Host response to alginate sheets: effect of alginate source

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OBJECTIVES

- Assess host response to alginate sheets implanted SC in rats
- Compare response to high-M alginates from different sources
- Compare different methods of fabrication

MATERIALS & METHODS

Alginates (all from *Macrocystis pyrifera*, F_M=0.60)

- NovaMatrix SLM-100 (FMC biopolymers, Philadelphia) **(Group 1)**
- Keltone HVCR (Monsanto, San Diego) **(Group 2)**
- *M. pyrifera* freshly harvested in San Diego, California **(Group 3)**
- Group 1 used as provided. Groups 2 and 3 alginates re-purified by Cerco Medical[1].

Sheet Fabrication[2]

- 1.5cm square sheets 300µm thick
- Encapsulating a polyester blood filter (for tear resistance)
- Gelled with 1.7% $CaCl_2$, pH 7.0
- Three sheet surface fabrication methods compared using preferred alginate

Animal Model

- Lewis rats
- Sheets attached by single suture in each corner.
- Each rat received one sheet subcutaneously (SC)
- Sheets recovered 14 days after implant

Endpoint: Gross observations of inflammation and fibrosis

REFERENCES

1 – http://www.isletmedical.com/pages/define_methods.htm
2 – Storrs, R et al. *Annals NY Acad. Sci.* **944**:252-266 (2001)
3 – de Vos, P et al. *Biomaterials*. 2006 Nov; **27**(32):5603-17

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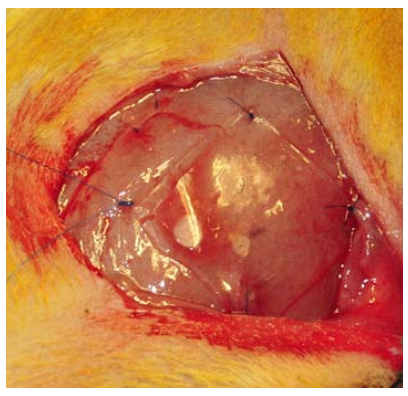
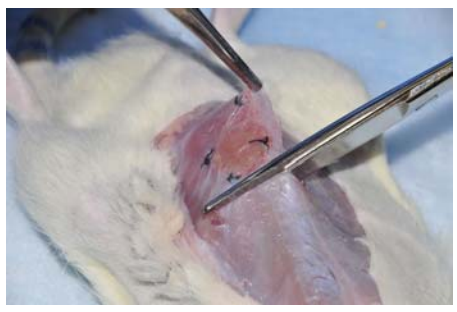
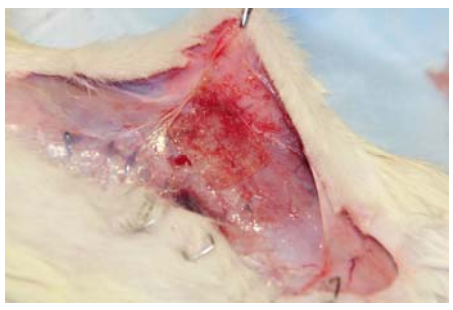
METHOD: Photographs of alginate sheets *in situ*





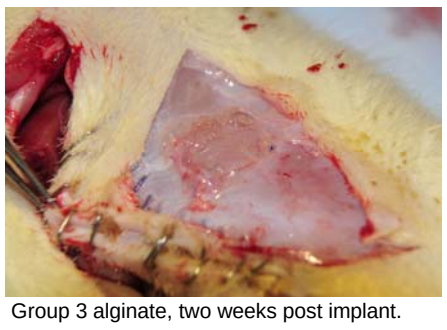
Subcutaneous alginate sheet at implant (L) and two weeks later (R). Keltone HVCR alginate (group 2).

RESULTS: Alginate source



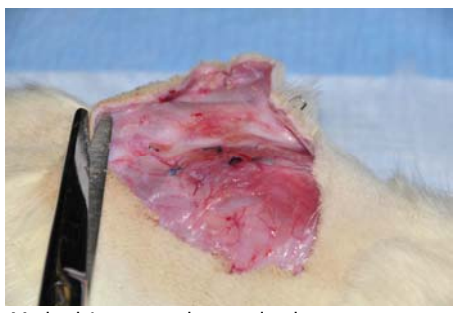
Group 1 alginate, two weeks post implant

Group 2 alginate, two weeks post implant

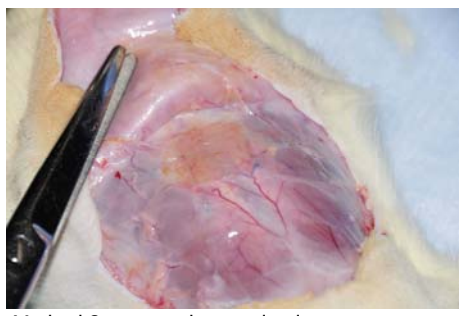


Group 3 alginate, two weeks post implant.

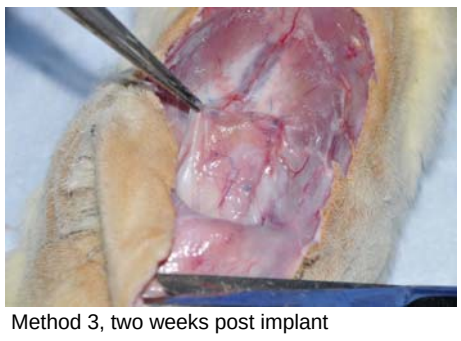
RESULTS: Fabrication Method



Method 1, two weeks post implant



Method 2, two weeks post implant



Method 3, two weeks post implant

CONCLUSIONS

Lewis rat reaction to alginate sheets depends on the source of alginate but not the sheet surface fabrication method.

Alginate re-purified from Keltone HVCR (Group 2) produced a smaller reaction when implanted SC.

DISCUSSION

The alginate formulation used in our previous experiments[2] is no longer available. Stability of alginate gels *in vivo* is dependent on a number of well known parameters[3] including alginate purity and molecular weight distribution. In this experiment **we compared alginate sheets** made with identical methods **using different alginates from three different sources**, then **different fabrication methods using the preferred alginate**. Sheets were implanted SC in Lewis rats for two weeks.

The observed fibrotic host response varied according to the alginate formulation. The repurified Keltone HVCR alginate (group 2) demonstrated the least reaction, while the NovaMatrix alginate produced the most significant response.

Three alginate sheet fabrication methods were then compared using the alginate from Group 2. Host reaction to Keltone HVCR sheets made by three methods was not significantly different.

FURTHER WORK

The goal of this project is to develop materials and methods for fabrication of an **Islet Sheet encapsulating primary islets that permits islet function for an extended time in the diabetic large animal.**

A significant reaction to the alginate sheet will lead to rapid islet cell death. Therefore research continues *in vitro* and *in vivo* to refine sheet fabrication to minimize deleterious reaction.