Quantification of the effect of Lipo-PGE₁ on angiogenesis

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* We have nothing to declare.
Current Use of Lipo-PGE$_1$

- Introduced in clinical practice - Carlson, 1973-

- Improves cutaneous microcirculation - Suzuki S, 1987-
- On blood flow, viscosity, fibrinolysis, platelet aggregation - Schrör, 1997-
- Potent hemodynamic effect in heart failure - Pacher, 1997-
- Reduce ischemia/reperfusion injury - Huk, 2000-
- Improve hemodynamic effects in heart failure/transplantation - Pacher, 1997; Haider, 2005-

- Diabetic neuropathy, leg ulcers - Toyota, 1993-
- Pph. arterial occlusive disease (PAOD) - Weiss, 2003-
- Diabetic murine hindlimb ischemia - Huang, 2008-
- Pulmonary hypertension & PAOD - Weiss, 2005-
- Collagen related skin ulcer - Murota, 2008-
- Renal injury - Stanek, 1997-
Successful composite graft for fingertip amputations using ice-cooling and lipo-prostaglandin E1

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: To confirm our previous report experimentally & scientifically
Materials and Methods

- 15 New Zealand white rabbits
- 2 groups
  - 8 experimental, 7 control

- Anesthesia
  - 5% Ketamine hydrochloride, 60 mg/kg

- Scaffolds implanting (S.C.) in the back
  - Merocel®
  - AlloDerm®

- Lipo-PGE$_1$ (Eglandin®) IV for 2 wks
  - Ear; marginal veins
  - 3 μg/kg/day
Merocel® as a scaffold
(Standard Nasal Dressing)

1 X 2 X 1.5 cm

2 X 2 X 1.5 cm
Mean clearance half time ($T_{1/2}$)

- At post-implant 2 wks
- Washout of radioactivity
- Collimated gamma-scintillation camera for 30 min
Histologic examination

- Extraction of implants at postop. 2wks
  - Merocel®, Alloderm®
  - Cut surface at the mid portion

- H & E staining

- Immunohistochemistry
  - CD31 (DAKO, Glostrup, Denmark) staining
  - Counting of the new vessels under light microscopy (x400)
    : 10 sites of HPF

- Statistical analysis
  - co-variants (ANCOVA) test by a specialist
RESULTS

\[^{99m}\text{TcO}_4^-\text{ clearance rate}\]

- Mean clearance half time \((T_{1/2})\)
  - in 1 X 2 X 1.5 cm \((p = 0.0125)\)
    : \(4005 \pm 2161.3\) (test), \(13840 \pm 4644.6\) (control)
  - in 2 X 2 X 1.5 cm \((p = 0.0413)\)
    : \(1560 \pm 1174.7\) (test), \(3405 \pm 807.03\) (control)

- Variance depended on the matrix size
$^{99m}$TcO$_4^-$ clearance rate

1 X 2 X 1.5 cm$^3$

2 X 2 X 1.5 cm$^3$

in 2 different sized Merocel®
Histological examination
(measurement of newly formed blood vv.)

- **Merocel® matrix**
  - in 1 X 2 X 1.5 cm (p = 0.0501)
    - : 11 ± 1.58 (test), 7.8 ± 1.71 (control)
  - in 2 X 2 X 1.5 cm (p = 0.02679)
    - : 20.19 ± 12.47 (test), 12.33 ± 3.25 (control)

- **Alloderm® matrix**
  - statistically unavailable
  - small in numbers at 2 weeks
(A) $^{99m}$TcO$_4^-$ clearance half time
(B) # of newly formed vvs. from Merocel® implants
Histopathology - H&E - (Merocel®)

Control group

Lipo-PGE1 group

X 400
Immunohistochemistry - CD31 - (Merocel®)

Control group

Lipo-PGE1 group

X 400
Immunohistochemistry
- CD31 - (Alloderm®)

Control group

Lipo-PGE1 group

# of vessels failed to show a significant difference between 2 groups.
Conclusion

Lipo-PGE$_1$ (Eglandin®)

= Alprostadil® (PGE$_1$) + Lipid microsphere

- Effective in angiogenesis
  - Composite graft survival
    in unreplantable fingertip amputation

- Improves microcirculation