

EFFICACIA DELLO STUDIO MORFOCINETICO DELL'EMBRIONE

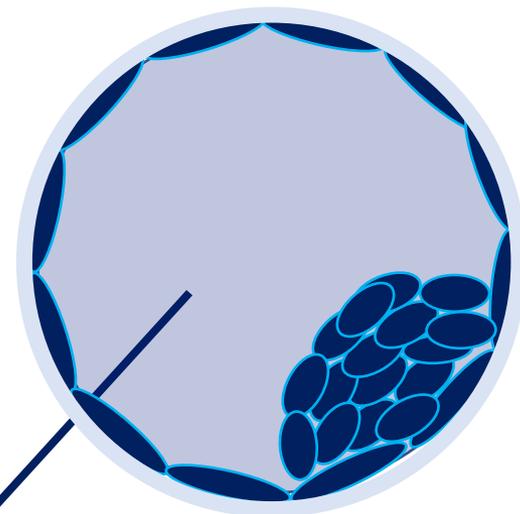
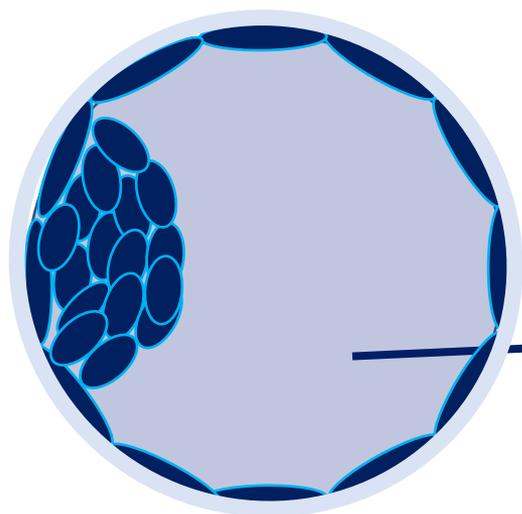
Federico Favero

Embriologo clinico, ARC-STER

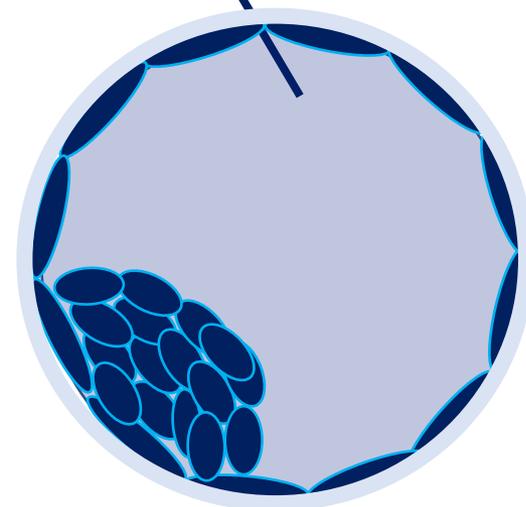
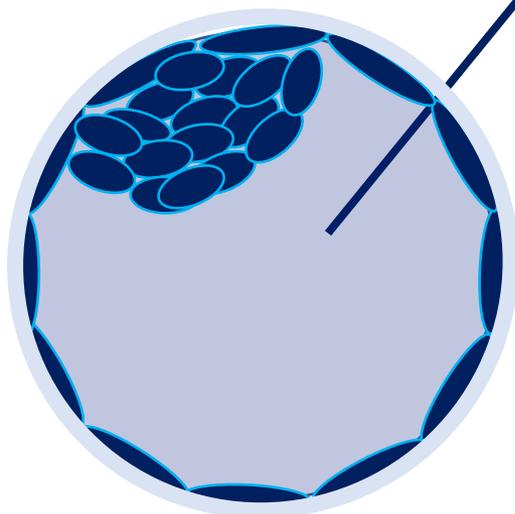
Delegato regione Veneto, SIERR



Marker non invasivi



NATO VIVO SANO?







INCUBATORE
(aumento chance)

TIME LAPSE SYSTEMS



MORFOCINETICA
(time to pregnancy - TTP)

INCUBATORE

- Accuratezza
- Sistemi modulari -> ridondanza
- Piastre dedicate (12-16 embrioni)
- Imaging ogni 5-20 min
- Luce: 500-600 nm



Non estrarre gli embrioni dall'incubatore - migliora la coltura? TL vs benchtop

Park et al., 2015

No benefit of culturing embryos in a closed system compared with a conventional incubator in terms of number of good quality embryos: results from an RCT

H. Park, C. Bergh, U. Selleskog, A. Thurin-Kjellberg, and K. Lundin*

- Transfer in D2
- IR simile
- Stesso n di embrioni di buona qualità

Barberet et al., 2018

Randomized controlled trial comparing embryo culture in two incubator systems: G185 K-System versus EmbryoScope

Julie Barberet, Pharm.D.,^a Jérémy Chammas,^a Céline Bruno, M.D.,^a Elodie Valot,^a Clarisse Vuillemin,^a Lysiane Jonval,^b Cécile Choux, M.D.,^c Paul Sagot, M.D.,^c Agnès Soudry, Pharm.D., Ph.D.,^b and Patricia Fauque, M.D., Ph.D.^{a,d}

- Miglior morfologia per embrio in TL (D2/3)
- IR non significativamente superiore
- > n blastocisti vitrificate (30% vs 25%)

MORFOCINETICA: VANTAGGI NEL MOLTIPLICARE LE OSSERVAZIONI

- Rilevazione eventi:
 - localizzati nel tempo (comparsa-scomparsa PN)
 - dinamici (movimento PN, DUC, RC..)
- Valutazione temporale

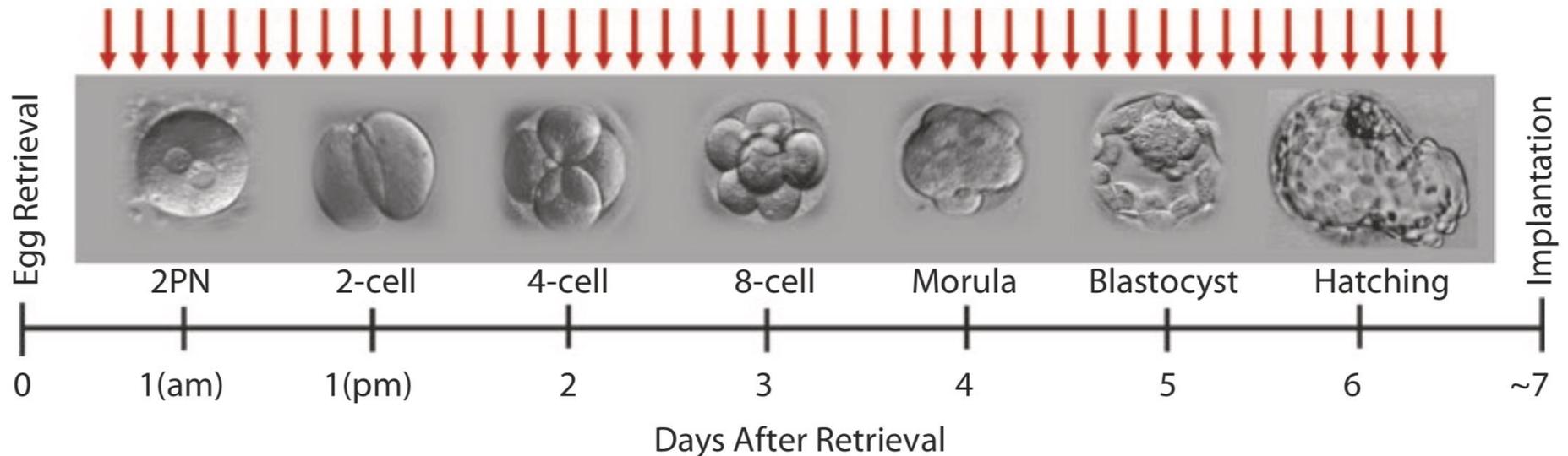


Image: Dolinko and Racowsky 2019

FERTILIZZAZIONE- parametri qualitativi

CYTOPLASMIC WAVE

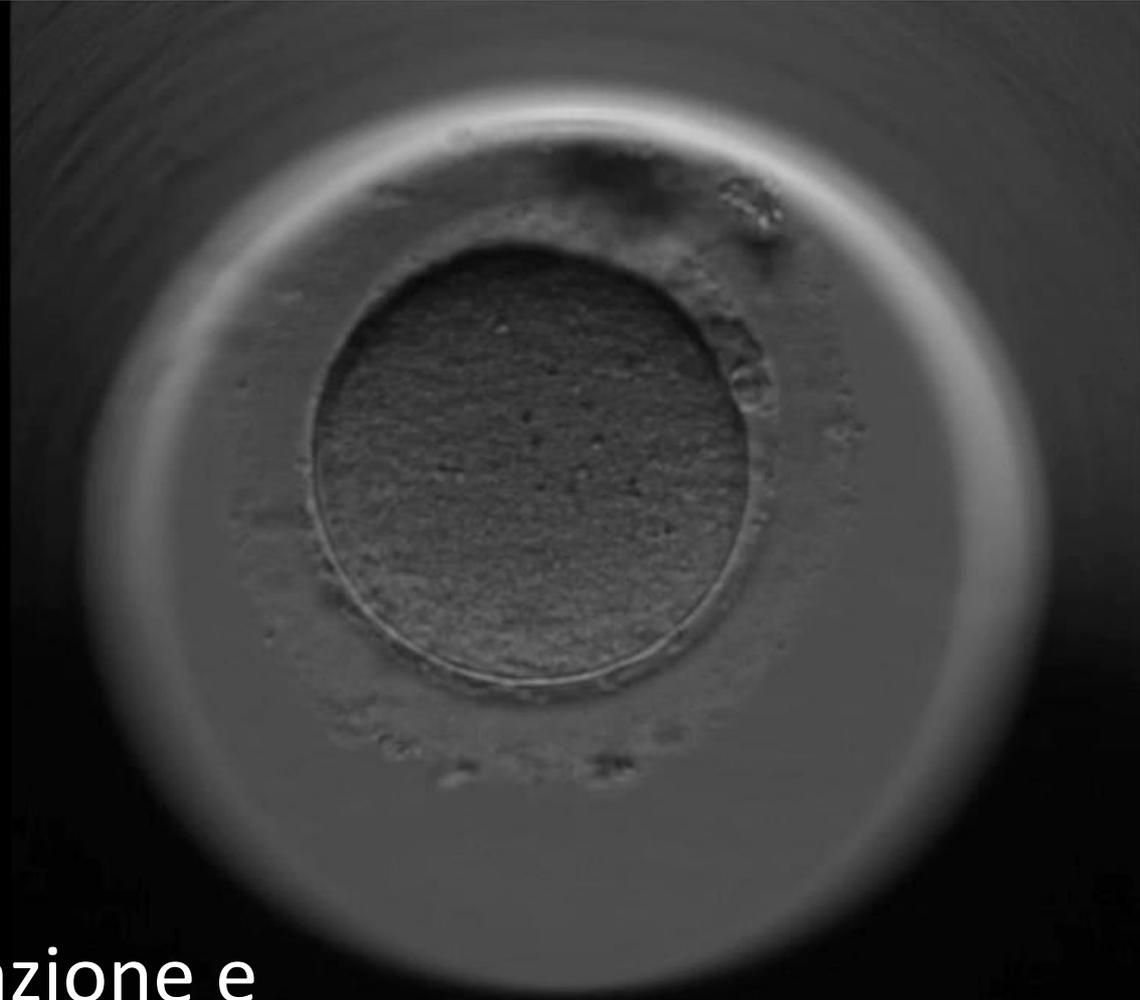
Tutti gli ovociti

2-3H dopo PBII

1h prima PN

Formazione dell'aster
Spermatocico.

Microtubuli per formazione e
allineamento pronucleo maschile



Coticchio et al., 2018

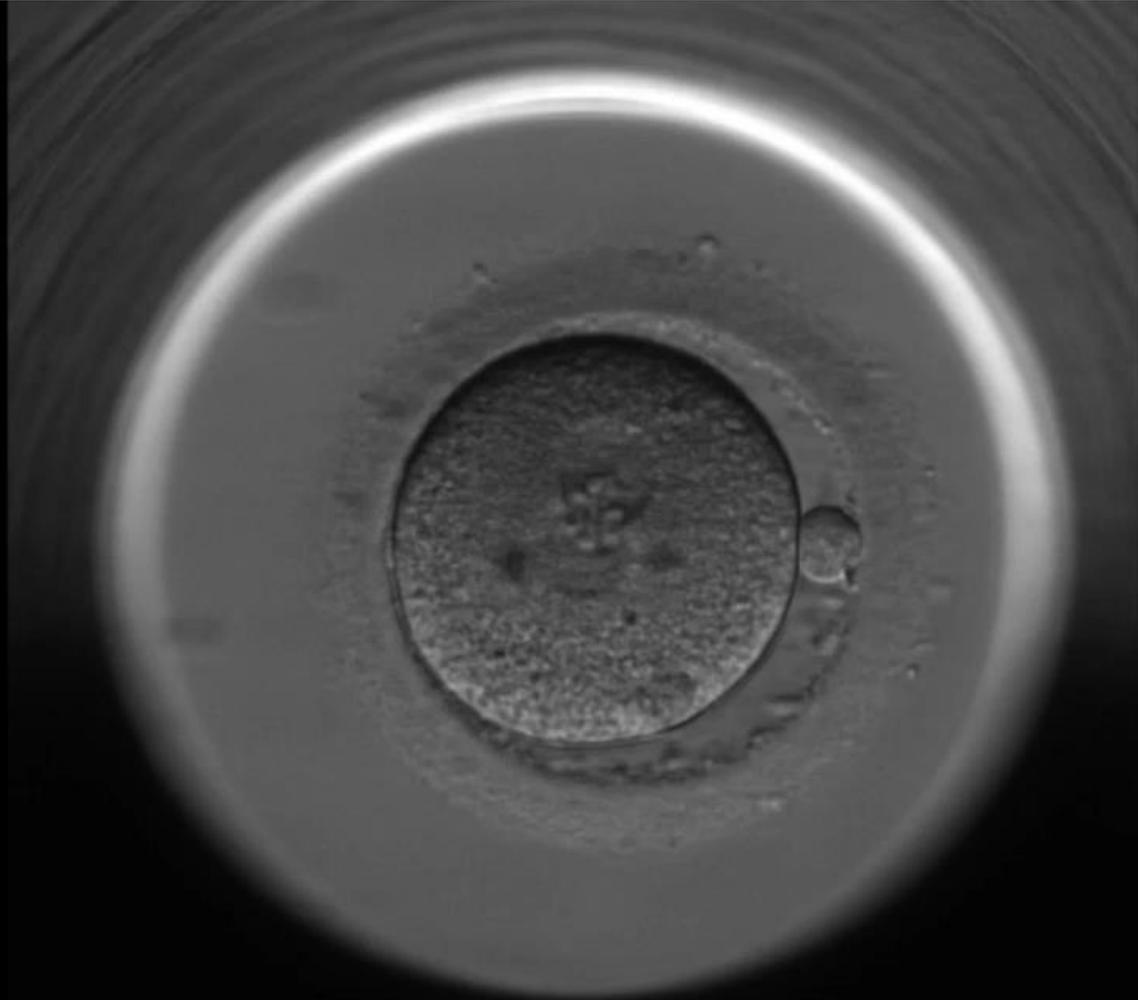
1.0h

FERTILIZZAZIONE- parametri qualitativi

AFFIANCAMENTO PN

Materno raggiunge
Il paterno

Dopo l'appaiamento
Si accentrano

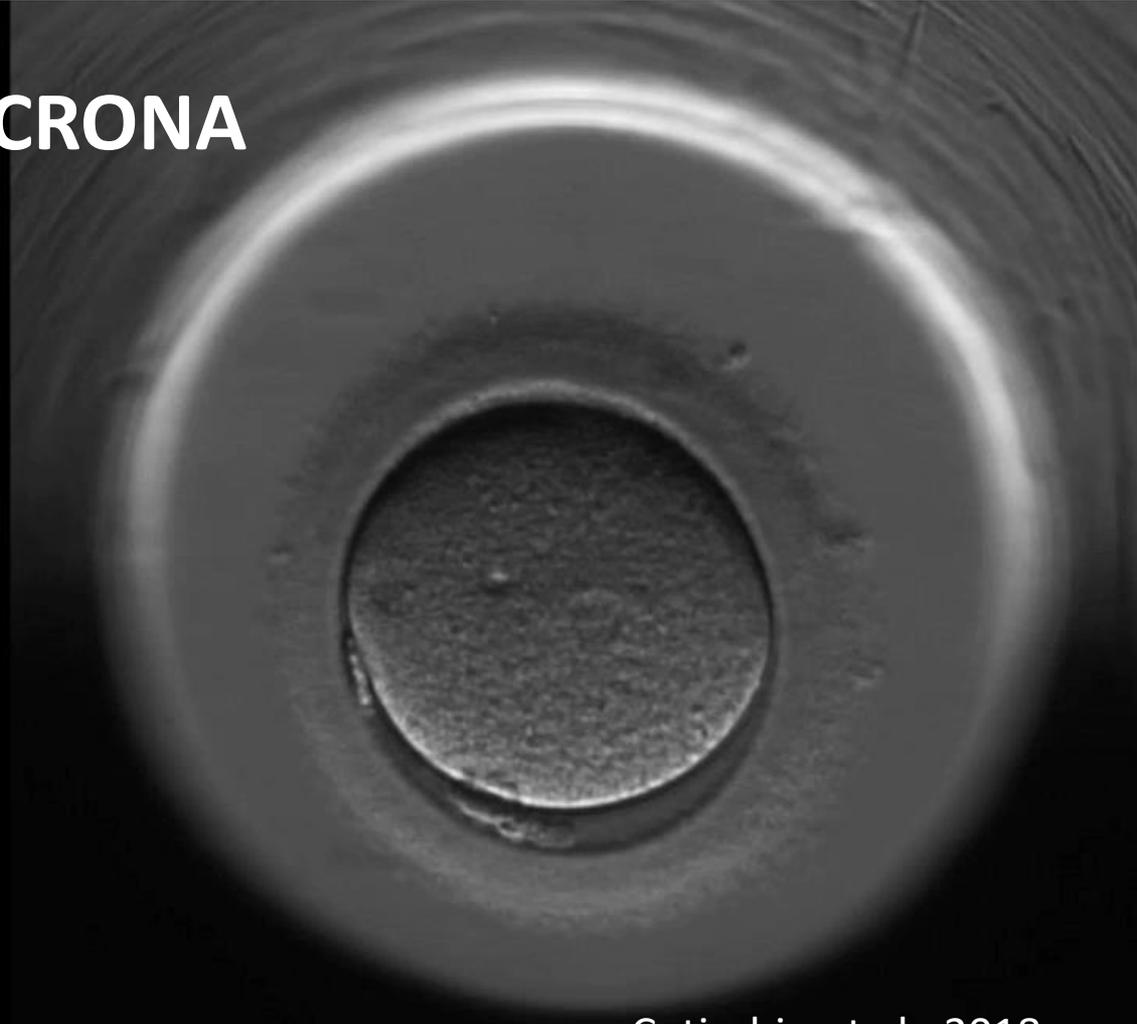


FERTILIZZAZIONE- parametri qualitativi

SCOMPARSA PN ASINCRONA

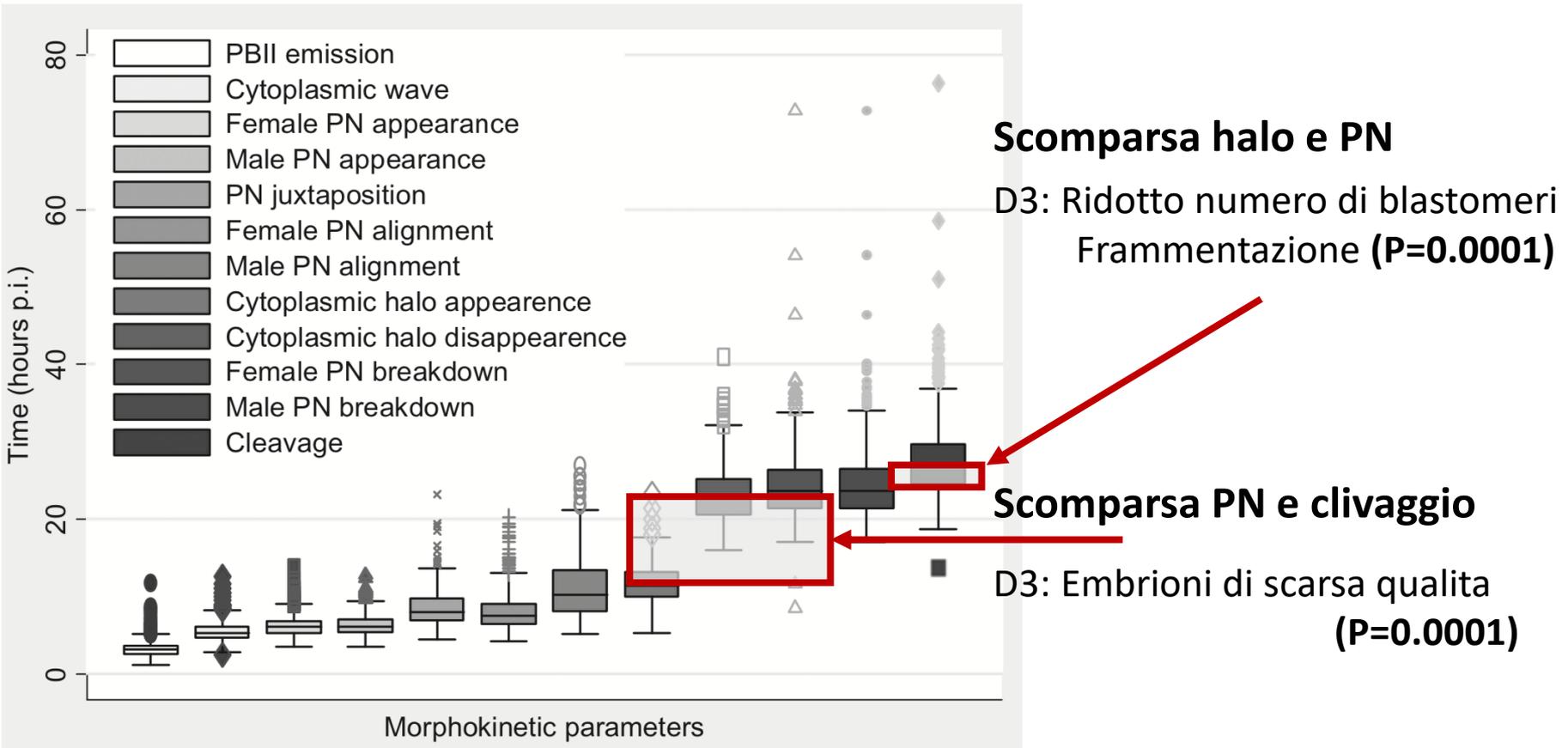
Spesso associato a:

- DUC
- Forte ritardo del primo clivaggio



FERTILIZZAZIONE – parametri temporali

Intervalli di tempo e qualità embrionaria



CLIVAGGIO – parametri qualitativi

RC: reverse cleavage
~10% embrioni

Blastulazione regolare

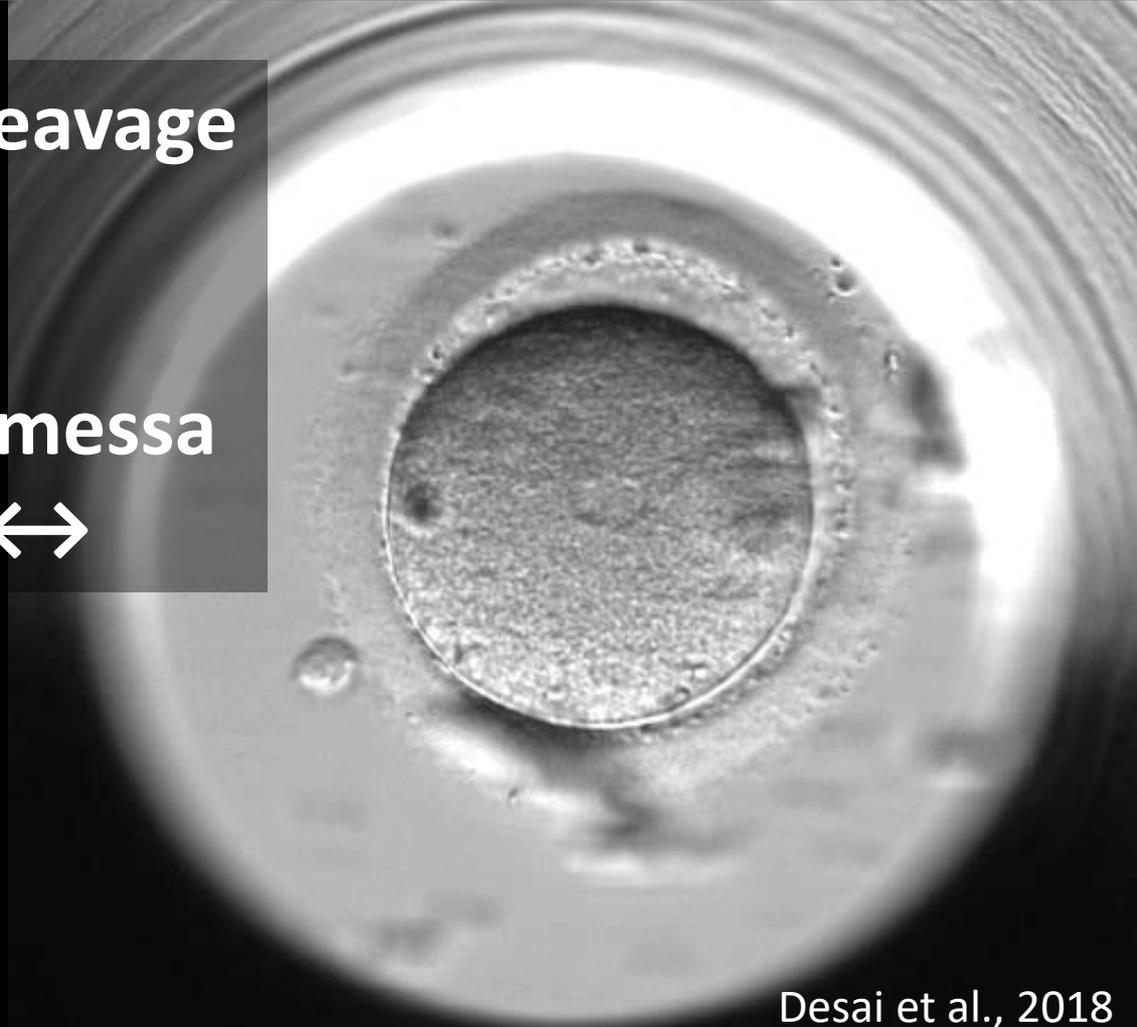


Desai et al., 2018

CLIVAGGIO – parametri qualitativi

DUC: direct uneven cleavage
~8% embrioni

Blastulazione compromessa
Aneuploidie in blasto ↔



Desai et al., 2018

CLIVAGGIO – parametri qualitativi

MULTINUCLEAZIONE

~35% embrioni

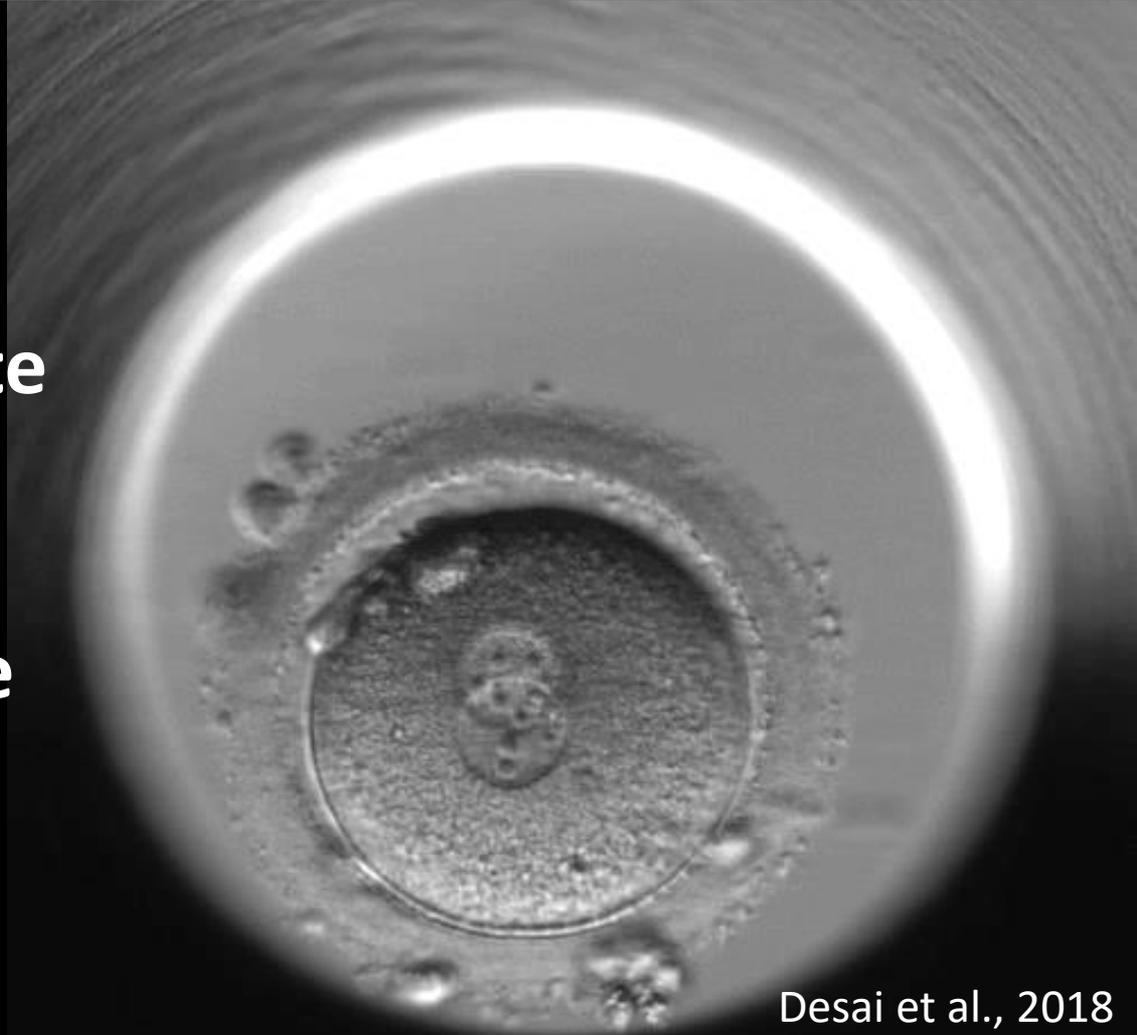
**Storicamente associate
a ↓ IR**

Blastulazione regolare

Aneuploidie ↔

Se con DUC, RC

Aneuploidie ↑



Desai et al., 2018

PARAMETRI QUALITATIVI: PLOIDIA?

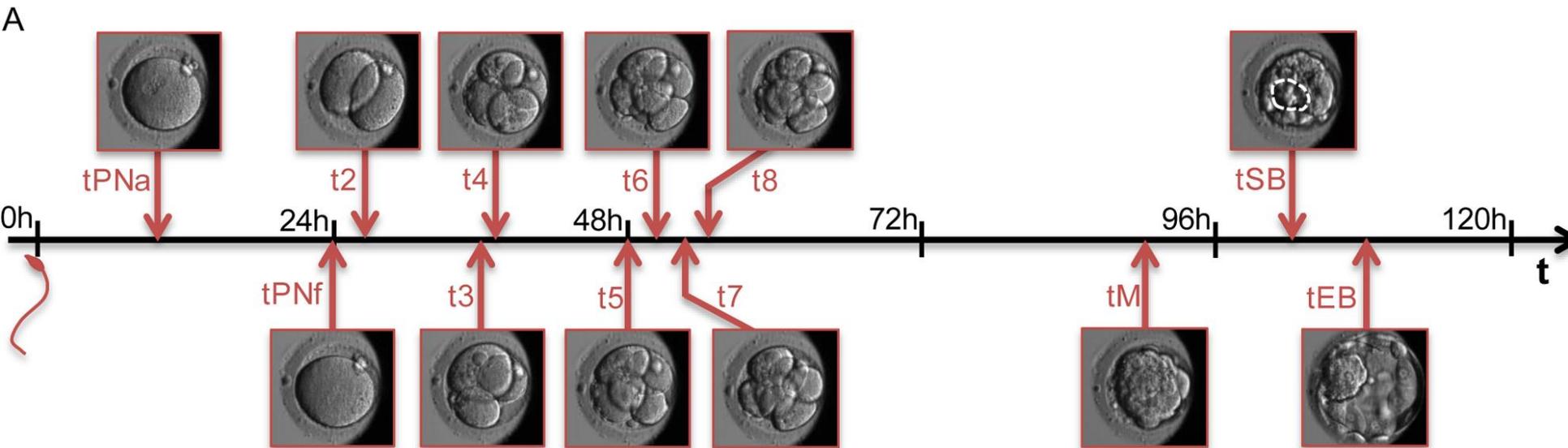
ANOMALIE DI CLIVAGGIO (RC, DUC, MN):

Da sole poco predittive, tranne DUC

2+ associate con >> aneuploidia

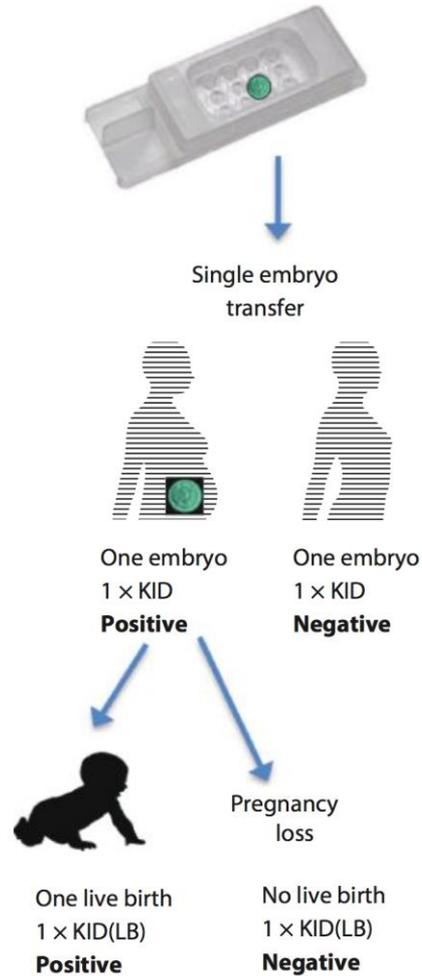
Meccanismi compensatori dell'embrione?

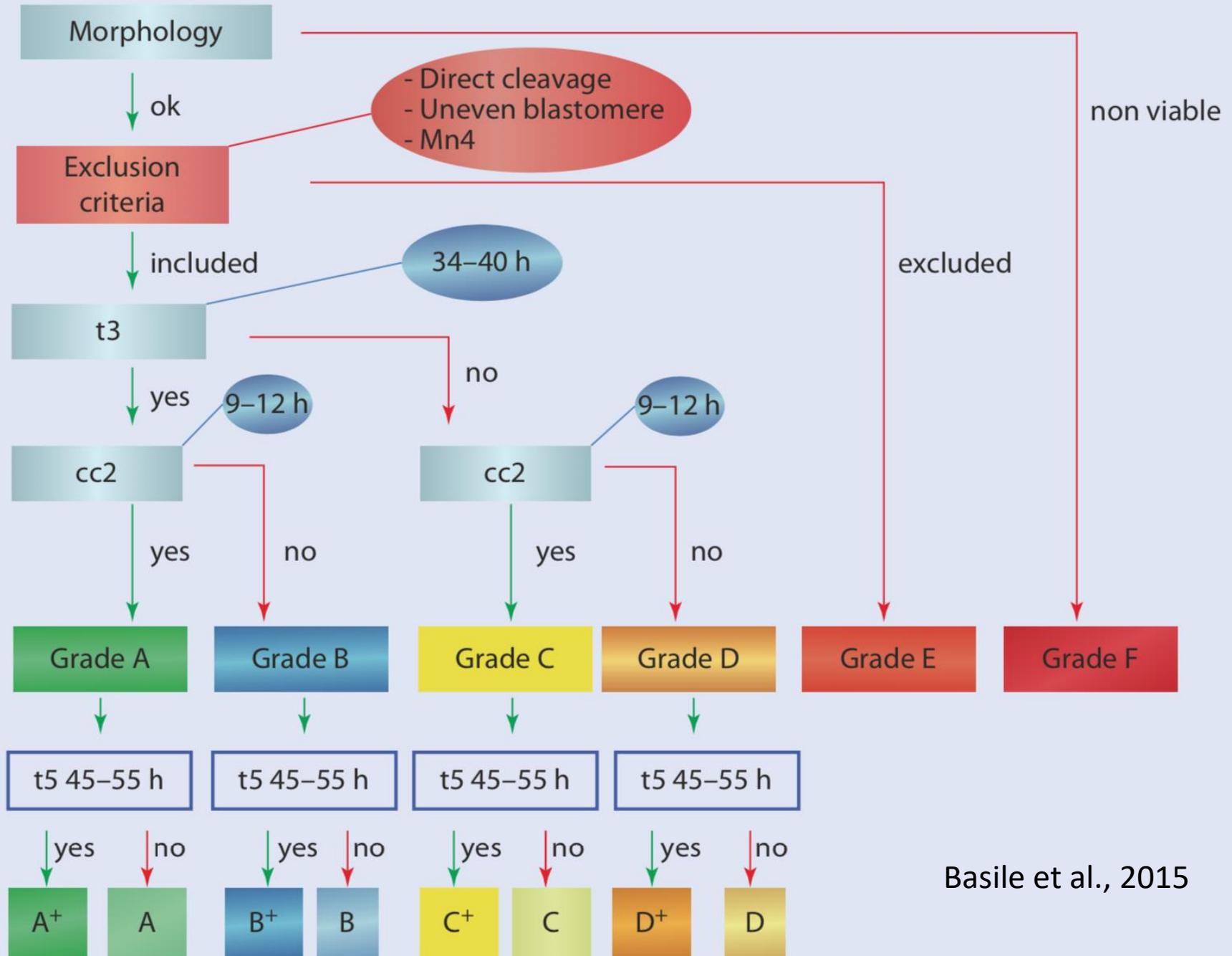
SVILUPPO – Parametri temporali



ALGORITMI

DISEGNO ALGORITMI

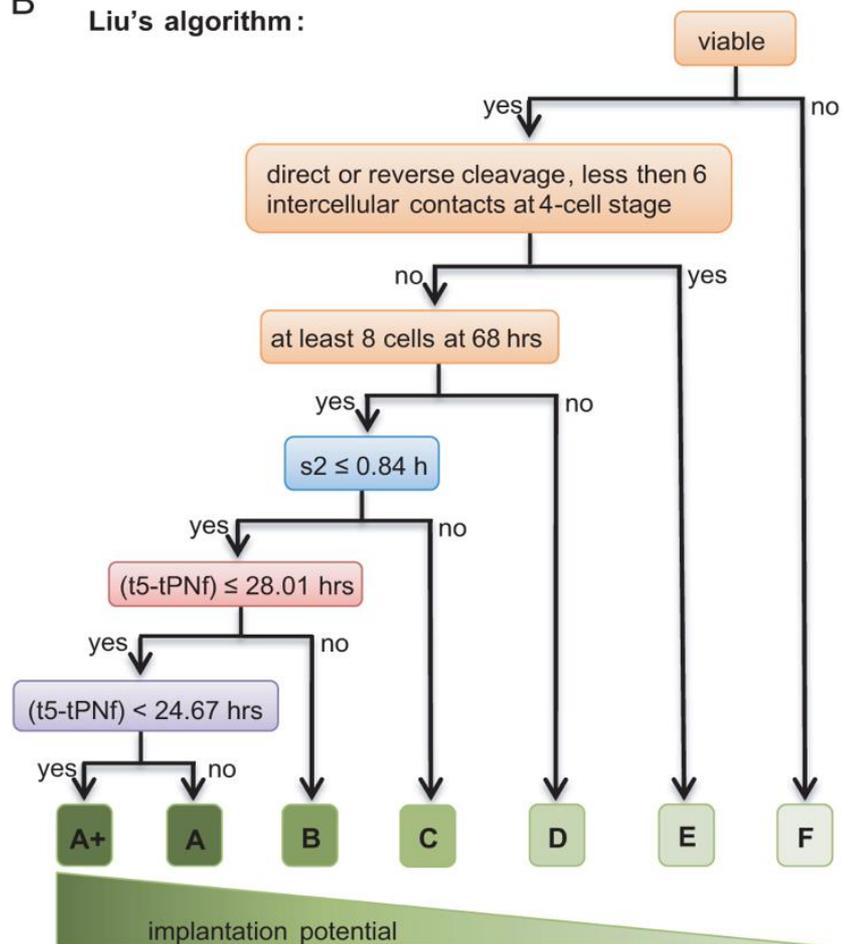




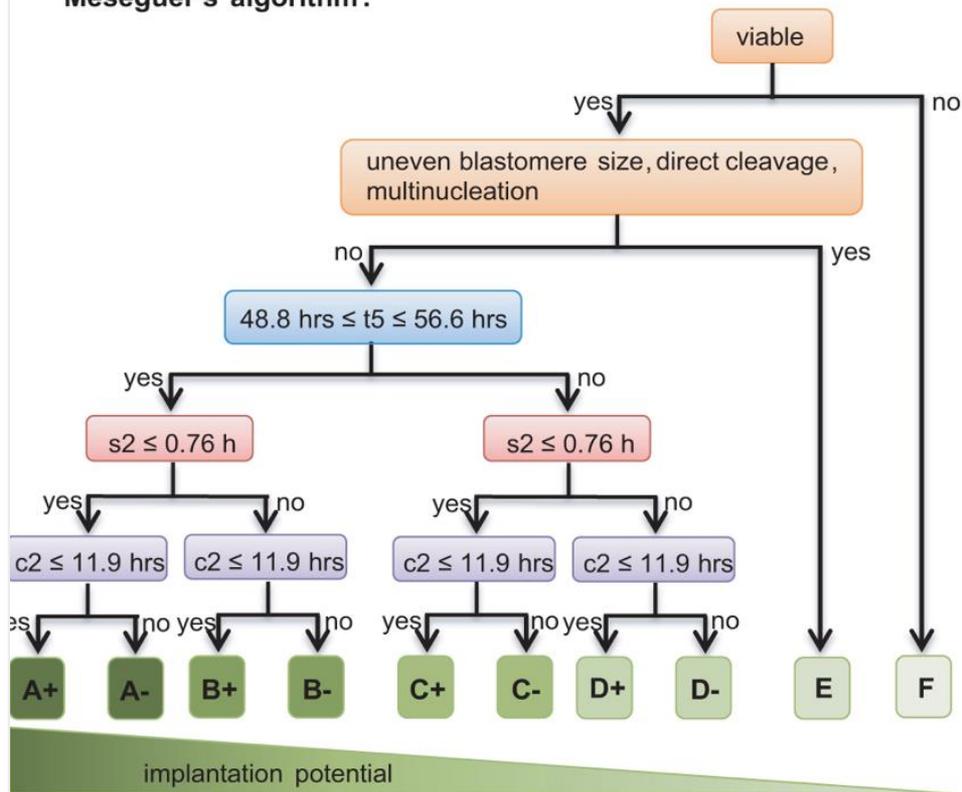
Basile et al., 2015

ALGORITMI - Impianto

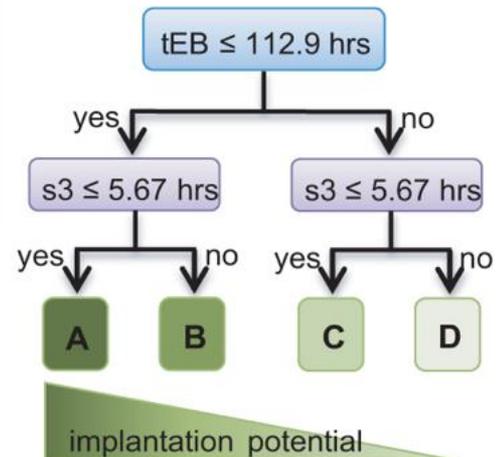
B Liu's algorithm:



A Meseguer's algorithm:



C Motato's algorithm:



RIPRODUCIBILITÀ ALGORITMI

Examining the efficacy of six published time-lapse imaging embryo selection algorithms to predict implantation to demonstrate the need for the development of specific, in-house morphokinetic selection algorithms

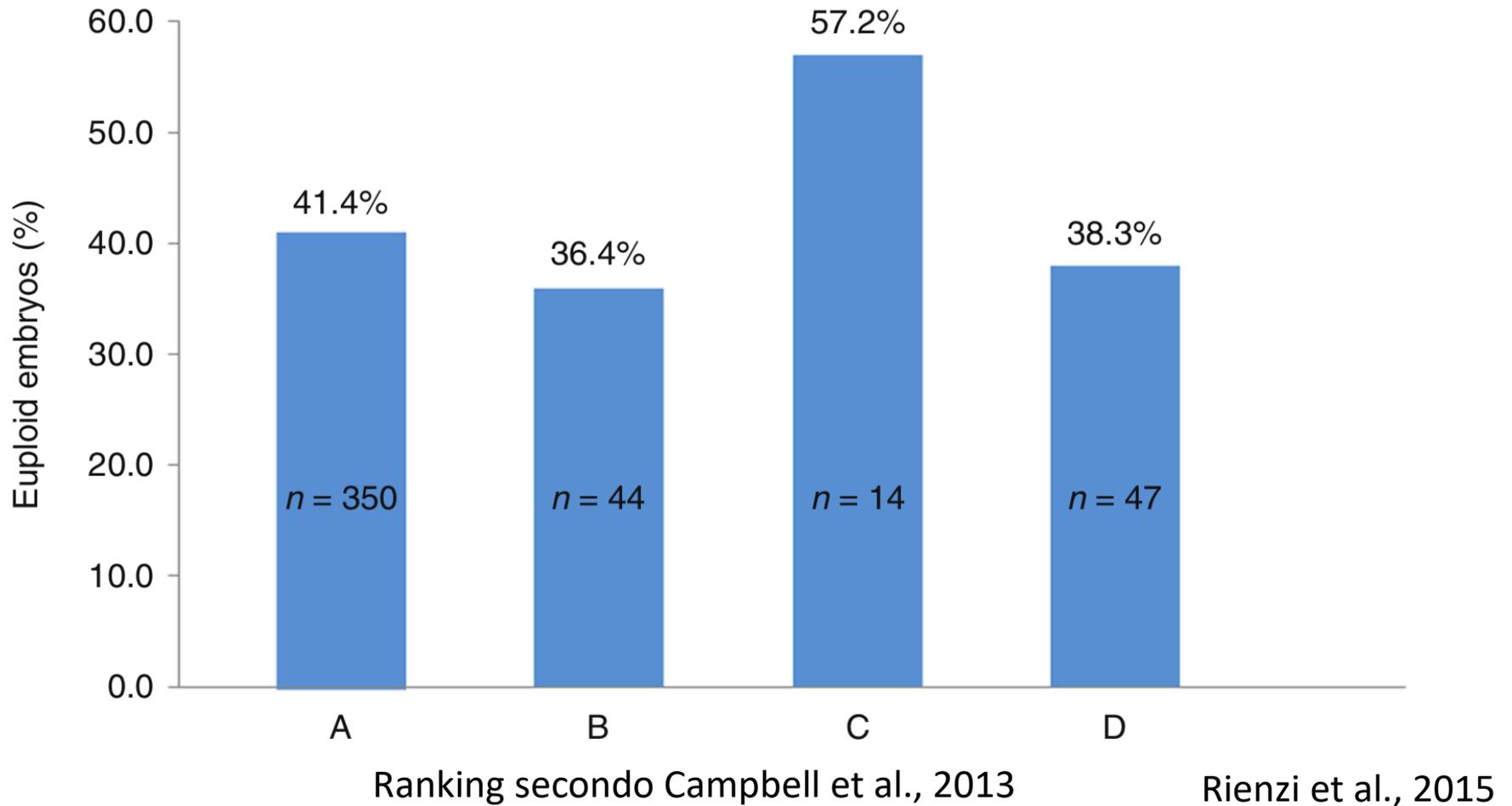
Amy Barrie, M.Sc.,^a Roy Homburg, M.B.B.S.,^a Garry McDowell, Ph.D.,^b Jeremy Brown, Ph.D.,^c Charles Kingsland, M.D.,^a and Stephen Troup, Ph.D.^a

^a Hewitt Fertility Centre, Liverpool Women's NHS Foundation Trust, Liverpool; ^b Manchester Metropolitan University, Manchester; and ^c Edge Hill University, Ormskirk, United Kingdom

IMPATTANO SULLA MORFOCINETICA

- Concentrazione di O₂ (Kierkegaard et al., 2013)
- Terreno di coltura (Desai et al., 2017)
- Protocolli di stimolazione (Munoz et al., 2013)
- Sesso dell'embrione (Bronet et al., 2015)
- BMI (Bartolacci et al., 2019)

MORFOCINETICA E PLOIDIA



OUTCOME CLINICI?

Cochrane Database of Systematic Reviews

Time-lapse systems for embryo incubation and assessment in assisted reproduction

Cochrane Systematic Review - Intervention | Version published: 29 May 2019 [see what's new](#)

TLS with conventional morphological assessment of still TLS images versus conventional incubation and assessment

TLS utilising embryo selection software versus TLS with conventional morphological assessment of still TLS images

TLS utilising embryo selection software versus conventional incubation and assessment

There is insufficient good-quality evidence of differences in live birth or ongoing pregnancy, miscarriage and stillbirth, or clinical pregnancy to choose between TLS, with or without embryo selection software, and conventional incubation. As the evidence is of low or very low-quality, our findings should be interpreted with caution.

Conventional morphology performs better than morphokinetics for prediction of live birth after day 2 transfer

TIME LAPSE: VANTAGGI NON DIRETTAMENTE CLINICI

- Workflow meno legato a tempi e luoghi
- Insegnamento
- Seconda opinione da altro operatore
- Strumento di ricerca

TIME LAPSE: VANTAGGI NON DIRETTAMENTE CLINICI



ANALISI PRELIMINARE DI UNO STUDIO SULLA CONCORDANZA INTRA- E INTER-CENTRO NELLA VALUTAZIONE EMBRIONALE STATICA

Coefficiente di correlazione intra-classe (ICC) tra operatori dello stesso centro e tra operatori di centri differenti.

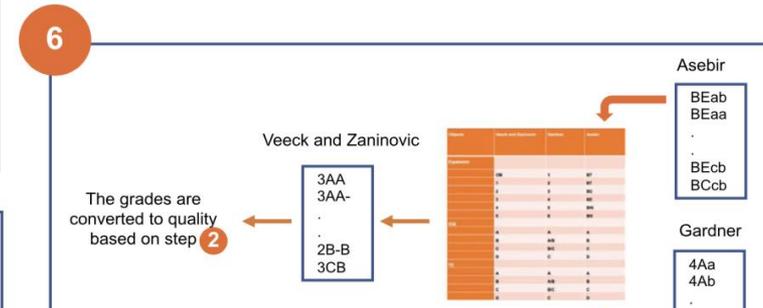
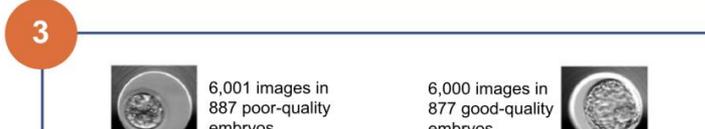
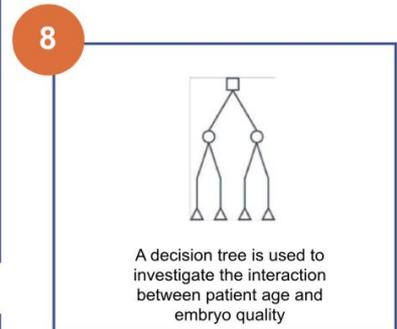
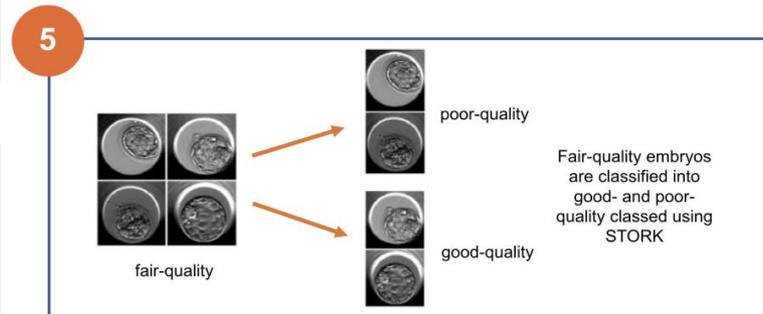
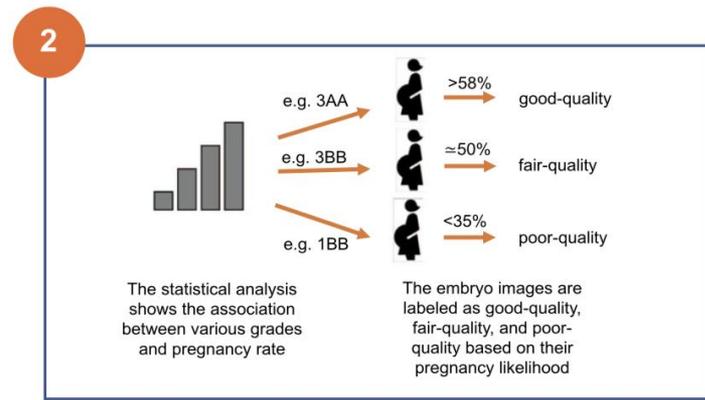
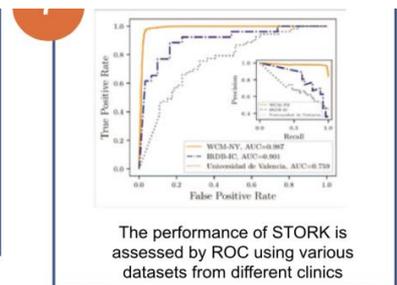
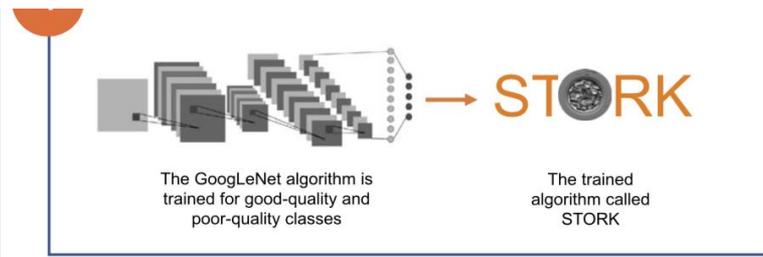
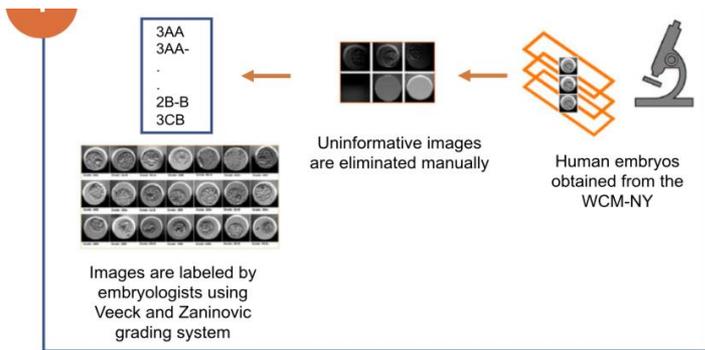
	Embrione allo stadio di cleavage		Blastocisti		
	<i>Simmetria</i>	<i>Frammentazione</i>	<i>Espansione</i>	<i>ICM</i>	<i>TE</i>
ICC <u>intra</u> -centro media±DS (min-max)	0.61±0.26 (0.1-1)	0.76±0.21 (0.29-1)	0.78±0.19 (0.41-1)	0.73±0.18 (0.34-0.97)	0.69±0.23 (0.16-0.96)
ICC <u>inter</u> -centro 95%CI	0.21, 0.14-0.31	0.56, 0.45-0.68	0.52, 0.41-0.65	0.58, 0.47-0.7	0.45, 0.35-0.58
Solo tra senior	0.25, 0.17-0.37	0.52, 0.38-0.65	0.52, 0.4-0.66	0.54, 0.43-0.67	0.44, 0.33-0.57
Solo tra junior	0.16, 0.1-0.26	0.6, 0.49-0.72	0.50, 0.39-0.63	0.61, 0.5-0.72	0.45, 0.34-0.58

Riproducibilità maggiore in centri dotati di TLSs

CAMBIO APPROCCIO: INTELLIGENZA ARTIFICIALE?

ARTICLE OPEN

Deep learning enables robust assessment and selection of human blastocysts after in vitro fertilization



The chance of a single pregnancy can be calculated as

$$P = \sum p_i \prod (1-p_j)$$

