

Improved embryo development and clinical pregnancy rates using a Geri time-lapse incubator with Geri single-step medium as compared to a conventional culture environment

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Introduction

The Geri time-lapse incubator, with its single patient-per-chamber design, continues to be utilised in Genea clinics and has been subject to enhancements to further improve upon its use and offer additional benefits. Besides providing an optimal environment for embryo development, offering fully uninterrupted culture when used in conjunction with Geri Medium, the incubator is now available with Geri Connect & Geri Assess, enabling users to view embryos and environmental data remotely. Further, Geri Assess 2.0 includes the automated annotations function to assist embryologists with making morphological assessments of embryos. The times of each of the developmental events are stored in Geri Connect & Assess and are also automatically inputted into an uploaded custom algorithm that uses morphokinetic analysis to determine the embryo quality, resulting in a score being given to each embryo. This score can be used to help embryologists make decisions on the viability of the embryos, potentially leading to increased pregnancy in the future as a consequence of transferring embryos that are more likely to implant and lead to healthy babies.

Geri Medium, the continuous culture medium available from Genea Biomedx, is now used in all Genea clinics as well as in customers' clinics globally. It is an optimised formulation that includes several key constituents that have been shown to promote embryo development, resulting in improved outcomes of embryo culture.

Geri Medium contains:

L-Carnitine: shown to have multiple advantages for developing embryos such as; increasing energy metabolism through facilitating the movement of fatty acids across the mitochondrial membrane; acting as a scavenger for damaging free radicals and; protecting against DNA damage by preventing mitochondrial dysfunction.¹⁻³

Glycine: allows embryos to maintain cell homeostasis and increases their ability to react to osmolality changes via importation using the GLYT1 transporter.⁴

Antioxidants: protect against oxidative stress by scavenging free radicals⁵. Geri Medium also contains all of the required constituents for glutathione production, not only important due to its function as an antioxidant, but also shown to have a critical role in the regulation of developmental signalling.⁶

As well as the obvious clinical benefits of using the uninterrupted, optimised system, efficiency gains can also be gleaned by using a combination of Geri with Geri Connect & Geri Assess alongside Geri Medium because embryologists are able to focus on higher priority tasks, rather than regularly moving embryos or assessing morphological development in the laboratory. In our own Genea clinics that have a

AIM

To determine if embryo development and clinical pregnancy outcomes are improved following uninterrupted embryo culture using the Geri incubator with Geri Medium, compared with conventional culture using a MINC incubator and Gems sequential media.

unique connection to Genea Biomedx, we have seen a decrease in foot traffic in the laboratory now that many tasks can be performed remotely. This has led to a more streamlined workflow, especially when several Genea Biomedx instruments are used alongside one another to standardise and automate a multitude of laboratory functions.

Method

This study was conducted across Genea clinics in Australia for data up until utilisation and included all 2PN's cultured in either the conventional culture environment using MINC (Cook) with sequential media (Gems, Genea Biomedx) or complete time-lapse culture environment using Geri with Geri Medium (Gems, Genea Biomedx). Utilisation refers to embryos at a blastocyst stage or greater which were deemed suitable by conventional morphological selection for transfer or vitrification (note that Geri's time-lapse morphokinetic capabilities were not utilised for the duration of this study).

To further investigate the results of pregnancy following embryo transfers, the data from Genea Canberra was studied in depth and is presented here.

This was a retrospective cohort study investigating embryo development and blastocyst utilisation of 46,653 normally fertilised oocytes across two culture systems used at different time periods. There were 21,645 2PN embryos cultured in the conventional culture environment from January 2015 to April 2016 and 25,008 in the complete time-lapse culture environment from April 2016 to April 2018. The additional data from Genea Canberra included 613 transferred embryos cultured in two culture systems used at different time periods, with 289 embryos transferred from the conventional culture environment from January 2015 to April 2016 and 324 embryos transferred from the complete time-lapse culture environment from April 2016 to January 2018. All results included embryos cultured following both IVF and ICSI.

Results

The results of the comparative study showed that there were statistically significant increases in total blastocyst number, good quality blastocysts and resultant utilisation rate when Geri Medium was used in Geri time-lapse incubator, thus offering undisturbed culture, compared to when using Gems sequential media in a conventional benchtop incubator.

As detailed in Table 1, the demographics of 2PN's between all groups were comparable in terms of 2PN age between the MINC & sequential Gems and Geri & Geri Medium groups. There was an increased number of total blastocysts on day 5 observed in all age groups when Geri Medium was used in the Geri incubator compared to when



All Genea Clinics: All Cycles	MINC & Sequential Gems Jan 2015 - Apr 2016			Geri & Geri Medium Apr 2016 - Apr 2018		
	<38	≥38	Combined	<38	≥38	Combined
Average 2PN Age	33.42	40.75	36.25	33.59	40.81	36.36
Average OPU Rank	1.70	2.38	1.97	1.62	2.38	1.91
Number of 2PNs cultured	13,283	8,362	21,645	15,392	9,616	25,008
Number of 2PNs transferred/frozen <Day 5	442	346	768	209	224	433
Total blastocysts on Day 5	38.9%**	25.6%**	33.8%**	52.3%**	37.8%**	46.8%**
G1/2 blastocysts on Day 5	27.8%**	17.0%**	23.6%**	38.6%**	25.6%**	33.6%**
Utilisation rate	45.1%**	35.8%**	41.5%**	56.4%**	46.3%**	52.5%**

Table 1: Summary of morphological assessments for embryos cultured in the MINC incubator using sequential Gems media or the Geri incubator using Geri Medium

**p<0.01

conventional culture was used. Specifically when considering the combined age group, the percentage of total blastocysts was 33.8% and 46.8% in the MINC & sequential Gems and the Geri & Geri Medium groups, respectively, representing a statistically significant increase ($p<0.01$). Furthermore, also in the combined age group, improved quality of blastocysts on day 5 was observed, with a higher percentage of grade 1 or 2 blastocysts in the Geri & Geri Medium group compared with the MINC & sequential Gems group, 33.6% and 23.6%, respectively. This was also a statistically significant difference ($p<0.01$). The utilisation rate of embryos cultured in the Geri & Geri Medium group was also higher than that seen in the MINC & sequential Gems group, 52.5% and 41.5%, respectively, also denoting a statistically significant difference ($p<0.01$). These data are graphically presented in Figure 1.

Of clinical importance, a statistically significant increase ($p<0.1$) in foetal heart pregnancy rate was observed in the Geri & Geri Medium group compared with the MINC & sequential Gems group, 37.3% and 30.1%, respectively, as presented in Figure 2.

Genea Canberra: Fresh Cycles	MINC & Sequential Gems Jan 2015 - Apr 2016			Geri & Geri Medium Apr 2016 - Apr 2018		
	<38	≥38	Combined	<38	≥38	Combined
Average Age	32.38	40.76	36.01	33.42	40.69	36.24
Average OPU Rank	1.64	2.23	2.35	1.59	2.69	2.02
Number Embryos Transferred	173	116	289	198	126	324
Foetal heart Pregnancies	39.9%	15.5%	30.1%*	46.5%	23.0%	37.3%*

Table 2: Summary of pregnancy outcomes following embryo culture using the MINC incubator & sequential Gems media or the Geri incubator & Geri Medium

*p<0.1

Conclusion

This study revealed statistically significant differences in embryo development outcomes between a traditional, sequential media culture system using a benchtop incubator and a completely uninterrupted, time-lapse system where the use of continuous culture medium was employed. This new data builds upon earlier findings that minimising the interruption of embryos during culture has a beneficial effect on their development and suggests that time-lapse systems should be used wherever possible, especially when additional benefits such as those relating to efficiency are realised. Moreover, a statistically significant increase in clinical pregnancy rate has now been observed, further promoting the use of the Geri incubator and Geri Medium to offer completely undisturbed embryo culture.

Blastocyst Quality and Utilisation

Combined Ages

■ MINC & Sequential Gems (Jan 2015 - Apr 2016)
■ Geri & Geri Medium (Apr 2016 - Apr 2018)

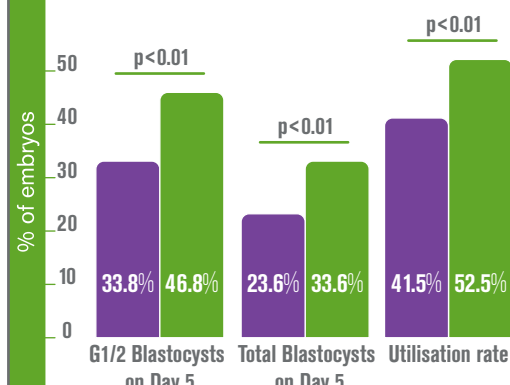


Figure 1: Blastocyst Quality and Utilisation - Combined Ages



Foetal Heart Pregnancy Rate

Combined Ages

■ MINC & Sequential Gems (Jan 2015 - Apr 2016)
■ Geri & Geri Medium (Apr 2016 - Apr 2018)

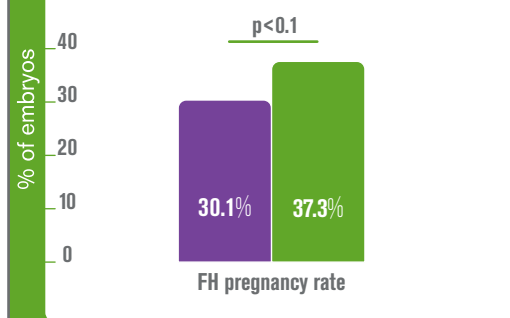


Figure 2: Foetal Heart Pregnancy Rate - Combined Ages

Limitations, reasons for caution

This was a retrospective analysis. As the analysis compared culture methods performed at different time periods, it is possible that other factors also influenced results. Prospective studies are required to confirm these findings.

Acknowledgments

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Competing Interest

The author is an employee of Genea Biomedx. Genea Biomedx is the manufacturer of the Geri system. Geri™ is a trademark of Genea Limited. ABN 82 002 844 448.

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