

Evolution Of The Biosynthetic Glove For Hand Burns

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Work done independently at different laboratories and universities - pictures of burn wounds used do not reflect identity of the patient - clinical studies were performed under IRB at Burn Centers on patients with an FDA cleared product (AWBAT, AWBAT Plus)

Competing Interests:

Aubrey Woodroof is the inventor of AWBAT Plus and CEO and Chairman of Aubrey Inc

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abstract

Methods – Use seamstress to design anatomical fit for glove and bootie, and tissue culture strategies to incorporate stem and cardiomyocyte cells into 3D matrices.

Conclusions - The AWBAT Plus glove is a biosynthetic glove expected to advance the art of hand burn management. Acute and chronic wound management may also be advanced by incorporating stem or other cell types into biosynthetic 3D Matrices to enhance the ideal properties required for skin substitutes (10, 11, 12 and 13).

Objective– Create a more effective biosynthetic glove for hand burns management. Advance the Art of Skin Substitutes.

Results – An almost perfect anatomical fit for the hand reducing operating room time and general anesthesia. A hydrophilic/hygroscopic moist, but not wet, wound healing environment which enhances healing.

Introduction

Hand burns represent an important wound with major potential for disability (1). The management of hand burns is multidisciplinary, requiring the expertise of surgeons, nurses, and occupational therapists. In addition to surgical excision and autografting, additional wound healing modalities are available for the care of hand burns including a bilaminate, biosynthetic glove. Motivated patients with burns limited to the hands can be managed on an outpatient basis at a burn center, where the requisite expertise in wound care, excision and grafting, and occupational therapy (OT) are available.

Plastic Surgeons, John Kucan and Martin Robson (2 - 7), envisioned biosynthetic gloves, booties and face masks in the early 80's. The first biosynthetic glove was created in 1981 from two flat sheets of Biobrane artificial membrane sewn together at Woodroof Labs Inc, Santa Ana, CA. The Biobrane glove has reduced surgical time after preparation for hand burns from

30–40 minutes per hand down to 5–10 minutes (8). Achauer (9) has emphasized the importance of early OT management which minimizes the need for later reconstruction. The Biobrane glove created has served the burn care community well (5 – 8) since the early 80's. Proper wound preparation of the acute hand burn is critical to success with a biosynthetic glove.

In 2009 at Aubrey Inc, Carlsbad, CA; a team of Biochemists, Bioengineers, Burn Nurses, Occupational Therapists, and a Seamstress were employed to advance the art of the biosynthetic glove. All known properties and attributes (10, 11, 12 and 13) identified to be important for temporary skin substitutes were utilized. Recently, new properties and attributes (14, 15) were formatted into a three piece anatomical design to better fit the complex asymmetric shape of the human hand including: (A) precision porous 3D silicone/nylon matrix. (B) advanced hydrophilic/hygroscopic moist, but not wet, healing environment.

The opportunity to satisfy unmet clinical needs by creating more complex "Combination Medical Devices" may be brought to fruition by incorporating living cells in the 3D matrix of AWBAT Plus or other biosynthetic matrices. The concept is being explored and preliminary results are reported here.

Background

During the 70's key properties of a Temporary Skin Substitute were identified by Tavis et al as well as the mechanism of adherence (13). Properties include – adherence (most important), stretchability, flexibility, stability (resistance to mammalian proteases), moisture control, sterile, non-toxic, transparent/translucent and long shelf life at room temperature.

In 1981, it was felt critical that the basic material for a burn glove, bootie or face mask (primary dressing) should possess all of the properties and attributes of an ideal Temporary Skin Substitute (see Figure 1). Film materials that possess these properties are bilaminate in contrast to mono-laminate.

Mono-laminate materials such as silicone and urethane membranes have good elongation properties but insufficient tensile strength, particularly the ability to hold sutures/thread. Materials with physical deficiencies and/or visual deficiencies (inability to see through the material) eliminated alginates, hydrocolloids and hydrogels for use as a primary dressing for a biosynthetic glove. Foams and gels are not useful to make prefabricated gloves. It was concluded that a porous bilaminate of silicone/nylon was the best material for the strength, stretchability, transparency and other desired properties.

Management of hand burns using Biobrane Gloves

Ten years of hand burn data, collected at the Adult Burn Centre of the Royal Adelaide Hospital in South Australia, has been analyzed retrospectively – including treatment method (conservative, Biobrane and excision and split skin grafting). This retrospective investigation revealed a gradual increase in the number of patients presenting with hand burns (from 68 in 2000 to 120 in 2009), but a progressive reduction in the proportion of hand burns being managed with grafting (55.9% to 18.3%) and a concomitant increase in those managed definitively with Biobrane (from 15.8% in 2000 to 52.5% in 2009). The proportion of those managed conservatively remained relatively static. There were no significant changes in mechanism of injury or patient demographics over this time period. A ‘jump’ in the trend towards Biobrane use occurred early in 2007, when Biobrane gloves became available in Australia. Although glove availability does not impact directly on outcome, it shortens markedly the operative time for definitive hand burn management with Biobrane.

We were intrigued as to whether this change in practice had any effect on outcome. An 18 month audit of outcome of all isolated hand burn patients – focusing on length of stay, time to return to work and other activity, scarring and patient satisfaction with their outcome, was undertaken. The prospective audit confirmed that hand grafting is not often performed and Biobrane outcomes are similar to the conservative treatment. Patients receiving skin grafts had longer inpatient stays, took longer to return to work and had greater dissatisfaction with appearance and function.

Biobrane treatment, and in particular the introduction of Biobrane gloves, has reduced the need for grafting in a proportion of hand burn injuries. The outcomes

with this material mirror less significant injuries treated conservatively, with the shift in hand burn management over the last 10 years having had major implications for South Australians.

Differential healing of semi-permeable skin substitutes

Pore marks on skin have been observed with the use of Biobrane (16). Greenwood (personal communication) has observed similar marks with other semi permeable materials and has used an optical biopsy technique that allows non-invasive assessment of skin by recording serial real-time visualization in horizontal “sections” (of chosen thickness in 2 micrometer increments up to 300 micrometers) from the surface of the keratin layer, through the epidermis, and into the superficial reticular dermis. Aside from avoiding patient discomfort and scar creation, its real-time images avoid the delay associated with pathology reporting and negate the need for histological processing which has deleterious effects on tissue biopsy structure, specifically dehydration, morphological change and artefact creation.

Semi permeable materials (Biobrane, AWBAT, meshed Integra, and meshed autograft) would be expected to have different rates of desiccation at the pore or mesh site as contrasted to the non-pore or non-meshed area. Greenwood and colleagues continue to study these healing phenomena and are preparing to publish and present their work. The rationale for meshing or increasing porosity is to ensure no fluid accumulates beneath the semi permeable temporary or permanent skin substitute which is believed to be a cause of infection. There is no perfect “skin substitute”, nor will there be until we can make skin substitutes that contain living pumps which can remove sub-membrane fluid when required (14).

Methods and Results

Presently, a number of materials are being evaluated for use as a Burn glove primary dressing.

- Biological materials – Cadaver allograft or porcine xenograft could be fabricated by the clinician into a glove however the process is time consuming.
- Alginates – Aquacell Ag+, being one of the better known alginate materials, has stability issues when on

the wound surface such as “shrinking.” That property alone is a significant disadvantage for use as a glove. The burned hand swells during the inflammatory phase of healing and needs relief as the volume of the hand increases.

- Plant derived products – such as BGC Matrix, Cellerate RX Gel are not commercially available as a glove. For the clinician to construct a glove from BCG Matrix will require expertise and time.
- Silverlon is available commercially as a burn glove. An advantage for this material would be antimicrobial protection which may be needed if the patient presents late.
- Temporary Skin Substitutes (Bilaminar composite materials, Bioengineered Alternative Tissues) – Biobrane, AWBAT and AWBAT Plus are available as biosynthetic burn gloves (see Table 1).

Future possibilities of using stem cells to create living 3D matrices

AWBAT Plus: Expansion of stem cells for clinical applications.

Preliminary data indicates that the AWBAT Plus provides an effective scaffold support matrix for the expansion of various cell types including embryonic stem cells (ES) and adipose-derived stem cells (ASC) from mouse and rat respectively (15). Both cell types displayed robust and confluent growth over the surface of the AWBAT Plus 3D matrix. Furthermore, the addition of beta-mercaptoethanol to the mouse ESC media stimulated the formation of embryoid bodies, introducing the possibility of differentiating the stem cells directly on the AWBAT Plus 3D matrix.

AWBAT Plus may fulfill a role in the *in vitro* generation of tissues for transplant. To date, tendons, cartilages and bladders have all been grown *in vitro*, mainly using collagen-based scaffold materials to direct the 3-dimensional growth of the seeded stem cells. AWBAT Plus could potentially be used in an analogous manner for the preparation of tissues including skin, tendons, cardiac tissue such as heart muscle and valves, ligaments, etc. This 3D precision porous silicone/nylon matrix offers several advantages over collagen scaffolds including stability in a biological environment, ease of handling and ability to be formed into various shapes without excessive processing. Coupled with a versatile, high performance cell culture vessel such as the Lampire Omni C3™ cell culture bag, tissues of almost unlimited shape and

configuration may potentially be grown *in vitro* using stem cells.

Although at the forefront of personalized medicine, the safety of stem cell-based therapies and transplants treatments has recently been questioned by possibilities that such cells could turn malignant. An increasing number of studies have identified aberrant stem cells at the heart of cancerous tumors, indicating that these self-renewing cells are responsible for the unregulated growth of the malignant cell population. Furthermore, several clinical cases have been published where stem cell transplantations have been implicated in subsequent tumor formation. This link between unregulated stem cell growth and cancer development would explain why tumors can regenerate, and also why tissues with a rapid turnover such as skin, blood and the lining of the gut are apparently more susceptible to cancer development. Obviously, further studies are required to understand how we can extend the use of stem cells for important clinical applications and expand the field of personalized medicine, without increasing the risk of cancer in patients.

AWBAT Plus and Cardiomyocytes - potential for replacing necrotic myocardium

The ability of human embryonic stem cells, derived, cardiomyocytes to attach and grow on the 3D matrix of AWBAT Plus was measured under different conditions. Human embryonic stem cells were differentiated into cardiomyocytes using an optimized regimen of growth factors, including activin A (protein) and bone morphogenetic protein, and after 2-3 weeks the cardiomyocytes begin to spontaneously contract (17, 18). The cardiomyocytes used in this experiment had begun the differentiation process about a month beforehand.

Beating cardiomyocyte colonies were seeded on approximately .5 cm x .5 cm square of AWBAT Plus. Each colony contained a few hundred to a few thousand cells which did not cover the patches, but provided enough colonies to assess attachment viability. Cardiomyocytes did attach to fibronectin coated AWBAT Plus and continued to beat spontaneously once attached.

A major challenge in optimizing AWBAT Plus as a cardiomyocyte scaffold will be increasing the number and density of nylon strands. As currently constructed, the nylon fibers are large (15/2 denier) in relation to

cell size. Another challenge is creating a 3D matrix thick enough to support enough cells, formed into muscle, that could attach to adjacent nylon fibers and contract/relax. The 3D matrix/cardiomyocyte complex would need to have good tensile strength and not be rejected. Another challenge, if the above can be accomplished, would be adequate vascular supply of the complex to support continued viability.

Conclusions

The AWBAT Plus glove may be the best current solution for mixed depth partial thickness burns. The future may bring an AWBAT Plus glove that contains living cells.

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- Amy Moss, OT, Project Leader; Victoria Vandenberg, RN; Karla Alvey, Seamstress – Co-Inventors of the AWBAT Glove

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Illustrations

Illustration 1

Figure 1 - The Biobrane glove - fabricated using two sheets of planar Biobrane was envisioned by Dr. John Kucan in 1981 (2).



Illustration 2

Table 1 - Evolution of the biosynthetic glove

Biosynthetic Glove	Date Created	FDA Classification	Porosity of the Silicone/Nylon Membrane	Biological Aspects
Biobrane	1981	Device	1.2% - crude pores w/ damaged 3D structure	Collagen peptide covalently bound
AWBAT	2009	Device	5.5%, precision pore w/ uniform 3D structure	Collagen peptide w/ no cross-linkers
AWBAT Plus	2010	Combination: Device & Drug	5.5%, precision pore w/ uniform 3D structure	Collagen peptide w/ no cross-linkers, Vitamin C & E, Chondroitin 4 & 6 Sulfate, Immuno-10

Illustration 3

Figure 2 - AWBAT Plus glove, a precision anatomical fit biosynthetic glove with three piece design.



Illustration 4

Figure 3 - AWBAT Plus Bootie, a precision anatomical fit with three piece design envisioned by Dr. Martin Robson in the early 80s.



Illustration 5

Figure 4- Photo's (Figures 4- 7) courtesy of Dr. Rajiv Sood and David Roggy, Wishard Burn Center, Indianapolis, Indiana. Pre-application of the AWBAT glove to properly prepared wound.



Illustration 6

Figure 5. Post application day 1. Provides a moist, but not wet, healing environment.



Illustration 7

Figure 6. Post application day 10 - immediately following removal of the AWBAT glove.



Illustration 8

Figure 7. Post application day 16.



Illustration 9

Figure 8. Post burn day 3. Glove applied in hydrotherapy room to partial thickness flame burn. Patient went home that afternoon. OT was pleased with the range of motion patient had upon discharge.



Illustration 10

Figure 9. Approximately 20 days out from injury. Partial thickness burns to bilateral hands



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