In vivo gelation of phenylboronic acid group-bearing polymer solution upon contacting soft tissue

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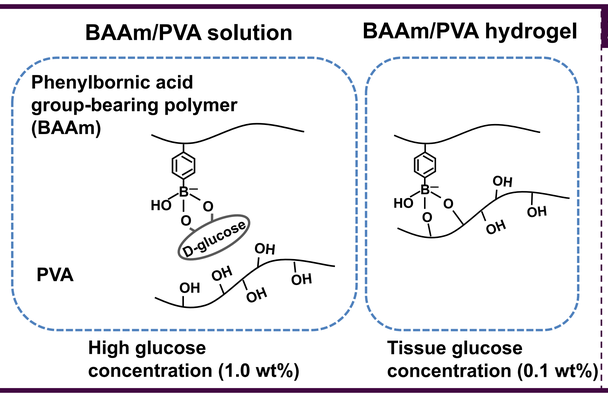
1. INTRODUCTION

Various anti-adhesion barriers including solutions, films and hydrogels have been developed so far. With increasing number of laparoscopic surgeries, in vivo gelation system which works in any shape is useful for adhesion prevention.

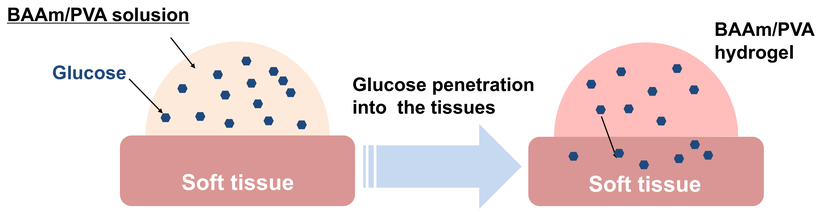
We focused on the reaction between the phenylboronic acid groups and diol groups. Polymers containing phenylboronic acid groups are widely used for gelation with polyol compounds such as poly(vinyl alcohol) (PVA) or sugars. Poly(acrylamide-*co*-*N*-acryloyl-3-aminoprophenylboronic acid (BAAm) binds to PVA and form hydrogels, and it also binds to glucose. The sol-gel state can be controlled by glucose concentration.

Herein, this sol-gel transition system is used to form hydrogels on soft tissues.



2. PURPOSE AND CONCEPT

Gelation due to decreasing glucose concentration

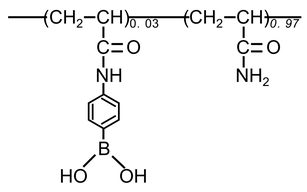


Once the glucose penetrates into the tissue, BAAm and PVA are expected to form hydrogels.

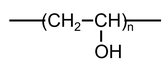
3. RESULTS & DISCUSSION

Effect of glucose concentration on gelation

BAAm
Mw: 54K



PVA
Polymerization degree: 580
Saponification value: 98%



BAAm/PVA solution
BAAm 1.0 w/w%
PVA 0.20 w/w%
Glu 1.5 w/w%

250 μL of injection

Dialysis for 2, 5, 10, 20, 30 min

Saline (Glu 0.1 w/w%)

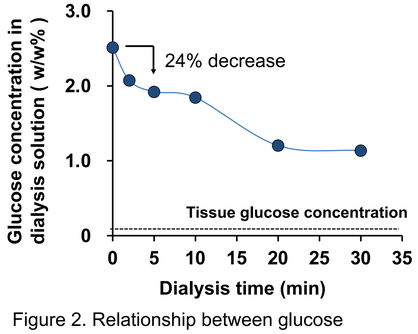


Figure 2. Relationship between glucose concentration and dialysis time.

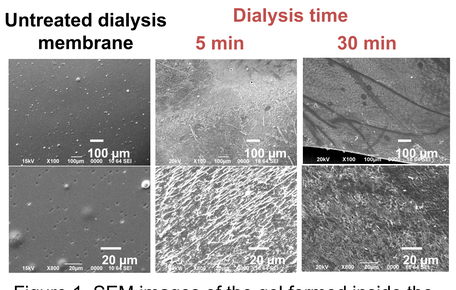


Figure 1. SEM images of the gel formed inside the dialysis membrane.

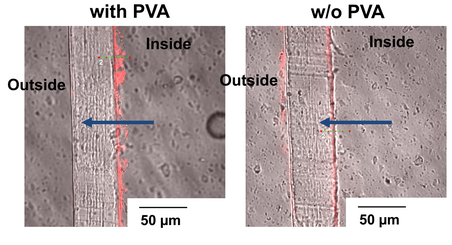
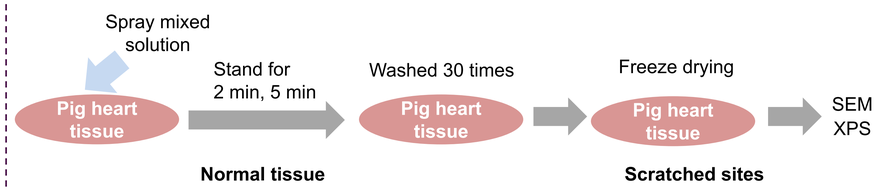


Figure 3. Cross section of dialysis membrane after 30 minutes dialysis (Frozen section).

It is considered that the hydrogels were formed by decreasing of glucose concentration at the membrane interface.

Evaluation of gelation on the surface of pig heart tissue



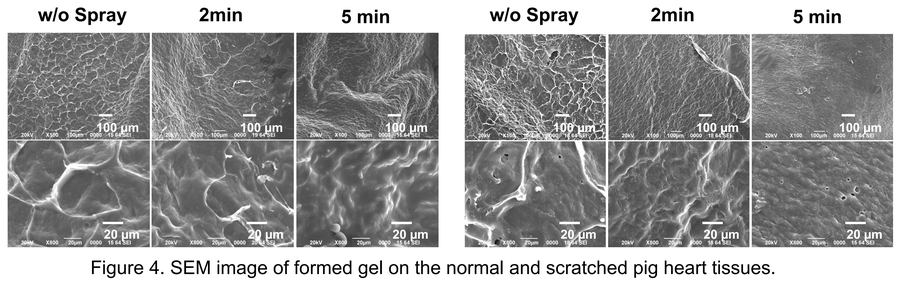


Figure 4. SEM image of formed gel on the normal and scratched pig heart tissues.

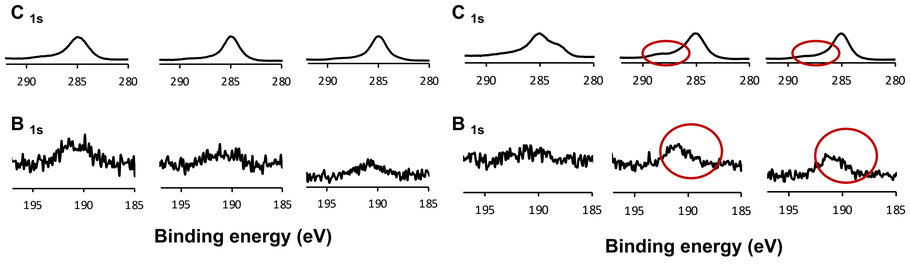
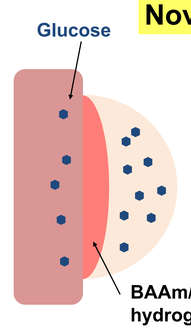


Figure 5. XPS spectra of the normal and scratched pig heart tissues surface.

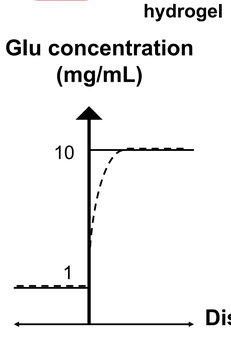
Hydrogels were formed on the tissue surface.
The gelation occurred remarkably on the scratched sites. This is probably because glucose penetrated into the tissue faster than normal tissue.

4. CONCLUSIONS

Novel *in vivo* gelation system



When the BAAm/PVA solution containing a high concentration of glucose comes into contact with soft tissue, the glucose immediately penetrates into the tissue.



Cross-linking between BAAm and PVA is thought to be due to decreasing of glucose concentration at the tissue interface.

We have developed the gelation system that induces gelation upon contacting soft tissue. This gelation system requires no artificial stimulations such as light, heat and pH.

The spontaneous gelation on the tissue surface enables a novel type of postoperative adhesion prevention.