Preparation and characterization of a decellularized dermis-polymer complex for the use in percutaneous devices

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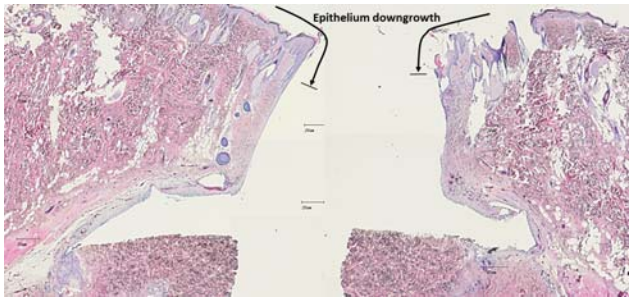
Introduction: Peritoneal dialysis is usually executed by implanting the flexible catheter directly the skin and peritoneal cavity. However, the problem with the flexible catheter is that the compatibility of the polymer and the skin tissue is too low which often causes the down-growth of the epithelial cells. This eventually causes the infection or even avulsion of the device. We tried to overcome this problem by preparing a percutaneous device based of a soft tissue-polymer complex using decellularized dermis as the soft tissue and poly(methyl methacrylaye) (PMMA) as the polymer. It is thought that it is possible to provide this device with tissue compatibility and maintainability of the flexible catheter within the device at the same time. We have reported that by putting MMA monomer into the dermis, it is possible to obtain a dermis-PMMA complex by simple bulk polymerization.[1)] In this report, we introduce the novel preparation method for decellularized dermis-polymer complex designed for the application as a percutaneous device and characterized its *in vivo* behavior.

Methods: The decellularized dermis was prepared using the high-pressure method. This was freeze-dried under reduced pressure overnight. Then, a hole in the center (θ = 4 mm) was made and the mixture of MMA, BPO, and DMPT with mole ratio of 200:1:1 was dropped around the hole to prepare a partial PMMA-dermis matrix. A silicone tube with inner diameter of 8 mm was placed on the hole and the mixture of MMA, BPO, and DMPT was poured to fill up the hole in the matrix and the tube. The matrix and the tube with MMA mixture was left in the air until the mixture polymerized and became very rigid (6 h). The silicone tube was cut open with a cutter to obtain a prototype percutaneous device with a PMMA rod tightly attached to the matrix (percutaneous device). This process was executed in the glove box, and the concentrations of O_2 and H_2O were below 0.1 ppm. The animal study was performed using wistar rats. Percutaneous devices were re-sterilized with high pressure in buffered saline (pH 7.4, 980 kPa) and implanted subcutaneously into the incision sites (n = 3), which were then immediately sutured with the PMMA rod sticking out from the rat. After 4, 8, and 12 weeks, the samples was then excised stained with Mayer's hematoxylin-eosin (H-E) stain and Elastic Van Gieson (EVG) stain. As a control, monolithic PMMA was also implanted.

Results: The swelling of tissue, clot formation, and keloid formation were not observed during the implantation period. The PMMA rod remained stable in the matrix, No rats died during the observation period. No sign of infection around the incised area was observed. Observation of the implant from the inside upon incision showed no sign of degradation of the matrix and no abnormal tissue formation around the implant.

After 4 weeks of implantation, the downgrowth of the cells stopped at the PMMA rod-tissue interface. An inflammatory response was visible between the PMMA rod-tissue and complex-tissue interface. The dermis part of the matrix, without PMMA, had integrated with the tissue, showing no clear interface. No infiltration of cells between the PMMA rod and complex was observed. However, the high downgrowth of the epithelial cells was observed for the monolithic PMMA. After 8 weeks of implantation, no further proliferation of the epithelium penetrating deeper into the tissue was observed. The number of the macrophages had decreased compared to the number at 4 weeks. Formation of fibrous capsules was observed around the complex and the PMMA rod. We could observe that the complex part and non-complex part of the implant were not separated by the infiltrated cells. After 12 weeks of implantation, the inflammatory response had almost completed, and the fibrous capsules had surrounded the device (Figure 1). Formation of blood vessels was clearly seen in the fibrous capsule layer. Further downgrowth of cells compared to that of 4 or 8 weeks was not observed at all. The PMMA rod and the matrix all remained stable inside the rat and did not come off when pulled perpendicularly. Further infiltration of the cells into the matrix did not occur, and foreign body giant cells were not observed.



Conclusions: We prepared a tissue-polymer complex with the flexible catheter firmly held by the stiff PMMA in the middle of the dermis. The suppression of downgrowth was successful. We believe that this tissue-polymer complex is suitable for use in percutaneous devices.

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References: K. Nam et al., *Mater Eng C*, Accepted.