

THE BIOMECHANICS OF ALLOMEND® ACELLULAR DERMAL MATRIX: BIOCOMPATIBILITY STUDY

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ABSTRACT

Dermal acellular matrices can successfully be used to replace or repair integumental soft tissues compromised by disease, injury or surgical procedures. A primary consideration when utilizing this biomaterial *in vivo* is its biocompatibility and immunogenicity, both of which influence its incorporation into the surrounding tissue.

In an animal model, AlloMend® ADM was implanted into 12 rats. There was no effect on metabolic function, and subsequent necropsy analyses indicated tissue incorporation and blood vessel infiltration with no untoward tissue reaction, including encapsulation (the formation of scar tissue), in each case.

Introduction

AlloMend Acellular Dermal Matrix (*Figure 1*) (AlloSource®, Centennial, CO), is produced through a proprietary process of cleaning, rinsing and decellularizing donated human dermal tissue, with significant removal of cellular debris (including DNA and RNA), proteins and antigens.¹ The process does not require the use of detergents or enzymes, thereby mitigating the possibility of harmful residuals in the tissue. Further, the product has been shown by biocompatibility testing to be non-cytotoxic. The decellularization process also inactivates microorganisms through cellular disruption, and as a result the likelihood of both immunogenic rejection and inflammatory response by the recipient is further minimized.

The tissue undergoes a terminal e-beam sterilization procedure, resulting in a 10⁻⁶ Sterility Assurance Level (SAL), meeting the same stringent sterility levels required by the U.S. Food and Drug Administration for implantable biomedical devices.

Because of its terminal sterilization, AlloMend Acellular Dermal Matrix (ADM) can be stored at room temperature for up to two years. Unlike some other acellular dermal matrices, the tissue is prehydrated and ready for immediate use without requiring a lengthy rehydration period. In addition, due to its handling characteristics, AlloMend ADM can be easily placed in a variety of anatomical areas.

The AlloMend ADM proprietary process results in a three-dimensional, collagen-rich, biocompatible, non-cytotoxic matrix that retains its biomechanical properties. This process and resulting properties help ensure it will be readily accepted by the recipient through subsequent revascularization and cell repopulation.

The purpose of this study was to evaluate the biocompatibility of AlloMend ADM through an animal model.

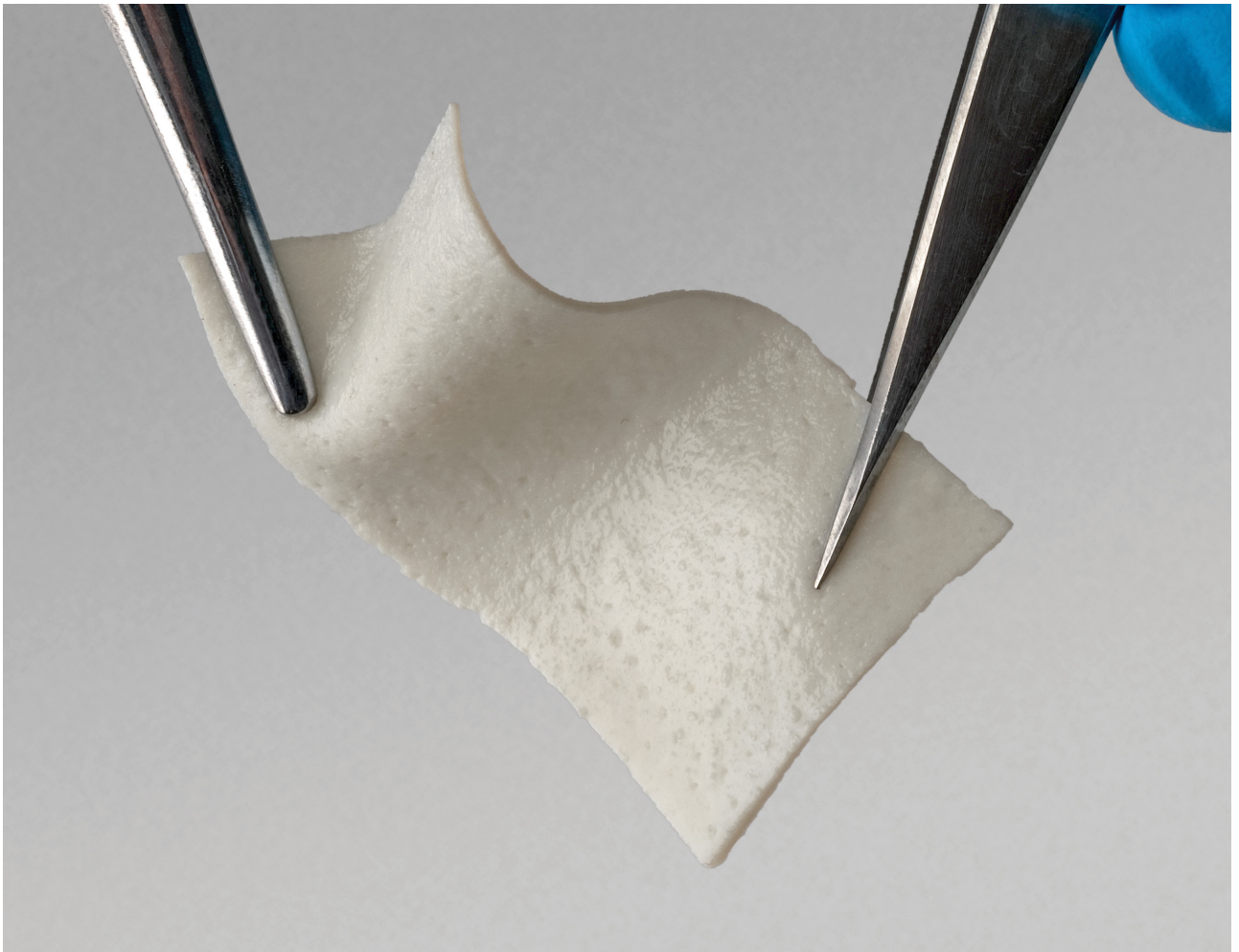


Figure 1. AlloMend ADM Tissue.

BIOCOMPATIBILITY

In an *in vivo* tissue graft environment, biocompatibility results in the incorporation of the implanted graft into the host tissue to the point where there is no discernible difference between the two in form and function. Vascularization and the absence of an immune response (a precursor to tissue rejection) are key factors indicating biocompatibility. In contrast, encapsulation is a foreign body response in which inflammatory cells surround the graft with resulting scar tissue.² Encapsulation is an indication of poor biocompatibility and this complication can necessitate a revision surgery.

Methods and Process

A standard *in vivo* study was conducted in which 12 rats were implanted subcutaneously with sections of AlloMend ADM from four different donors (*Figure 2*). A doctor of veterinary medicine monitored the animals' well-being and conducted the clinical assessments of the animals following the implantation procedures.

The animals were sacrificed at three time intervals: two weeks, six weeks and twelve weeks post-implementation. After euthanasia the implants (*Figure 3*) were removed and submitted to a board-certified veterinary pathologist for a histological assessment of the integrity of the implant and the infiltration of

blood vessels into the graft. Standard, documented procedures^{3,4} were used in the assessment.

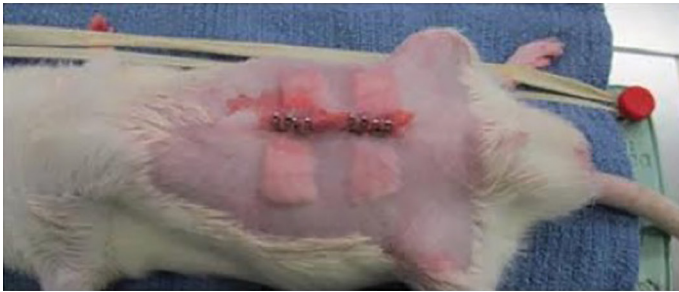


Figure 2. Initial implant of AlloMend ADM at time 0.



Figure 3. Implanted AlloMend ADM at 14 days.

Results

Two days after implantation procedures, visible swelling and erythema were resolved normally, an initial indication of graft incorporation. Similarly, all of the animals gained weight at rates consistent with normal rats, evidence that the grafts did not inhibit metabolic growth. At the time of explantation, all of the animals were deemed healthy by the veterinarian, suggesting there was no significant immunogenic response to the graft.

Upon necropsy, all animals were determined to have developed normally during the period and no untoward tissue rejection was apparent. Histological examination of the explanted tissue indicated cell and vessel infiltration for all three time periods (*Figures 4 and 5*). No significant levels of graft encapsulation were observed, indicating the absence of inflammatory response tissue rejection.

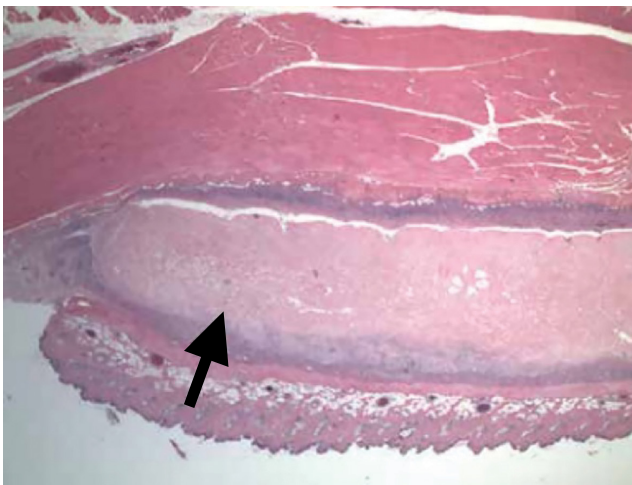


Figure 4. Graft implantation (arrow) at two weeks.

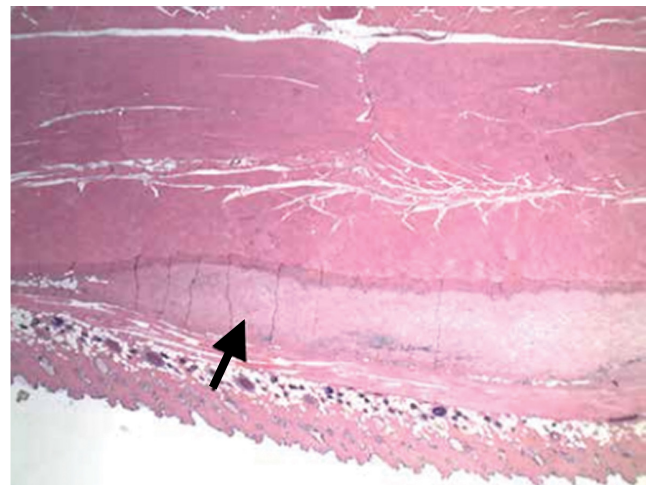


Figure 5. Graft implantation (arrow) at 12 weeks.

Infiltration of blood vessels into the grafts was apparent, providing further evidence of tissue incorporation. This vascularization was confirmed through immunohistochemistry staining (*Figure 6*) for the presence of Von Willebrand factor (vWF), a key component of the blood clotting cascade and a reliable

marker protein for endothelial cells of blood vessels.⁵ Thus, the presence of vWF in blood vessels is a strong indication of vascularization.⁶

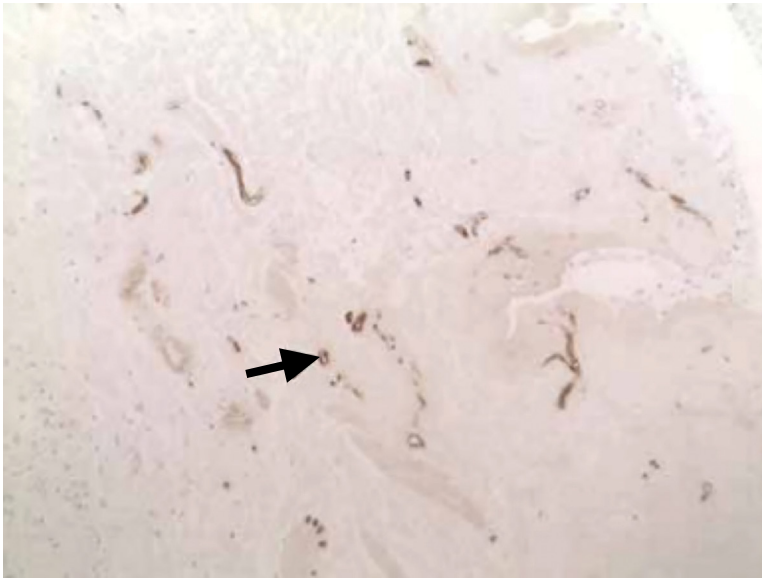


Figure 6. Immunohistochemistry staining for Von Willebrand Factor in an AlloMend graft at six weeks. Arrow indicates a blood vessel.

Finally, even though AlloMend ADM was implanted without suturing and no encapsulation was found, the grafts stayed in place with very little evidence of migration, suggesting there was incorporation of AlloMend ADM.

Implications

The lack of untoward biocompatibility response to the implanted AlloMend ADM stands in contrast to the histological record of implanted synthetic mesh materials, which due to their synthetic nature would remain a foreign body and never be fully incorporated. In fact, the use of synthetic mesh has led to relatively high incidences of infection^{7,8} even years after implantation.⁹

Conclusion

This animal study demonstrates the biocompatibility of AlloMend ADM. No untoward tissue reaction or encapsulation was found. There was strong evidence of tissue incorporation and blood vessel infiltration. No infections were noted nor was there a discernible impact on metabolism; animal growth and development subsequent to implantation were normal.

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