

# TECH NOTE GERI ASSESS® 2.0

An automated software tool to support embryologists in embryo assessment

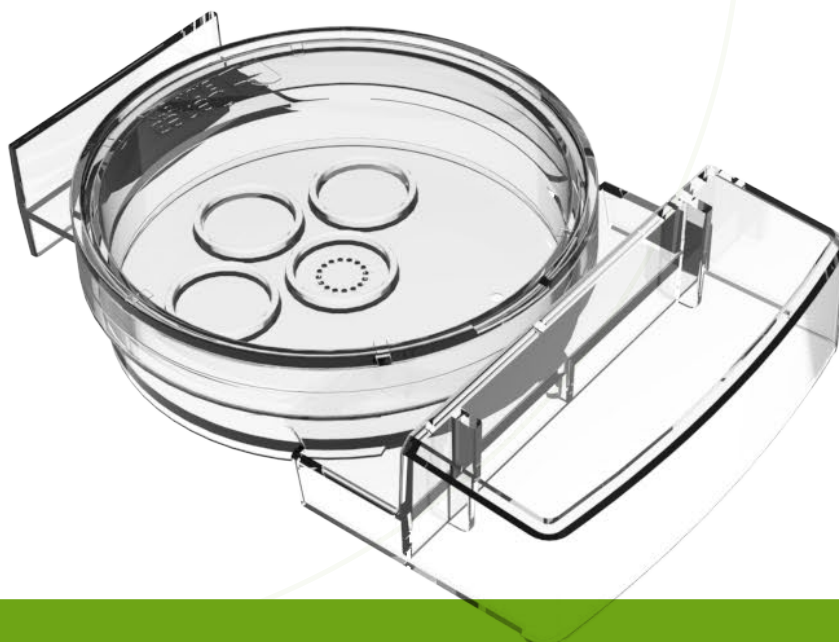
Introducing time-lapse technology into the embryology laboratory brings detailed insights and data about embryo development to embryologists. Geri Assess® 2.0 is an embryo development assessment tool that automatically detects and annotates key morphokinetic events and observations as they occur. The software was developed to utilise the images generated by time-lapse technology, guide embryologists to key developmental events and assist in embryo ranking.

## > Principles of Geri Assess® 2.0

During time-lapse culture the Geri® incubator captures multiple high-resolution images of embryos at specified time-points. Geri Assess® 2.0 software utilises the sharpest images from the Geri® incubator and performs standardised automated annotations of an embryo's key developmental events and observations as they occur.

### HOW?

The Geri Assess® 2.0 automated annotation software was developed using an artificial intelligence deep learning technique called convolutional neural network (CNN), which is inspired by biological neural networks. CNN is commonly applied to image analysis and pattern detection. Essentially, the software was taught to classify embryo images into classes such as 6-cell, hatching blastocyst etc. using thousands of human embryo images. It then analyses and classifies the images into categories and compares adjacent images to each other to track consistent developmental patterns. The performance of the software was validated against manual annotations performed by experienced clinical embryologists (QRTM213 Geri Assess® 2.0 Annotation Accuracy Tech Note).



## WHAT CAN GERI ASSESS® 2.0 DETECT?

Embryo development is dynamic; events are defined as discrete cell cleavage events that an embryo should achieve throughout its growth from pronuclear to blastocyst stage. Observations refer to events which can occur during embryo development and may be transient (e.g. reverse cleavage) or ongoing (e.g. fragmentation) in nature. A full list and definition of key developmental events and observations annotated by Geri Assess® 2.0 are shown in *Table 1* and are based on published recommendations<sup>2</sup>.

Application of these defined key developmental events and observations can facilitate standardised comparison of embryo development within and across laboratories.





Icon	Event or Observation*	Definition of the Event or Observation
	PN Appearance	The first frame where appearance of at least one visible PN is identified
	PN Disappearance	The first frame where disappearance of all visible PNs is identified
	2-cell division	The first frame where 2 discrete membrane-separated blastomeres is identified
	Reverse Cleavage*	The first frame where the embryo has returned back to 2 discrete membrane-separated blastomeres after a cleavage or a failed cytokinesis event (applicable for 2-cell stage only)
	3-cell division	The first frame where 3 discrete membrane-separated blastomeres is identified
	4-cell division	The first frame where 4 discrete membrane-separated blastomeres is identified
	5-cell division	The first frame where 5 discrete membrane-separated blastomeres is identified
	6-cell division	The first frame where 6 discrete membrane-separated blastomeres is identified
	Morula Transition	The first frame where appearance of cellular compaction and blurring of distinctive individual cell membranes is identified
	Early Blastocyst Transition	The first frame where appearance of blastocyst cavitation is identified
	Expanded Blastocyst Transition	The first frame where appearance of clearly expanded blastocyst with a minimum diameter of 167 µm is identified
	Hatching Blastocyst Transition	The first frame where appearance of cellular hatching, shown as trophoblast cells extruding from the zona pellucida, is identified
N/A	Fragmentation*	A set of five consecutive images where the embryo is identified as having cellular fragmentation present in ≥15% of its volume (defined as extracellular membrane-bound cytoplasmic structures <45 µm diameter in a Day-2 embryo and <40 µm diameter in a Day-3 embryo). This event could appear several times or persist on the development timeline.

Table 1 - Key developmental events and observations and their definitions automatically annotated by Geri Assess® 2.0. Observations are marked with an asterisk \*.



## > Geri Assess® 2.0 Timeline

For easy visual identification and assessment by the embryologist, Geri Assess® 2.0 presents the annotation results with graphical icons placed on the Timeline Bar as shown in *Figure 1*. Each embryo has a dedicated Timeline Bar and to assist in embryo comparisons, Timeline Bars for a cohort of embryos from the same patient can also be viewed simultaneously. For fragmentation which can occur numerous times or persist for a period of time, a continuous blue bar is placed on the timeline to reflect the event's presence. Only the annotations falling inside the pre-defined time ranges specified for each event are included in the Timeline Bar, guiding embryologists to the key developmental events and observations detected by Geri Assess® 2.0. These pre-defined time ranges were established around recommended review times<sup>1</sup>. The pre-defined time ranges as seen in *Figure 2* are meant as a guide only and shouldn't be interpreted as a definite reflection of embryo viability. All out-of-range annotations are visible on the Geri Assess® 2.0 tab of the Patient Review page with a warning triangle to alert the embryologist that a closer inspection and manual annotation modification may be required (see *Figure 3*).

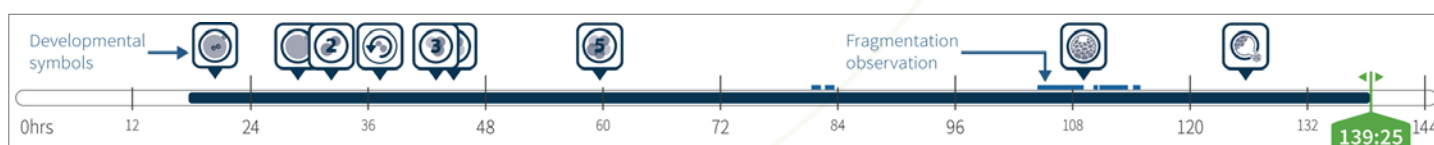


Figure 1 - Geri Assess® 2.0 Timeline Bar of an embryo showing only annotations falling within the pre-defined time ranges.

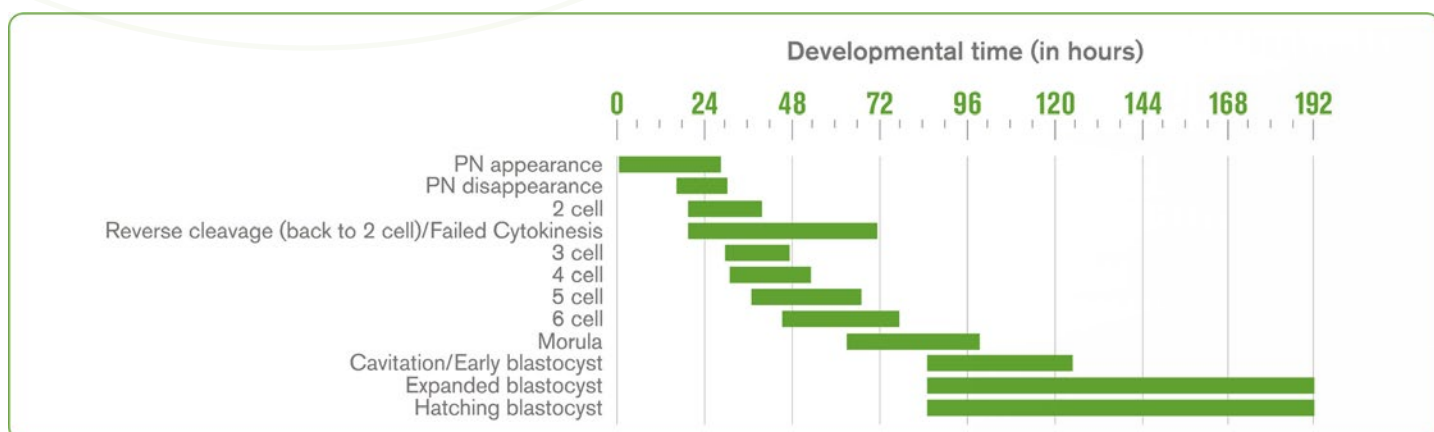


Figure 2 - Pre-defined time ranges for determining inclusion of key developmental event annotations by Geri Assess® 2.0

## > Geri Assess® 2.0 and Custom Scoring Algorithms

By using morphokinetic data in combination with known embryo outcomes, statistical patterns can be established and defined by algorithms which generate a score for each embryo. Once defined, the algorithm can be applied to all embryos to assist embryologists in ranking a patient's embryos.

Geri Assess® 2.0 provides a custom algorithm feature that enables users to upload and apply both published and/or user defined algorithms, i.e. algorithms based on a laboratory's own data set. The user can upload single or multiple algorithms and have embryo scores displayed individually or as a combined average. Custom scoring algorithms can be used with data generated by automated or manual annotations. Basile *et al.* (2015)<sup>3</sup> can be used as an example to give detailed information on establishing and utilising morphokinetic algorithms in the embryology laboratory.

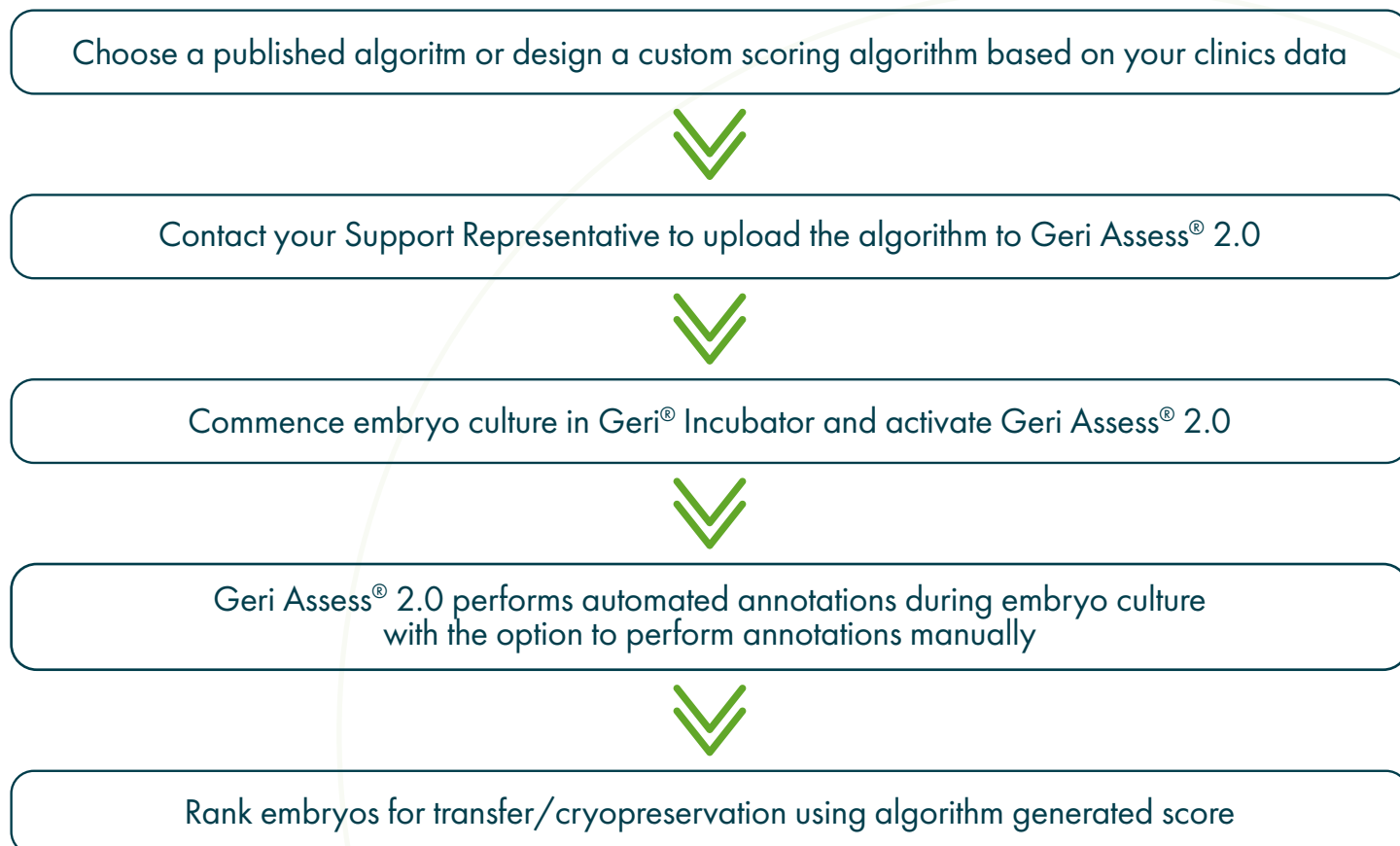
Events	ESTIMATED	MODIFIED
PN appearance	20:50	
PN disappearance	29:00	
2 cell	32:10	
3 cell	42:00	
4 cell	43:35	
5 cell	59:45	
6 cell	81:25	
Morula	105:20	← Out-of-range annotations
Early blastocyst	108:50	← Out-of-range annotations
Expanded blastocyst		
Hatching blastocyst	125:35	
<b>Observations</b>		
Reverse Cleavage	36:40	
Fragmentation	10:35	8%

Figure 3 - Example of Geri Assess® 2.0 tab of a Patient Review page of the Timeline Bar from Figure 1 showing all of the automated annotations, including the out-of-range annotations with the warning triangle



## > Using Geri Assess® 2.0 in the embryology laboratory

The following flowchart presents a snapshot of how Geri Assess® 2.0 would be used in the embryology laboratory.



### CONCLUSION

Geri Assess® 2.0 embryo assessment tool provides automated annotations to guide embryologists to key developmental milestones and facilitates standardised comparison of embryo development within and across laboratories.

## > REFERENCES

1. ALPHA scientists in Reproduction medicine and ESHRE SIG of Embryology (2011). *Istanbul consensus workshop on embryo assessment: Proceedings of an expert meeting.* Human Reproduction 26 (6): 1270-1283
2. Ciray H.N. et al. (2014). *Proposed guidelines on the nomenclature and annotation of dynamic human embryo monitoring by a time-lapse user group.* Human Reproduction 29 (12): 2650-2660
3. Basile, N. et al. (2015). *The use of morphokinetics as a predictor of implantation: a multicentric study to define and validate an algorithm for embryo selection.* Human Reproduction 30 (2): 276-283