Guidelines for getting started with models in Compare & Select

The use of models for embryo evaluation can be a strong and time saving tool aiding embryologist and lab technicians in decision-making regarding which embryo to transfer or freeze. The EmbryoViewer® software presents the user with the possibility to create clinic-specific models tailor made to their own IVF practice. The evaluation criteria already implemented for embryo selection in a specific clinic can be converted into a model in the Compare & Select feature of the EmbryoViewer software.

What are the advantages of using models?

Embryo viability and implantation success is generally agreed to be reflected by embryo morphokinetics. Models provide a fast and unbiased interpretation of embryo morphokinetics and can assist the user in deciding what embryo to transfer, freeze or discard. Furthermore, the use of models may also aid in standardizing embryo selection amongst lab personal in large clinics or amongst cooperating clinics. Models shared amongst clinics should always be validated on clinic specific data before clinical implementation. It should also be noted that accurate and consistent annotations are necessary in order to gain full benefit from implementation of models in a daily routine.

Time-lapse embryo evaluation – how to get started using models

Most IVF clinics already have a specific and robust set of selection/de-selection criteria that was used for embryo selection in the daily routine before implementing the EmbryoScope™ time-lapse system. Most likely these criteria are based on single observations of cell numbers and morphology at certain time points after insemination. Such criteria can easily be transferred to the EmbryoViewer software if the incubation conditions (e.g. oxygen and carbondioxide level, temperature and media) are comparable to the standard incubator. This means that the same criteria are used but that the software assists in the identification of those embryos that are selected or de-selected. The following will provide a guide for entering de-selection and selection criteria to Models tab sheet of the EmbryoViewer software for use in Compare & Select.

How to design a model

For a detailed description of the models in Compare & Select, please refer to the EmbryoViewer software User Manual.

Define the model

1. Open the EmbryoViewer software, choose the Settings menu and choose the Models tab sheet
2. Name your model in the text box "Model Name"
3. Choose the model type in the drop down menu "Model Type" (either additive, multiplicative or hierarchical)
4. Enter in your name or initials in the text box "Creator"
5. You can make a note about your model in the "Model Description" box

Defining variables by creating custom expressions

1. Click the "New" button to the right of the "Custom Expressions" box. A window will appear with the header "Custom Expressions" (Fig 1).
2. Enter a name for your variable in the "Name" box. The name can be up to eight characters long and consist of letters and numbers, but must start with a letter.
3. Define the custom expression in the "Expression" box using the variables (t2 to t9, tM, tSB, tB, tEB and/or tHB), the four standard arithmetic operators (+ - * /) and brackets (e.g. t5-t3). Or use the build-in function "cells(t)" which will give the annotated number of cells at a given time "t" (e.g. cells(28)).
4. Click OK
5. The name and the custom expression will now show up in the "Custom Expressions" box on the model page.

Defining variables, weights and intervals

Defining variables, weights and intervals are done in the "Model Definition" box. Please refer to the EmbryoViewer software User Manual for detailed instruction on how to practically create a model in the Model Definition box.

1. Variables, including those defined as custom variables, are chosen in the "variable" column drop down menu.
2. Weights are assigned according to variable prioritization in the "Weight" column.
3. The minimum and maximum values of the target interval is defined in the "Min" and "Max" columns. If the value of the variable is inside the target interval it will get the assigned weight.

Example: How to design a simple additive model with an exclusion criteria, three selection criteria and three information variables.

After choosing "Additive" in the "Model type" box, the following criteria are used (example shown in Fig. 2):

Exclusion criteria (assigned a low negative weight)
1. Embryos are generally evaluated as normal if they have two pronuclei. Therefore, embryos NOT showing two pronuclei is generally avoided. Embryos with abnormal number of PNs can be excluded by choosing the variable "NOT2PN" and setting a low negative weight (e.g. -100). This means that if the embryo is annotated as having two PNs it gets the weight 0 and if not it gets the weight of -100.

Selection criteria (assigned a positive weight, here 1)
2. If embryos in your clinic are usually monitored for cell number at 28 hours after fertilization, and two blastomeres at this stage is considered favorable the

"cells28" variable can be defined in the Custom Expression box (name: "cells28"; expression: "cells(28)" (will return the number of cells annotated at 28 hours)). Minimum and maximum should both be 2 (for two cells) and assigned the weight 1. Similarly, if embryos are considered favorable if having 4 cell at 44 hours and 8 cells at 68 hours, such variables can be defined in the Custom Expressions box, and appropriate values set for min/max parameters.

Information variables (weight = 0)
3. Information variables denotes variables in a model that do not have a clear priority and are not yet used for selection or de-selection, but still are interesting to the user. These variables can be assigned the weight 0, and thus they will not be contributing to the final score of an embryo evaluated by the model. In the example below information variables are multinucleation at the two cell stage (MN2), multinucleation at the four cell stage (MN4) and relative size of blastomeres at the two cell stage (UNEVEN2).
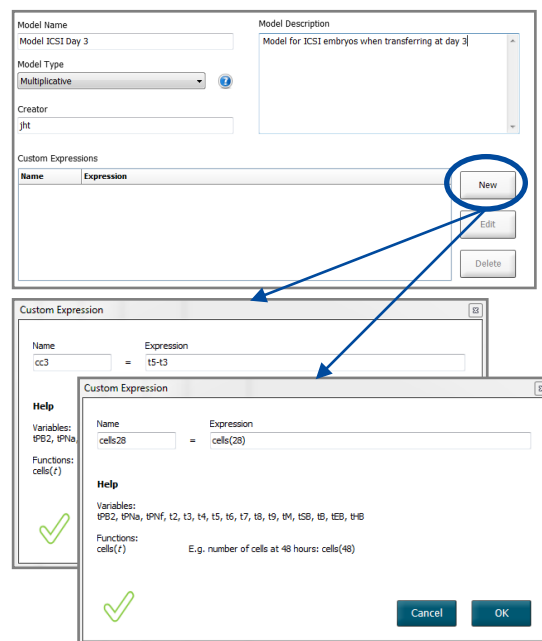

Fig 1: When the expression is recognized and approved by the software as a valid expression a green checkmark will appear in the lover left corner.

Fig 2: The final score of an embryo will appear in the Compare & Select page upon selection of the model. The score is a sum of the weights assigned for each variable and therefore reflects how well each embryo fits the criteria set up in the model. The simple model will give a model score of 1, 2 or 3 if it fulfills one, two or three of the selection criteria and not fulfills the de-selection criterion.

NOTE: the model and timings depicted only serves as a guidance how to design a model and they should not be used in clinical practice without validation.

Model Definition

Variable	Weight	Min	Max	Description	P(Variable)
NOT2PN	-100			Avoid	-100, if NOT2PN is TRUE 0, if NOT2PN is FALSE
Cells28h	1	2.0	2.0	Prefer	1, if 2.0 ≤ Cells28h ≤ 2.0 0, if 2.0 > Cells28h or Cells28h > 2.0
Cells44h	1	4.0	4.0	Prefer	1, if 4.0 ≤ Cells44h ≤ 4.0 0, if 4.0 > Cells44h or Cells44h > 4.0
Cells68h	1	8.0	8.0	Prefer	1, if 8.0 ≤ Cells68h ≤ 8.0 0, if 8.0 > Cells68h or Cells68h > 8.0
MN2	0			Information	
MN4	0			Information	
UNEVEN2	0			Information	

Score = P(NOT2PN) + P(Cells28h) + P(Cells44h) + P(Cells68h)