Introducing a G185 incubator into the IVF lab: a practical perspective

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OVO FERTILITÉ

K-Systems
ASRM
Atlanta
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INTRODUCTION - WHO WE ARE?

CLINIQUE OVO
- OVO Fertility
- OVO Labo
- OVO Biosurance
- OVO Prenatal
- OVO R&D
- OVO Consulting
- OVO Foundation
INTRODUCTION - WHO WE ARE?

• OVO Fertility
  – Opened in 2003
  – 800 cycles IVF / ICSI per year
    • Fresh and Frozen IVF
    • Natural cycle IVF
    • Egg donation cycles
    • Surgical sperm retrieval
    • PGD
INTRODUCTION – Fertility Laboratory

• 5 Embryologists, 1 Andrologist
• 6 Hereaus Heracell 240 incubators

• Laboratory restructure in August 2008
  – Improve layout
  – Increase cycle capacity
  – Improve results
INTRODUCTION – Fertility Laboratory
PRODUCT REQUIREMENT

• Need additional incubators

• Considerations
  – Space
  – Usable internal area
  – Efficiency for IVF
  – Cost
PRODUCT REQUIREMENT

- Available space for 2 Hereaus Heracell 240
- Is this the best option?
PRODUCT REQUIREMENT

• Heracell 240

  – Large capacity but don’t use this volume
  – Large capacity incubators associated with increased loss of gas and temperature
PRODUCT REQUIREMENT

• Space efficient tri-gas incubator
• Equivalent or improved embryo culture conditions
• Use of 100% gas
  – CO₂
  – N₂
  – Use of current gas lines
PRODUCT REQUIREMENT
PRODUCT SELECTION

• Temperature recovery time
  – Chamber opened for specific time
  – Chamber closed and recovery monitored every minute
  – Minimum measurement 1 minute

<table>
<thead>
<tr>
<th>Time chamber opened</th>
<th>Recovery Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>10 seconds</td>
<td>No effect seen</td>
</tr>
<tr>
<td>20 seconds</td>
<td>No effect seen</td>
</tr>
<tr>
<td>40 seconds</td>
<td>No effect seen</td>
</tr>
<tr>
<td>60 seconds</td>
<td>2 minutes</td>
</tr>
<tr>
<td>120 seconds</td>
<td>3 minutes</td>
</tr>
</tbody>
</table>

• Ronny Janssen – unpublished data
PRODUCT SELECTION

• Gas recovery
  – Chamber opened
  – Repeated every 10 minutes
  – Chamber closed and recovery monitored every minute
  – Minimum measurement 1 minute

<table>
<thead>
<tr>
<th>Gas</th>
<th>Recovery Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbon Dioxide</td>
<td>3 minutes</td>
</tr>
<tr>
<td>Oxygen</td>
<td>3 minutes</td>
</tr>
</tbody>
</table>

• Ronny Janssen – unpublished data
## PRODUCT SELECTION

<table>
<thead>
<tr>
<th>Particle Size</th>
<th>G185</th>
<th>Reference Incubator</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0.3µm</td>
<td>0.5µm</td>
</tr>
<tr>
<td>Particle Count</td>
<td>17380</td>
<td>472</td>
</tr>
</tbody>
</table>

• Ronny Janssen – unpublished data

| Maximum permitted particles per m³ equal or greater than tabulated size |
|---------------------------|-----------------|-----------------|-----------------|
|                           | At rest         | In operation    |
| Grade | 0.5µm | 5.0µm | 0.5µm | 5.0µm |
| A     | 3520  | 20   | 3520  | 20   |
| B     | 3520  | 29   | 352000 | 2900 |
| C     | 352000 | 2900 | 3520000 | 29000 |
| D     | 3520000 | 29000 | Not defined | Not defined |

Volume 4 EU Guidelines for GMP Medicinal Products for Human and Veterinary use- annex 1 (feb 2008)
PRODUCT SELECTION

• Janssen’s data demonstrated
  – Faster recovery of chamber gas and temperature
  – No significant impact on other chambers when opening
  – No significant difference in % fertilization rate in sibling oocyte study (vs. Heracell 240)
  – Increase in % ‘good quality’ embryos
INITIAL SETUP
INITIAL SETUP

• Used existing gas line (100% CO$_2$ and N$_2$)

• No increase in gas usage
  – One x 6.24m$^3$ N$_2$ / 1.5 days
  – Addition of Heracell incubators had seen gradual increase in gas use from 1 x N$_2$ / 5 days up to 1 x N$_2$ / 1.5 days

• No need for pre-mixed gas
  – Cost and order issues
  – Additional gas line requirement
INITIAL SETUP

• Considerations and Concerns
  – External validation of temperature, gas levels
  – Lack of humidification
  – ‘User Comfort’
VALIDATION

• External temperature and gas validation
VALIDATION

• Lack of Humidification
  – Evaporation of media?
  – Changes in media osmolarity?
  – Use of water dish in each chamber?
  – Use of oil overlay sufficient?
VALIDATION

- Mouse embryo assay
  - 1 cell mouse embryos
  - Compare results with Heracell
  - Average % blasts in G185 = 91%
  - Average % blasts in Heracell = 84%
  - Subjective blast scoring
VALIDATION

• Sibling Oocyte Study (n=20)
  – IVF / ICSI
  – G185 vs. Heracell (2 units)
  – %2PN 63.9% vs. 65.6% (NS)
CLINICAL USE

• G185 included in rotation of incubators
• Recent media study necessitated different %CO₂
  – G185 used for specific CO₂ requirement
CLINICAL USE

• Future considerations
  – Additional 2x G185 planned
  – Cabinet for three units
  – Gradual replacement of Heracell units
CONCLUSION

• Easy integration of benchtop incubator into established IVF lab
• Minimal learning curve for use of benchtop incubator
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  – Patrick Chebli

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  – Vincent Attallah