Introduction

Cryopreservation of embryos is an essential component of assisted reproductive technologies. However, especially manual vitrification is a high-skill and labour intensive procedure with varying results between embryologists and clinics.

The Gavi® system was designed to automate key steps of the vitrification process. It standardises and controls key parameters, namely temperature, exposure time to cryoprotectants and cooling/warming rates. The latter two are particularly strong determinants of embryo survival, and their control is crucial for optimal vitrification.

Besides anticipated improved clinical outcomes due to standardisation, a further advantage of the automation is the reduced timeframe required for embryologists to achieve high survival rates consistently, when compared to manual systems.

This paper describes retrospective analysis of data collected during implementation of two new vitrification systems to the flagship Genea clinic in Sydney, Australia. The first data set is from the implementation of the current gold-standard manual Cryotop® system in 2009-2010, the second data set from the implementation of Gavi® system in 2015-2017.

Methods

Performance: Gavi® clinical study included infertile couples undergoing IVF and Preimplantation Genetic Screening (PGS), who were randomly allocated to have either their best embryo vitrified using the Gavi® and their second best using the Cryotop® system, or vice versa (maximum two embryos per patient were included in the study). Vitrification was performed using Gavi® as per manufacturer’s instructions, or the open Cryotop® protocol as described previously. Embryo recovery and survival rates, defined as >75% or 100% of cells survived, were subsequently compared, as were single embryo transfer outcomes.

Competency: To evaluate the training perspective, embryo survival results across >25 embryologists at the early stages of both systems implementation were analysed retrospectively. The average experience level of the embryologist (x-axis), the average blastocyst cell survival % (y-axis) and the number of embryos warmed were used to generate a model to define outcomes as per embryologist basis.

Results

Performance: Embryo recovery and survival rates of blastocysts vitrified using the Gavi® system were comparable to those vitrified using the Cryotop® system (Figure 1). In addition, the number of blastocysts with 100% cell survival was significantly greater (p<0.05) when the Gavi® system was used. Pregnancy rates (βHCG and Foetal Heart) were likewise comparable between the two groups, with average patient ages of 36.01 (Gavi®) and 36.03 years (Cryotop®) (Figure 2). The number of live births were 126 and 111 and on-going pregnancies 18 and 25 in Cryotop® and Gavi® groups, respectively, by May 2018.

Competency: Although embryo recovery rates were initially lower with Gavi®, it reduced the variability of the outcomes between embryologists, and competency for blastocyst cryosurvival was achieved faster with Gavi® than with Cryotop® (Table 1 and Figure 3). Moreover, embryo recovery rates improved soon after the initial teething problems in this world-first implementation of the new system were addressed, and now stand at 99.8% (518/519) since Gavi® was implemented into routine clinical use.
After a total of 361 embryos had been vitrified during the implementation stages of both systems, with Gavi®, 82% of 25 embryologists achieved an average embryo survival of ≥95% (mid-point of competency and benchmark values1), regardless of experience level. With Cryotop®, only 36% of 28 embryologists achieved this, representing a statistically significant difference (p<0.001).

**Figure 2:** Pregnancy outcomes from euploid single embryo transfers for Cryotop® and Gavi® systems

**Figure 3:** Recovered embryo survival by freeze scientist - Gavi® vs Cryotop®

**Table 1:** Comparison of early stage implementation - Gavi® vs Cryotop®

### Conclusions

Laboratory and clinical outcomes of blastocysts vitrified using Gavi® are comparable to those vitrified using Cryotop®.

Gavi® reduces variability between embryologists and shows that through standardisation, embryologists can achieve and exceed performance levels representing the mid-point (≥90%) of the competency (≥90%) and benchmark (≥99%) blastocyst cryosurvival considerably faster. This leads to a marked reduction in the time taken to achieve vitrification competency with Gavi® compared to Cryotop®.

Since its implementation into Genea clinics, Gavi® system has greatly minimised variation between embryologists at different experience levels2. Its ability to revolutionise vitrification by standardising outcomes is likely to provide the same benefits to all clinics, regardless of size and cryopreservation experience.

**References**