A Comparative Study Between Microskin Autograft, Cultured Autologous Keratinocytes and Meshed Split Thickness Skin Autograft, in Burn Wound Coverage

Thesis

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LIST OF ABBREVIATIONS

CEA	Cultured Epidermal Autograft
EGF	Epidermal Growth Factor
FBS	Fetal Bovine Serum
Fig.	Figure
HEPA	High Efficiency Particulate Air
H & E	Hematoxline and eosin
KBM	Keratinocytes Basal Medium
P/S	Penicillin / Streptomycin
STSG	Split Thickness Skin Graft
TBSA	Total Body Surface Area

Introduction

Introduction

Advances in the critical care, resuscitation, ventilation, and nutritional management have improved survival after severe burn. However, the extensive damage caused by massive burns still constitutes a major surgical challenge for wound coverage and healing ***(Atiyeh Bishara et al., 2005).***

Methods for handling burn wounds have changed in recent decades. Aggressive surgical approach with early tangential excision and wound closure is being increasingly applied. Surgeons now face the challenge of excising and grafting larger burns with limited autograft availability. In such cases, it is necessary to find alternatives to conventional split-thickness skin autografts ***(Ronfard et al., 2000).***

Transplantation of split-thickness skin grafts (STSG) harvested from healthy donor sites is the standard method for burn wound closure and remains the mainstay of treatment to provide permanent wound coverage ***(Holmes et al., 2003).*** Even though harvesting of autologous skin grafts is associated with additional scarring ***(Gajiwala et al., 2004),*** autologous split-thickness

graft is still considered the ideal skin replacement ***(Pellegrini, 1999).***

In some severely burned patients, the burns are so extensive that donor site availability is limited by the disparity between burned and unburned tissue. This may be further complicated by donor site unsuitability for harvest (e.g. face, hands, feet, axilla, perineum) so that the surgical treatment of these patients becomes a very difficult task. Furthermore, dermal thickness may limit the number of harvests at any one site to three or four times, and the time required for re-epithelialization delays recropping. Such limitations have driven the search for alternative means to resurface the burn patient and achieve healing ***(Williamson et al., 1995).***

The Meek–Wall dermatome was described in 1958 and allows cutting of postage stamp skin grafts suitable for grafting of an area larger than the donor site. This method was eclipsed, however, by the introduction of meshed skin grafts which are less time consuming and easier to perform ***(Raff et al., 1995). Tanner et al., (1964),*** presented the technique of meshed skin graft by which they could cover three times the donor area with good take, improved drainage, and rapid epithelialization of the interstices. The meshed split thickness skin graft might be

expanded up to 1-6 or 1-9 ratios to cover extensive burns ***(Hurt and Erikson, 1986)***, but this is associated with decreased take, excessive scarring and poor cosmetic appearance ***(Alexander et al., 1981, and Herd et al., 1987).***

Based on the antigenic disparity between the epidermis and the dermis, several methods were described to cover burn wound by homo- and autografting. These include using alternate strips of homo- and autografts ***(Jackson, 1954)***, the Chinese concept of intermingled auto-allografting ***(Yang et al., 1980 and 1982).*** However, these techniques could achieve only limited expansion in surface area. ***Zhang et al., (1986)***, described a technique that enabled skin cover to be obtained in patients who had suffered major burns. This technique involved using finely minced autografts on the undersurface of cadaveric allografts. Their published results demonstrated a major advance in burns surgery management. However, this technique has not been widely applied, partly because of the risks associated with HIV and hepatitis transmission and also the problems of obtaining fresh allograft tissue. Large expansions result in delayed healing, scar hypertrophy, and contracture. Such problems have been overcome somewhat by overlaying the interstices with allograft or synthetics. The autograft

resurface the wound and the overlay is subsequently rejected ***(Tanner et al., 1969).***

When donor sites are not sufficient to prepare enough meshed grafts, the permanent coverage of burn wounds with cultured autografts becomes life saving ***(Pellegrini et al., 1999).*** Fortunately, considerable progress has been made in the culture of human keratinocytes and it is now possible to obtain large amounts of cultured epithelium from a small skin biopsy within 3 to 4 weeks ***(Ronfard et al., 2000).*** The ability to grow keratinocytes *in vitro* and generate cohesive sheets of stratified epithelium which maintains the characteristics of authentic epidermis was developed by ***Rheinwald*** and ***Green*** in ***1975*** and is the most commonly used technology for producing graftable epithelium ***(Ronfard et al., 2000).***

The cultured keratinocyte sheets have several drawbacks. Three to five weeks are required to prepare sheets before being ready for grafting ***(O'Connor et al., 1981).*** Cultured epidermal cells separated by dispase II fail to attach or proliferate on dermal collagen membrane ***(Boyce and Hansbrough, 1988),*** do not show hemidesmosomes ***(Aihara, 1989),*** and show microscopic blebbing at the basal side, which might represent cell injury and affect cell function and/or attachment

(Compton et al., 1989). Cultured keratinocytes tend to differentiate as cultivation progresses and this could be another reason for poor graft attachment ***(Kumagai et al., 1988).***

The time needed to use cultured keratinocytes to cover a burn wound was reduced to 3 weeks by late 1980s and early 1990s ***(Compton, 1993). Stark et al., 1995*** developed suspension in Fibrin glue and reduced the time for clinical use to 14 days. Some groups approached the reduction in time by developing a technique of delivering a suspension of cells to the wound surface reducing the laboratory culture time to 5–7 days ***(Dvorankova et al., 1998). Wood et al. (2006)*** stated that in Western Australia, the technology developed rapidly from the use of confluent epidermal sheets that comprised predominantly of keratinocytes to the use of pre-confluent cells in suspension delivered as an aerosol onto the wound surface (now called Cell Spray).