Clinical outcome after culturing human preimplantation embryos in incubators with individual chambers compared to standard incubators; randomised trial

Janssens R, Souffreau R, Haentjens P, Van de Velde H and Verheyen G

Universitair Ziekenhuis Brussel

Vrije Universiteit Brussel

Centrum voor Reproductieve Geneeskunde

Introduction

- Standard incubators UZ Brussel

- Triple gas (6% CO_2 – 5% O_2)
- Large capacity (inertion)
- Heated door
- Stable atmosphere, fast recovery (CO_2 –temp)
  - → Infrared CO_2 sensor
  - → Gas tight split doors
- No humidified atmosphere
- HEPA - VOC filters
- Safety
  - → Independent monitoring (temp- CO_2)
  - → Remote alarm system
  - → UPS

Universitair Ziekenhuis Brussel
Vrije Universiteit Brussel

Centrum voor Reproductieve Geneeskunde

Introduction

- 2010: 4500 retrievals – blastocyst culture
  → 10 incubators
  → 8 for culture
  → Space limitations

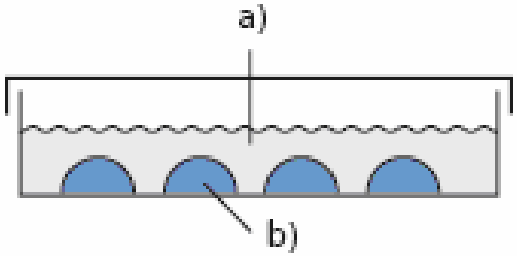
- Gardner et al., - “we prefer a limit of four cases per incubator.”
  (Textbook of Assisted Reproductive technologies, second edition)

Universitair Ziekenhuis Brussel
Vrije Universiteit Brussel

Centrum voor Reproductieve Geneeskunde

Effect of high door opening frequency on microdrop culture

- Temperature and pH changes in microdrops
  → - 0.3°C
  → - 0.08 to + 0.05 pH



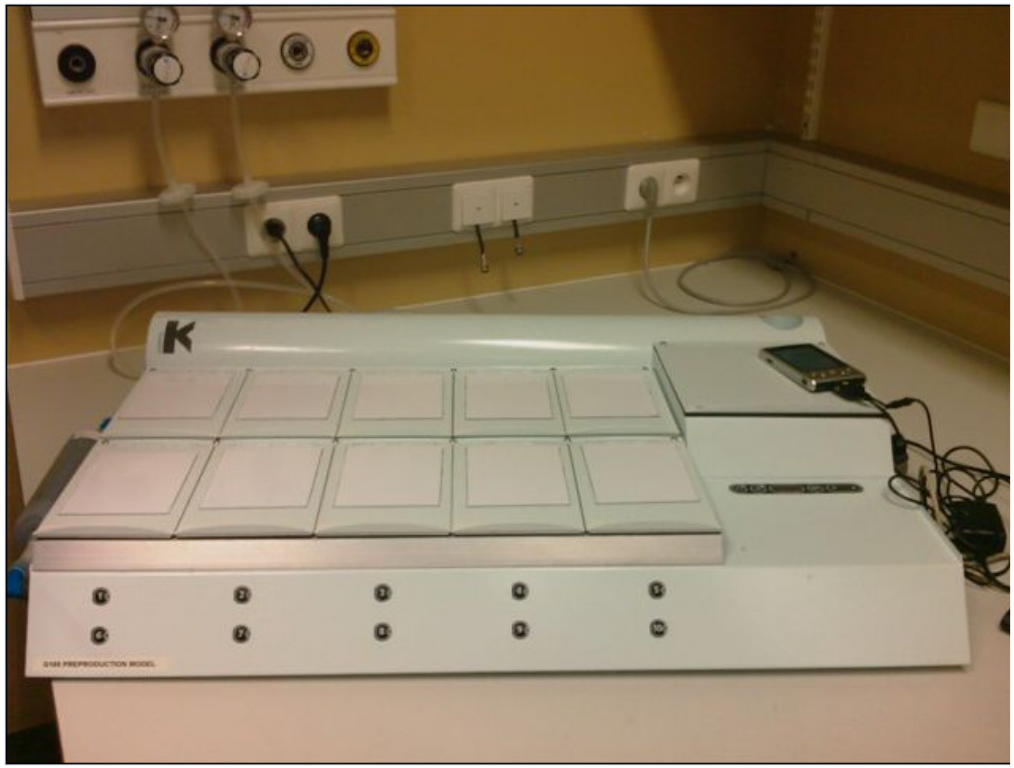
- No one has identified and characterized a precise pH optimum for the culture of human embryos (7.1 – 7.4)
- Temperature optimum?

(A. De Bisschop, 2007)

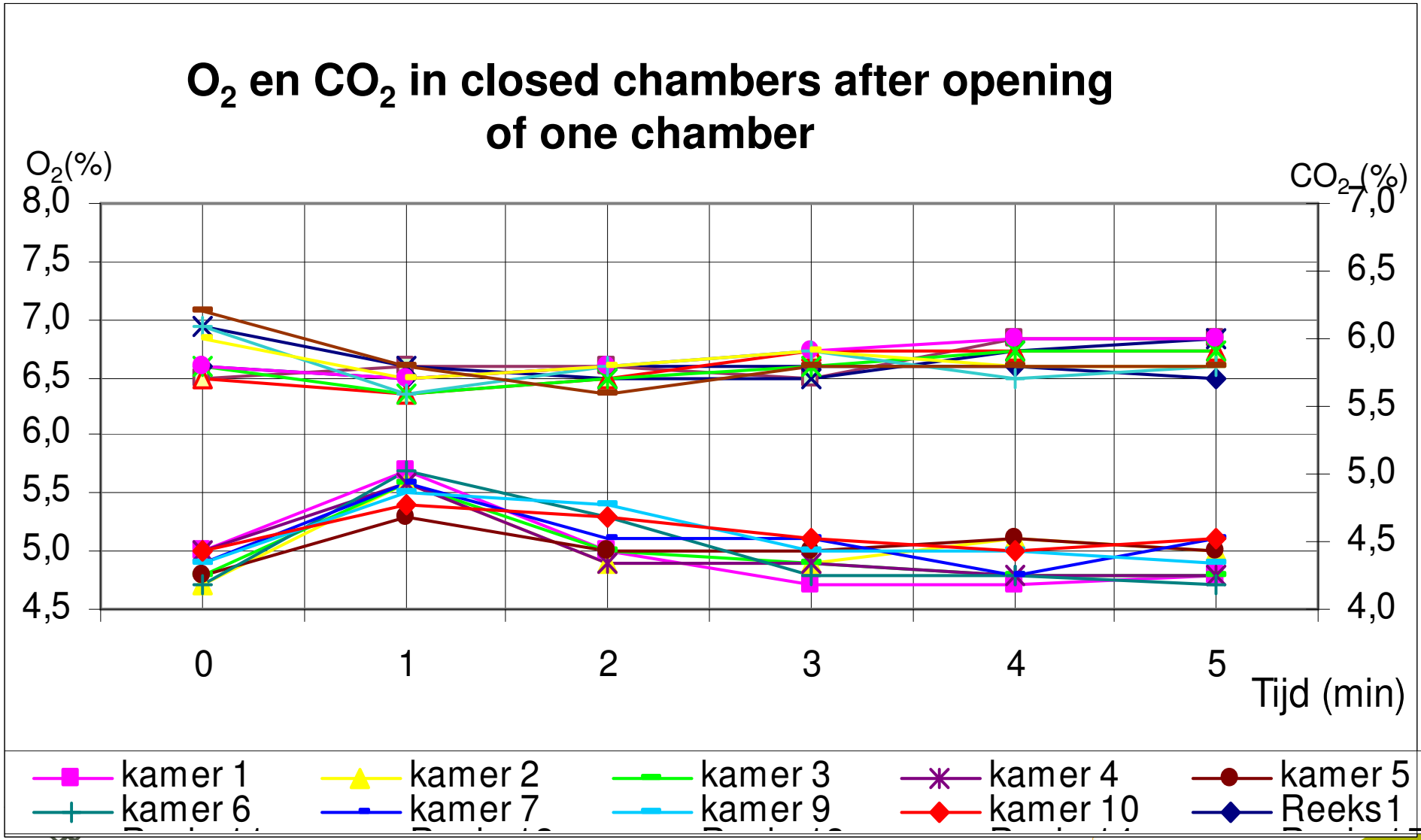
G-185

- Triple gas
- Integrated gas mixing unit (N_2 – CO_2)
- 10 individual chambers
- Direct heat transmission
- Photo-oxidation
- HEPA + VOC filters

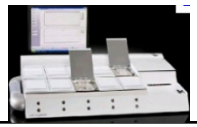
- No humidification!
- Independent Vaisala CO_2 probe

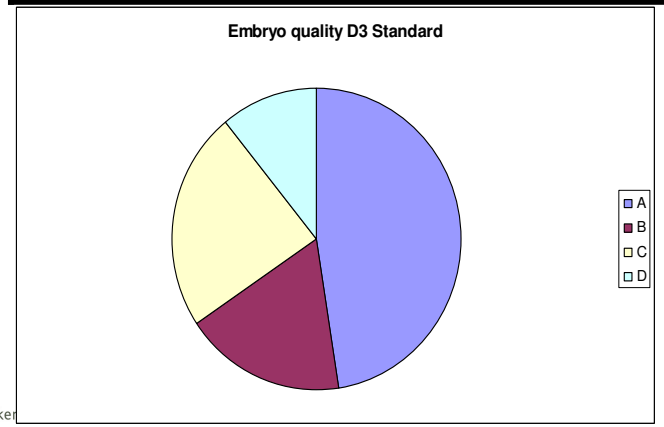


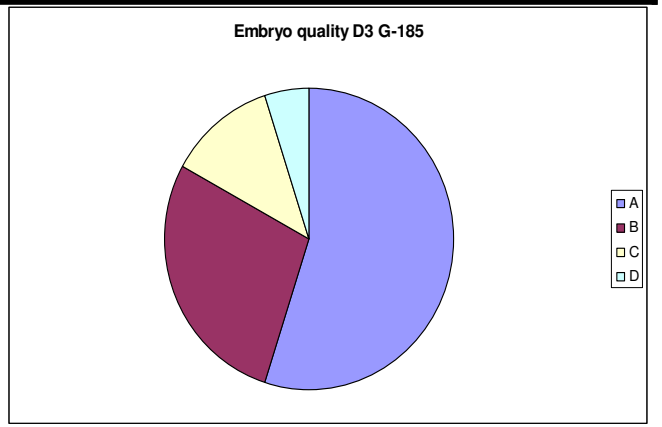
Impact of opening one chamber on gas concentrations



Sibling oocyte study (n=24)

	Heracell 240 N (%) 	G-185 N (%) 	
Injected (inseminated)	133	126	
Deg	10	11	
1PN	2	9	
2PN	90 (67.7)	86 (68.3)	NS
3PN	2	3	





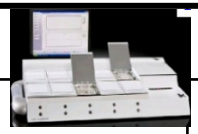
Universitair Zieken
Vrije Universiteit Brussel

Centrum voor Reproductieve Geneeskunde

RCT

- June – december 2010
- IVF/ICSI, 6 COC, ejaculated semen
- Standard Incubator (SI): Heracell 240i – Thermoforma (37.0°C – 6% CO_2 – 5% O_2) without humidified atmosphere with continuous monitoring
- Semen: 90 – 45% discontinuous gradient (Spermient, Cook)
- Microdrop (25µl) culture media (Sage) under paraffin oil (Ovoil, Vitrolife)

Results

	SI 	G-185 	p
Randomized	155	157	
Excluded	17	17	
Cycles	138	140	
Age (av ± SD)	34.4 ± 5.2	33.1 ± 4.7	
COC (av)	1508 (10.9)	1632 (11.6)	
Inseminated	1221	1338	
Degenerated (%/ins)	57 (4.7%)	63 (4.7%)	ns
2PN (%/ins	921 (75.4%)	1004 (75.0%)	ns
N ET	134	135	
N +hCG	53	69	
%/cycle	39.0	50.4	P=0.058*
%/ET	39.6	51.1	P=0.057**

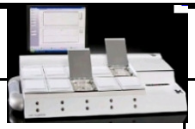
Universitair Ziekenhuis Brussel
Vrije Universiteit Brussel

*** +11.4% (95% CI, -0.3% to + 23.1%)**

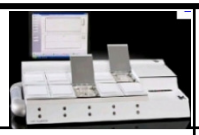
****2 +11.6% (95% CI, -0.3% tot+23.4%)**

Centrum voor Reproductieve Geneeskunde

Results

	SI 	G-185 	p
Cycles	138	140	
N ET	134	135	
D3	95	80	
D5	39	55	
Embryos replaced	270 (2.0)	220 (1.6)	
N +hCG	53 (39.0%)	69 (50.4%)	P=0.058
?	2	4	
Bioch/misc	8 (+1 late misc)	11	
EUG	1	1	
Evolutive	42 (-1)	53	
Sac FHB	55 (21.1%)	63 (29.6%)	P=0.033
Singleton	31	45	
Twin	9	9	
Triplet	1		

Embryo quality

	SI 	**G-185** 	
2PN	921	1004	
Grade A	472 (51.2%)	580 (57.8%)	P=0.008
Grade B	259 (28.1%)	244 (24.3%)	
Grade C	139 (15.1%)	140 (13.9%)	
Transferred	270	220	P<0.001
Frozen	259	366	P<0.001
Embryo utilisation rate	529 (57.4%)	586 (58.4%)	

Conclusions

- Culture in the G-185 resulted in a trend towards higher pregnancy rates
- The G-185 incubator maintains optimal physiological activity and homeostasis during embryo culture
- This reduction in embryonic stress results in better embryo quality and increased implantation potential

Conclusions

- The G-185 is a good alternative for embryo culture
  - → Consumes less gas
  - → Takes less space
- We consider a gradual replacement of all our standard incubators

Time outside the incubator is problematic

The future: Controlled work environment

- Integration of functions: workbench – incubator – microscopes

- Enclosed box = improved environmental control (Temp /pH / pollutants /microbes/ particles)