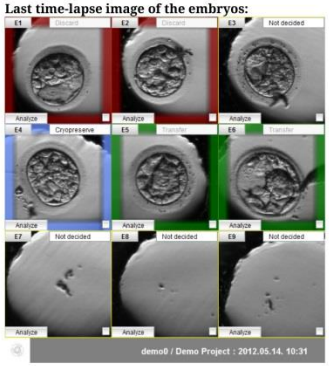
Patient name: Mrs. Patient Date of birth: 10/05/71	Date of aspiration: 09/05/12 14:10 Date of time-lapse cycle: 10/05/12 12:40 14/05/12 10:31 3 d 21:51 Date of report creation: 27/04/13 12:13

TIME-LAPSE EMBRYO MONITORING REPORT
SUMMARY

Date of fertilisation: 09/05/12 14:10
Method of fertilisation: IVF and ICSI

Start of the time-lapse cycle: 10/05/12 12:40
End of the time-lapse cycle: 14/05/12 10:31

Last time-lapse image of the embryos:



Number of eggs retrieved: 8
Number of eggs fertilized: 6 IVF: 3 ICSI: 3
Number of PGDs: 0

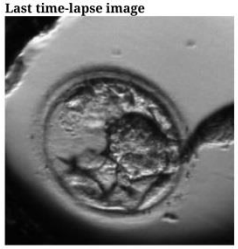
Number of embryos transferred: 2 E5 E6
Number of embryos cryopreserved: 1 E4
Number of embryos discarded: 2 E1 E2
Number of embryos not-decided: 4 E3 E7 E8 E9

Notes:

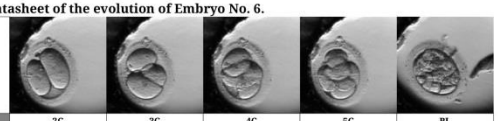
Patient name: Mrs. Patient Date of birth: 10/05/71	Date of aspiration: 09/05/12 14:10 Date of time-lapse cycle: 10/05/12 12:40 14/05/12 10:31 3 d 21:51 Date of report creation: 27/04/13 12:13

TIME-LAPSE EMBRYO MONITORING REPORT
Transferred Embryo (No. 6.)

Last time-lapse image

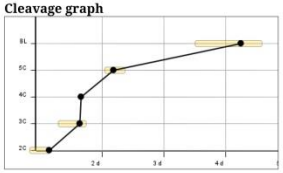


Summary datasheet of the evolution of Embryo No. 6.

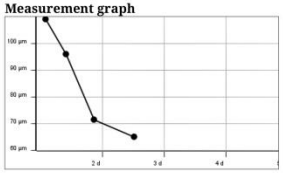


Status	2C	3C	4C	5C	BL
Cleavage time	27:40	39:30	40:00	52:30	101:50
Reference time	20:00	31:00	-	49:00	84:00
Measurement	28:00	42:00	-	57:00	110:00
	-	-	-	-	-

Cleavage graph



Measurement graph



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FEEL FLEXIBLE – MONITOR AND ANALYZE WHERE YOU ARE

SCIENTIFIC EVIDENCE

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TIME-LAPSE MONITORING SIGNIFICANTLY INCREASED PREGNANCY RATES

STUDY DESIGN

- Prospective cohort trial
- 239 women (≤42 y) undergoing ICSI cycles
  - Patients randomized into TLM group (30%) or Conventional group (70%)
- 2- or 3-day culture
  - TLM group: Primo Vision dishes
  - Conventional group: Nunc dishes
- Evaluation and selection for transfer
  - 1-3 embryos transferred per patient
  - TLM group:
    - Without removing the embryos from the incubator
    - t2, t3, t4, t5, t8; cc2, cc3; s2, s3
  - Conventional group:
    - Morphological evaluation at 44h and 68 h

Morphokinetic parameters of early embryo development via timelapse monitoring and their effect on embryo selection and ICSI outcomes: a prospective cohort study (Siristatidis C. et al., Greece; J assist reprod genet)

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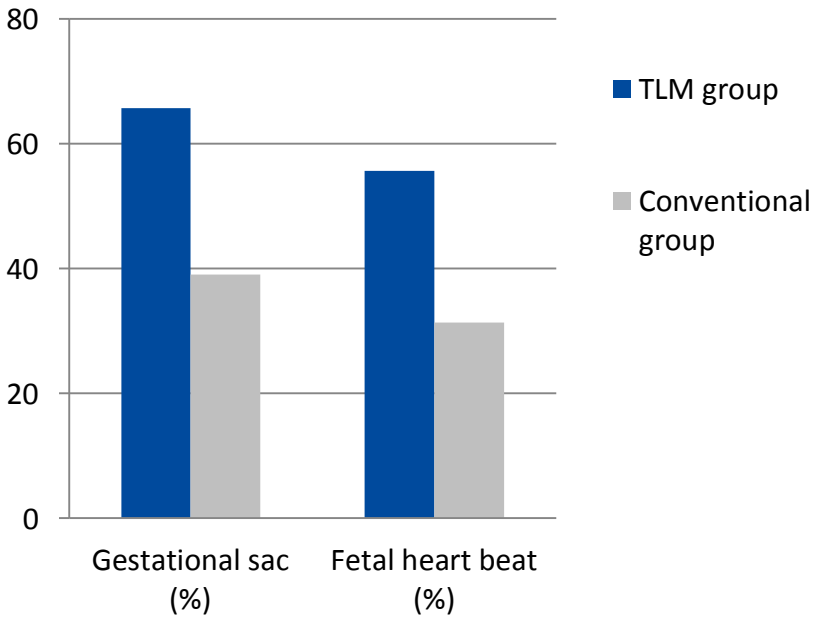
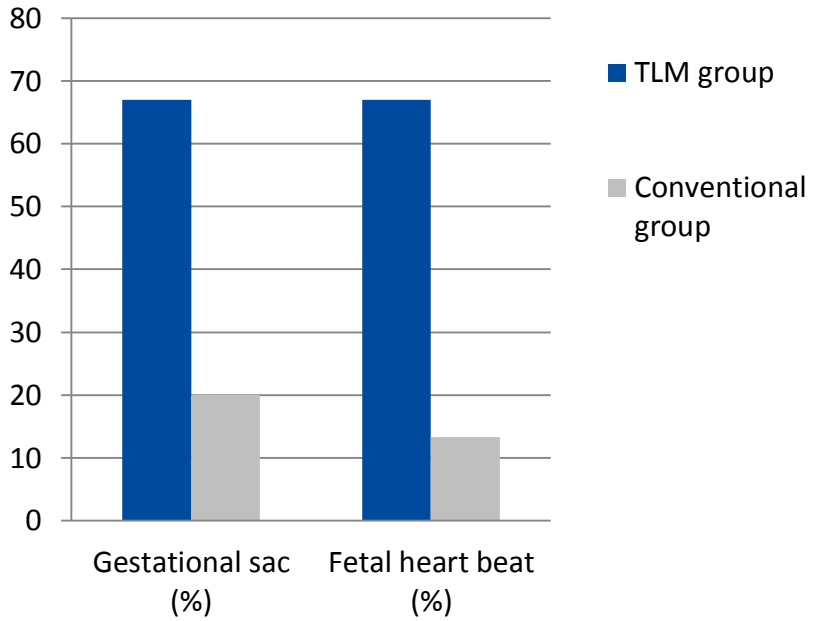
TIME-LAPSE MONITORING SIGNIFICANTLY INCREASED PREGNANCY RATES

OUTCOME



OUTCOME IN PATIENTS > 40 Y



Morphokinetic parameters of early embryo development via timelapse monitoring and their effect on embryo selection and ICSI outcomes: a prospective cohort study (Siristatidis C. et al., Greece; J assist reprod genet)

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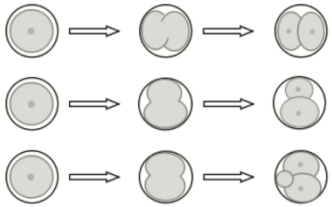
CLEAVAGE PATTERN PREDICTS DEVELOPMENTAL POTENTIAL OF DAY 3 HUMAN EMBRYOS PRODUCED BY IVF

1 Retrospective analysis for model building

- 345 embryos were studied for abnormalities in division behaviour
- Two categories formed, based on the impact of abnormal division behaviours on daughter cells (whether they take part in blastocyst formation or not)

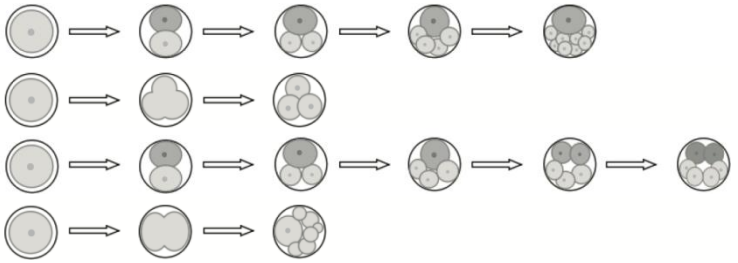
CATEGORY 1 – abnormal division behaviours with low impact on blastocyst formation:

- Distorted cytoplasmic movement
- Uneven blastomeres
- Big fragment



CATEGORY 2 – abnormal division behaviours with high impact on blastocyst formation:

- Developmental arrest
- Direct cleavage
- Disordered division
- Fragmentation



Yang S.T. et al., China; Reprod Biomed Online, 2015

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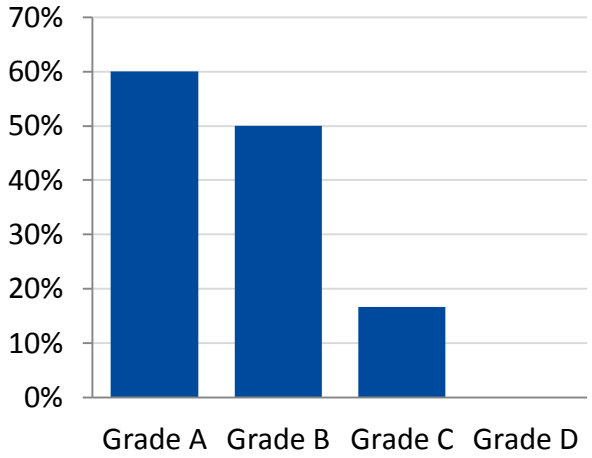
CLEAVAGE PATTERNS OF THE FIRST THREE CLEAVAGE CYCLES CAN PREDICT THE DEVELOPMENTAL POTENTIAL OF EMBRYOS ON D3

2 Prospective observational study

- Based on the retrospective study results a hierarchical classification model was developed
  - Embryos were classified into Grade A – F, based on the type of abnormal division:
    - Belongs to Category 1 or 2?
    - Occurs in 1st, 2nd or 3rd cleavage cycle?
- Correlation of embryo grade and implantation was studied in 144 KID embryos of 70 women
  - Significant decrease in the implantation rate of embryos of lower grades

Implantation rate



(Grade E and F embryos were not transferred)

Yang S.T. et al., China; Reprod Biomed Online, 2015

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STUDIES SUPPORTING GROUP CULTURE

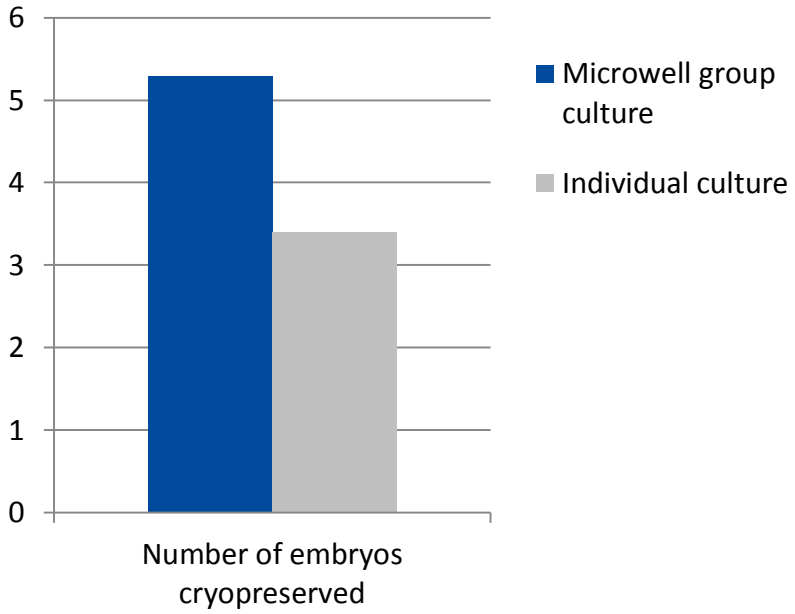
COMPARISON OF CULTURE IN GROUP IN A MICROWELL GROUP CULTURE DISH OR INDIVIDUALLY IN DROPLETS

Results from an intermediate analysis

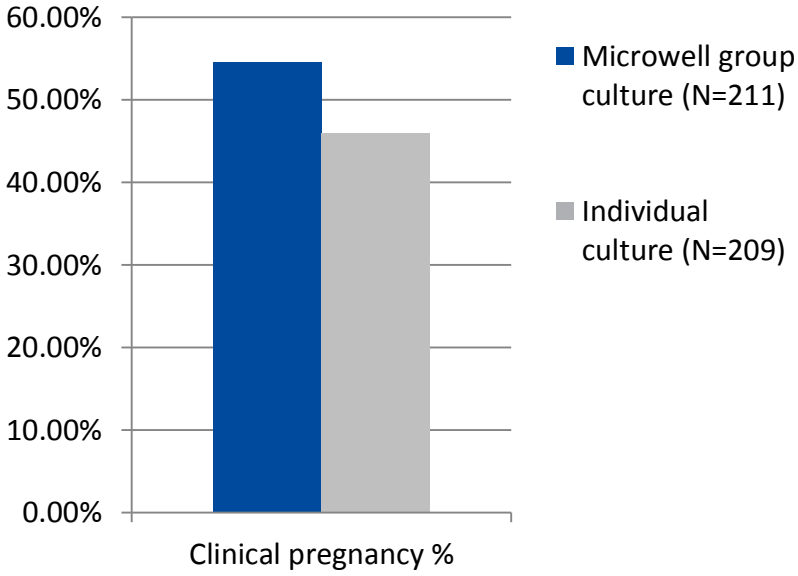
- Prospective randomized study
- Comparison of group culture vs individual culture
  - 3-day culture
  - Group culture in Primo dish — 211 transferred embryos
  - Individual culture — 209 transferred embryos

GROUP CULTURE IN PRIMO DISH ALLOWS SIGNIFICANTLY BETTER CULTURE CONDITIONS FOR THE EMBRYOS

Higher proportion of embryos available for cryopreservation (p=0.002)



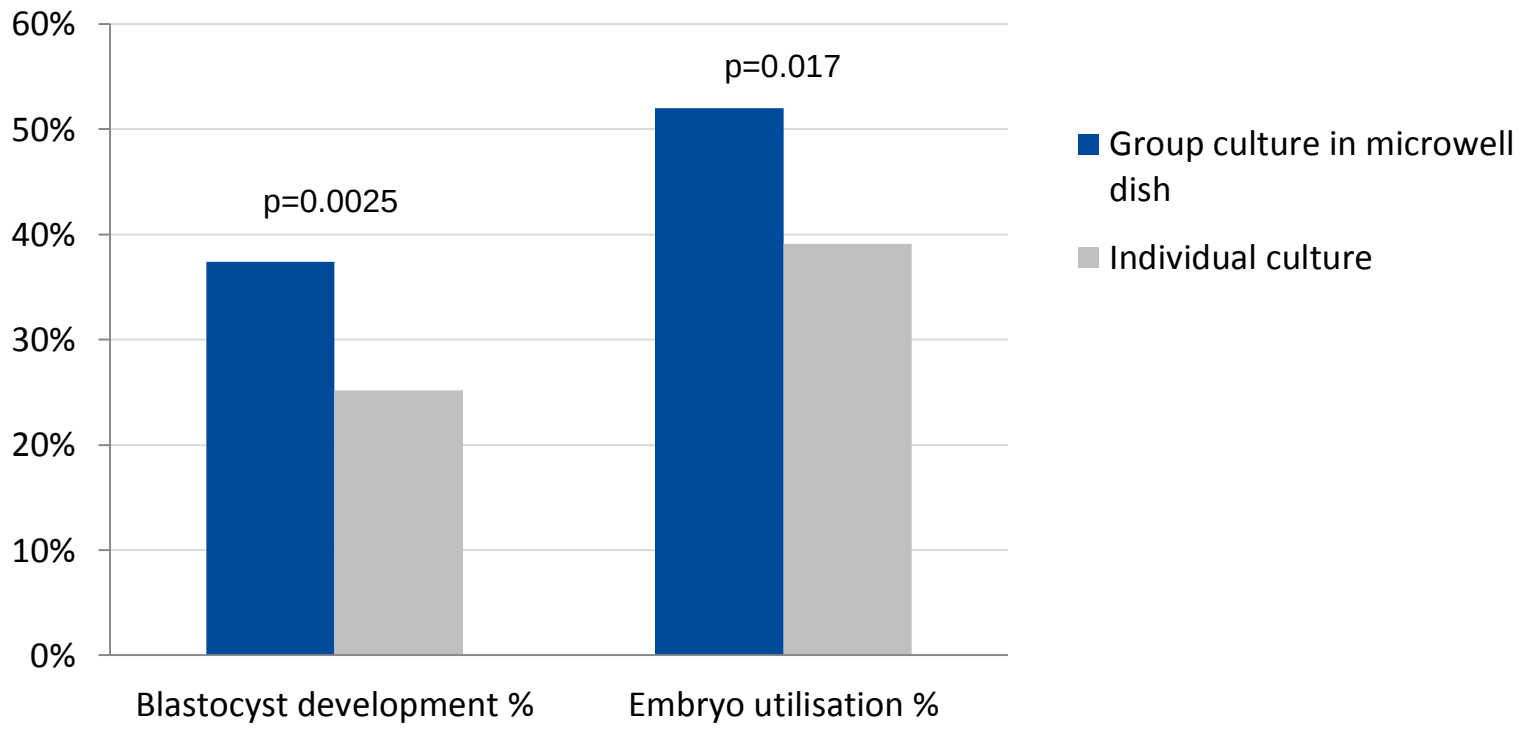
Higher clinical pregnancy rate 54.5% vs. 45.9% (p=0.06)



COMPARISON OF SINGLE EMBRYO CULTURE OF GROUP CULTURE USING A MICRO-WELL GROUP CULTURE DISH

- Prospective randomized study
- 5-day culture
  - group culture (85 embryos) vs
  - individual culture (85 embryos) in the same dish
- Group culture in the Primo dish
  - higher expanded blastocyst rate (p=0.0025)
  - higher proportion of „A" grade ICM and TE (p<0.0001, p=0.0007)
  - higher rate of embryo utilisation (p=0.017)

GROUP CULTURE IN PRIMO DISH ALLOWS SIGNIFICANTLY BETTER CULTURE CONDITIONS FOR THE EMBRYOS



Ergin E. et al., P 117 Randomized controlled comparison of single embryo culture versus group culture using a micro-well group culture dish in humans, ESHRE 2014

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SUMMARY

SUMMARY

- Good for the embryo
  - Stable conditions
  - Reduced handling
  - Controlled environment
- Good for the embryologist
  - Catch abnormal cleavages
  - Improved selection and deselection
  - Easy to use system
- Good for the clinic
  - Modular, flexible system
  - Improved workflow
  - QC tool
  - Archiving tool
  - Service tool

Attila, born in May, 2010
World's first time-lapse baby assessed with Primo Vision V2

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