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Near-infrared (NIR) analysis of Day 2 Single Embryo Transfer Culture Media Samples: Blind Validation of Multi-linear Regression Algorithm

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Objective: Non-invasive metabolomic profiling of embryo culture media using NIR spectroscopy correlates with the reproductive potential of embryos. This technology assesses modifications of the chemical composition of the embryos surrounding medium using spectroscopy and generates a value termed the ViaMetrics-ETM score. In the current study our objectives were to: (i) develop a model for the calculation of the ViaMetrics-E score for embryos transferred on day 2 and (ii) determine whether a blinded analysis of day 2 embryo culture media using this model could predict their reproductive potential.

Design: NIR analysis of Day 2 media samples and correlation with fetal cardiac activity (FCA).

Materials and Methods: SETs (n=181) were performed on Day 2 at the Kato Ladies Clinic, Tokyo, Japan. Day 2 embryos were assessed by morphology and the best single embryo transferred. After SET the embryo media and a blank were cryostored. NIR spectral analysis was performed based on technology involving two steps: 1. Computation of a mathematical formula (multi-linear regression) that correlates key NIR spectral regions to an embryos metabolic viability. The methodology serves to identify spectral differences between transferred embryos which did (+) and did not (-) result in FCA. A genetic algorithm determines these spectral regions, which are expressed as independent variables in a multi-linear regression. A dependent variable, ViaMetrics-E score is calculated from the resulting regression. 2. Blind validation of the multi-linear regression algorithm on the NIR spectra of an independent set of Day 2 culture media.

Results: NIR spectroscopic analysis of spent culture media of embryos with proven reproductive potential demonstrated higher ViaMetrics-E scores (mean + SD) in both studies.

ViaMetrics-E scores of pregnant & non-pregnant patients

Study	N	ViaMetrics-E Score FCA +	ViaMetrics-E Score FCA -	P value (T-test)
Model Development	121	0.34 ±0.17	0.24 ±0.16	0.002
Blinded Assessment	60	0.33 ±0.18	0.26 ±0.15	0.048

In the blinded assessment the algorithm had an accuracy of 72% in identifying viable and non-viable embryos. When the 60 blinded samples were separated into quartiles, of increasing ViaMetrics-E scores, there was a positive correlation between ViaMetrics-E scores and positive FCA (Pearsons; P<0.05).

Conclusions: Findings of the current study suggest that the ViaMetrics-E score can provide an independent parameter that may significantly improve embryo assessment.

Non-Invasive Metabolic Profiling of Day 5 Embryo Culture Media adds to the Discriminatory Power of Blastocyst Culture for Single Embryo Transfer

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Objective: We have recently reported that non-invasive metabolomic profiling of embryo culture media using near infrared (NIR) spectroscopy correlates with the reproductive potential of embryos in IVF (Seli et al., 2007). This technology assesses modifications of the chemical composition of the embryos surrounding medium using spectroscopy and generates a value termed the ViaMetrics-E score. In the current study, we hypothesized that the use of a ViaMetrics-E score could further assist in determining the most viable embryo in addition to extended culture to blastocyst.

Design: NIR analysis of Day 5 embryo culture media samples and correlation with pregnancy outcome.

Materials and Methods: Single embryo Day 5 transfers (n=137) were performed at the Fertilitetscentrum, Gothenburg, Sweden and Shady Grove Fertility RSC, Rockville, Maryland, USA. Day 5 embryos were assessed for SET based on morphology. After SET a media sample from the transferred embryo and a blank were collected and cryostored. Media NIR analysis and a genetic algorithm were used to identify spectral regions, for eg. -SH, C=C, -CH, -OH, and NH groups, that discriminated most between transferred embryos that did and did not result in pregnancy (fetal cardiac activity detected at 12 weeks of gestation). Relative ViaMetrics-E scores were calculated by quantification of these spectral regions, adjusting for parallel blank media controls.

Results: The overall pregnancy rate from the two clinical sites using SET was 69/137 (50.4%). When the transferred embryos ViaMetrics-E scores were assessed, we found a large variability in metabolic profiles (range: -

A significant (Pearsons: P<0.001) positive correlation was observed with increasing ViaMetrics-E score quintiles and their associated implantation rates (Table 1).

ViaMetrics-E scores of day 5 embryos & implantation rates

ViaMetrics-E Score	Pregnant	Not Pregnant	Implantation Rate (%)
<0.2522	7	19	26.9
0.2522-0.4451	6	21	22.2
0.4451-0.5415	13	14	48.1
0.5415-0.7004	21	6	77.8
>0.7004	22	8	73.3

Conclusions: The ViaMetrics-E score helps discriminate between day 5 embryos, confirming that the embryos metabolism varies widely regardless of morphology. The added armory of metabolomic profiling by NIR spectroscopy, coupled with bioinformatics, to current morphological assessment protocols seems to allow a greater discrimination for selection of embryos for transfer, and has considerable promise to improve IVF outcomes.

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Christmas/2009 Trading

Gytech will close for 2008 at 5pm on Tuesday 23rd December and resume normal trading at 8.30am on Monday 5th January 2009.

Gytech would like to wish all of our loyal customers a happy holiday and safe and successful 2009.