Using Ovine Extracellular Matrix in Difficult to Close Excisions of Common Skin Cancer: an Evolving New Technique

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ABSTRACT

Squamous cell (SCC) and basal cell (BCC) skin cancer are common presentations in elderly patients. Skin cancer are often located in sun exposed areas where damage from exposure has occurred. The sun exposed areas are often difficult to close or would require more complex measures to cover. Skin grafts or rotation flaps are commonly employed for coverage. Having tumor free margins is required to anticipate avoiding local recurrence. Mohs techniques examine the surgical margin to ensure that lesions are completely excised. When reliable frozen section is not available for immediate confirmation, permanent section may be used. Excising lesions and implementing radial identification allows margin localization of involved margins for re-excision. Divided into quartets, directed re-excision can be undertaken with minimal disturbance to the healing wound bed. Use of an ECM device (Myriad™, Aroa Biosurgery, Auckland, New Zealand) accelerates healing and leaves a cosmetically acceptable result that affords margin examination and re-excision with minimal disturbance to healing wound. Here we present an evolving technique of excision of common skin cancers utilizing ECM Matrix Graft technology and healing. This technique affords margin identification utilizing permanent section examination. Subsequent margin identification and re-excision if necessary is localized to individual quadrants of the excision site allowing more precise re-excision and not disturbing the grafted wound site. Healing seems accelerated and cosmetic appearance is acceptable to patients.

INTRODUCTION

Surgical excision of common skin cancers continues to evolve in technique. The introduction of readily available and cost effective Extracellular Matrix Grafts (Myriad™, Aroa Biosurgery, Auckland, New Zealand) that orchestrate healing can be integrated into a treatment plan in difficult to close skin cancer excisions. Certain areas of the body do not lend themselves to simple closure without tension and a high risk of dehiscence leaving an open wound. Immediate grafting or flap closure carries with it the chance that permanent sections of the margins could be found involved with micro extensions of tumor.[1-3] These micro extensions then raise the risk of local recurrence. Re-excision of a positive margin at an excision site where a skin graft was applied risks the skin graft to disruption and failure. It is likely that the graft will not be mobile enough to cover the excised area without undermining the graft from its new attachments. The graft of a re-excision is more

likely to heal with a tissue deformity at the operative site. Additionally, finding a positive margin in the pathology after flap closure is further complicated by locating with certainty the exact point of the involvement given the re-arrangement of tissue.[3] By incorporating an of the shelf ECM graft device, surgical excision can be completed and the excised area can be grafted with an Extracellular Matrix Graft Device immediately.[4] Permanent section evaluation and review can then be completed. If margins are incompletely excised, i.e., positive, directed and limited re-excision can be performed. Re-excision has not lead to a delay in healing. Once removed, the newly created defect can then be grafted by adding ECM graft material to the defect, filling the void and complement healing. In this way, surgically applied skin and rotated skin flaps are not disturbed or compromised as would be the case when re-excision after those more involved procedures are performed. In the event that grafting or flap closure is warranted, the use of an Extracellular Matrix Device does not preclude subsequent procedures from being utilized.[4] In the event of simple skin grafting, a granulated bed can be achieved with the use of an ECM graft device which would more readily accept a skin graft.

MATERIALS AND METHODS

The area about the skin cancer can be mapped out for resection. Using a 4 mm margin, the skin lesions can be excised full thickness to include epidermis, dermis and subcutaneous tissue.[1,5,6] Where appropriate, underlying fascia or other connective tissue can be removed en bloc.[1,5-10] The tissue specimen would then be prepared for quadrant margin examination.[2] The specimen can be oriented to identify each quadrant margin in a clockwise fashion. The specimen is oriented identifying the 12 to 3 quadrant, the 3 to 6 quadrant, the 6 to 9 quadrant, and the 9 to 12 quadrant margins for examination.[11-13] The quadrants are separated by notching with the scalpel to further separate the individual quadrants during examination. Sutures are used to identify each individual quadrant so that each unique margin can be identified by the pathologist and separated from each of the other quadrant margins. Each quadrant margin is uniquely identified, as demonstrated in Fig. 1. The specimen is then examined microscopically by means of permanent section. Each distinct margin edge can then be identified as part of the specimen evaluation and noted by specific quadrant. Paraffin block permanent section examination was utilized with anticipation that in the event of a positive quadrant margin, repeat resection could be more specifically identified and directed to remove margin edge in that quadrant with minimal disturbance to the ECM tissue device graft. This method avoids incongruity between frozen section evaluation and subsequent permanent sections.

At the time of excision, the tumor and resection margins are mapped out to allow for an adequate margin (Fig. 2a). Wide excision of the lesion is performed taking full-thickness tissue to obtain a deep margin as well as skin margin (Fig. 2c).

After skin tumor removal, the full thickness defect is then filled with a layered ECM-device tissue graft (Myriad™, Aroa Biosurgery) tailored such that it fits and fills the tissue defect (Fig. 2c,d). The ECM tissue device graft is then secured about its perimeter with an absorbable 4-0 monofilament suture. The ECM tissue device graft would be hydrated with saline solution. With placement and hydration, the ECM device absorbs blood elements into the graft from the surrounding tissues as visually noted by its red color (Fig. 3A-C). A bolster tie over dressing constructed of antibiotic impregnated petrolatum gauze and cotton

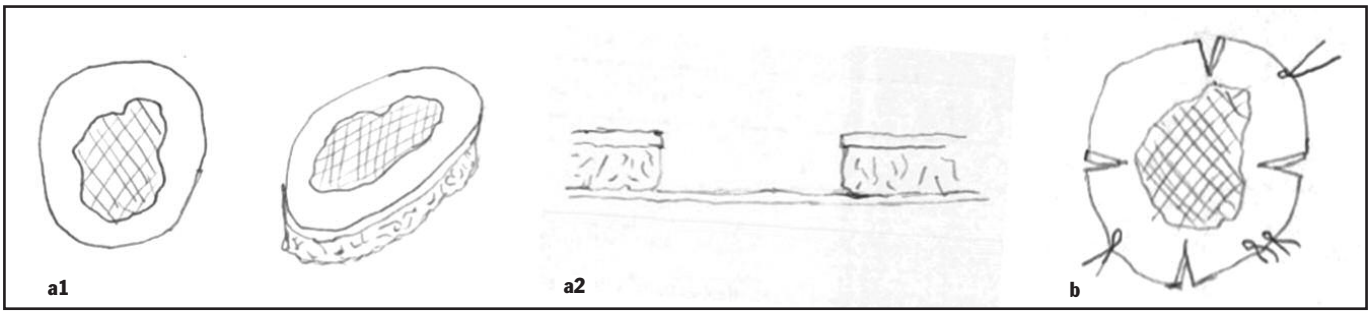

Figure 1. (a1, a2) Complete full-thickness excision planned with appropriate margins. (b) Specimen oriented and knotched to identify margins.

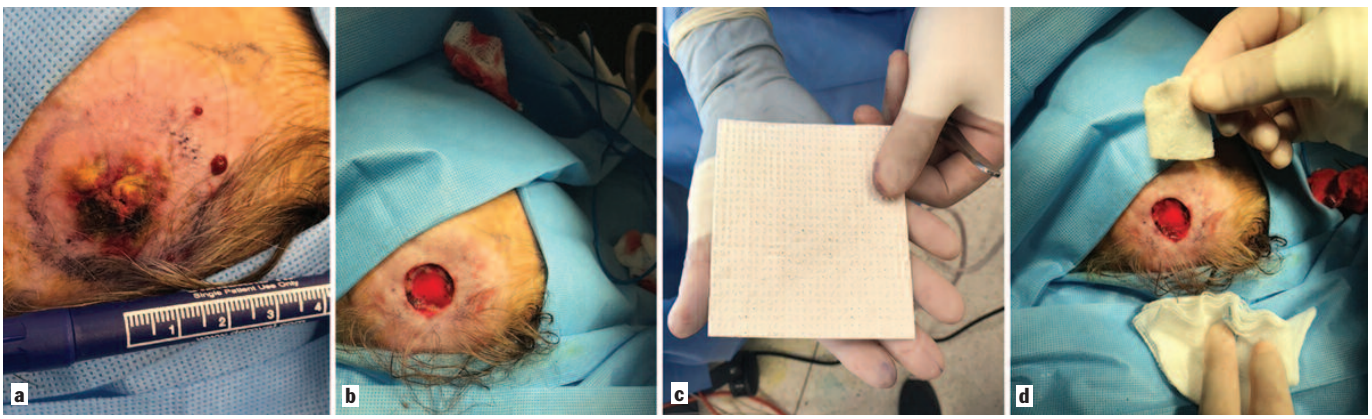

Figure 2. (a) Mapping and measuring resection margin. (b) Excision. (c,d) Layering of ECM tissue device graft.

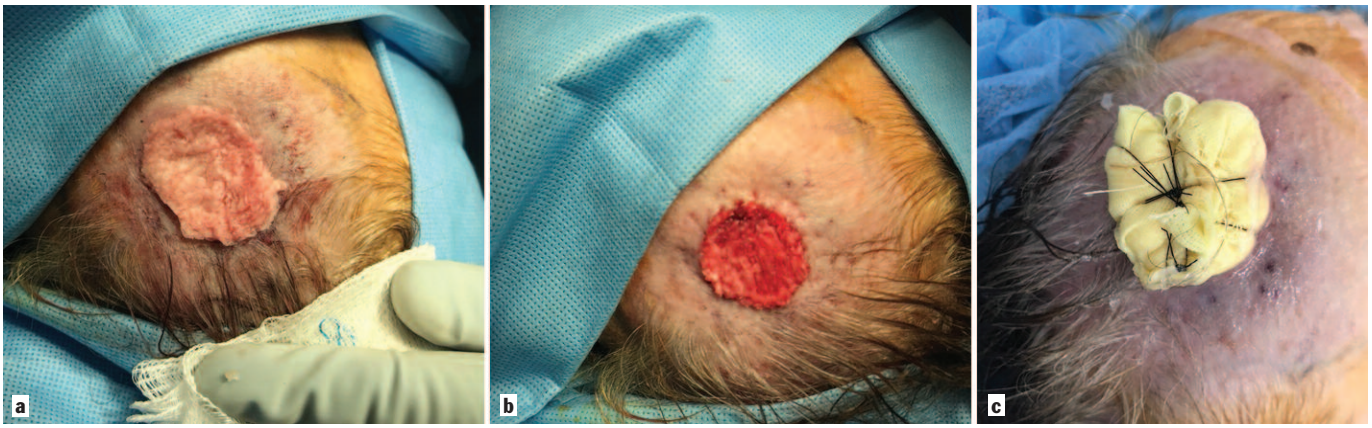

Figure 3. (a) Graft is applied and hydrated. (b) Graft immediately uptakes blood elements from wound. (c) Secured with monofilament absorbable suture and bolster dressing created and tied.

gauze was applied over the ECM tissue device graft. The bolster is secured and anchored with nylon sutures. The secured bolster dressing covers the ECM device and applies pressure to the graft holding it in place and to ensure contact of the ECM tissue device graft to the base of the wound defect (Fig. 4).

Full thickness excision of the basal cell skin cancer is achieved. Attention to removing the tumor with adequate skin margins can be applied without modification to accommodate simple closure techniques (elliptical excision). Excision with intent on maintaining the resection margin to achieve complete excision is more the focus and avoids taking extra skin and tissue in anticipation of closure. Given the planned use of an ECM device to fill the defect, deep margin removal can be more complete as the ECM device has been shown to fill and cover vital structures with good results.[14,15] Excision of deeper structures to bone or fascia can be performed with confidence that underlying structures will be covered at the conclusion of the operative procedure. In this manner complete excision of skin, Subcutaneous tissue and fascia exposing bone or other structures can be performed if required.[3]

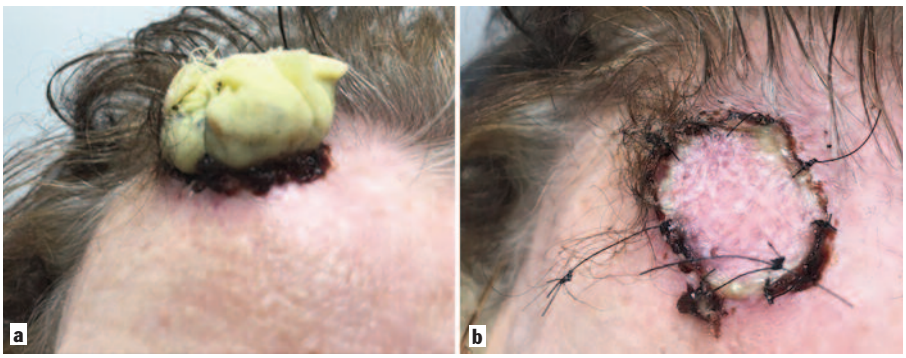

Figure 4. (a) 2-week follow-up visit. (b) Bolster is removed, graft is pink and becoming infiltrated with host cells.

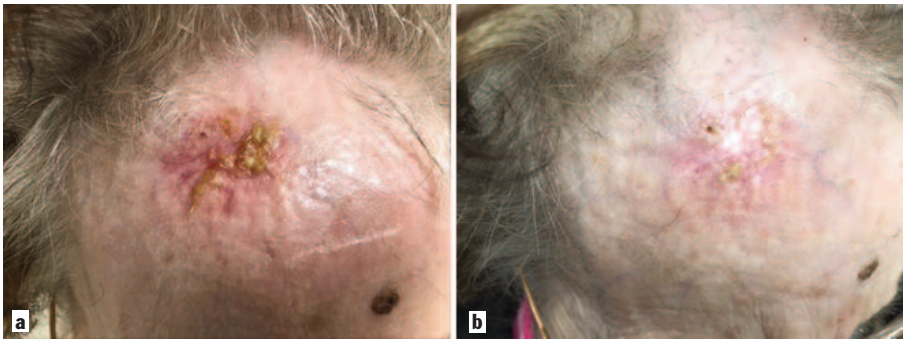

Figure 5. (a) Graft at 5 weeks. (b) Graft at 6 weeks. Healed and defect filled with little tissue loss deformity. Skin covered and level with surrounding skin.

In the event of a positive margin, planned re-excision specific to the involved quadrant can be performed. Directed re-excision results in less tissue removal that total re-excision. If a tissue deficit is created, additional ECM device can be applied to fill that defect without jeopardizing healing.

RESULTS

Patients are followed weekly. The bolster dressing is left in place for 2 weeks undisturbed. Antibiotic ointment is applied around the contact perimeter of the skin -bolster dressing. This helps to avoid drying of the ECM device. At 2 weeks, the dressing is removed and the graft material is examined. The ECM device is pink and looks viable as cellular infiltration has been initiated and occurred into the structure of the device (Fig. 5). Cellular signaling and remodeling of the ECM material is occurring. This remodeling of the ECM has been demonstrated to produce and result in factors that have major roles in healing. Degradation of the ECM releases multiple factors that play a role in orchestrating healing. Of these products, a group of leucine-rich proteoglycan factors are released. These molecules bind to growth factors and collagen affecting multiple essential cellular functions.[16-18] Cell differentiation, proliferation, and migration are but some of those functions. These processes affect collagen synthesis and scar formation. A specific factor, May-Day has been identified from remodeling of the provisional ovine ECM device that attracts endogenous mesenchymal stem cells to the device which may help further understand the role of a provisional matrix in wound healing.[16] Using a device to attract endogenous stem cells may help

explain the healed outcomes where by the excision site is repaired and seems to match well to surrounding tissues.[17] Evident in the excisions is that this type of secondary healing prompted by the ECM device allows the site to fill in avoiding the tissue deficit commonly seen in other techniques (Fig. 5).

DISCUSSION

Managing common skin cancers requires resection with negative margins in order to reduce the rate of recurrence.[1,2,5,7-11] Complete excision of skin cancer using this technique can proceed without undo concern over excising the lesion in an elliptical manner to accommodate for simple closure. The lesion is excised with emphasis on obtaining negative margins. Such a perimeter based excision leaves a tissue defect shape that traditionally has either been allowed to granulate, followed by skin grafting. Allowing the wound to granulate, particularly if the depth of the wound is periosteum or fascia can take a considerable amount of time. This delays grafting and time to a healed outcome. Negative pressure wound therapy (NPWT) can sometimes be used to help accelerate this process. NPWT however results in added therapy and the application of the mechanical device to the wound area. The matching of donor skin harvested to cover the defect can also be problematic as typically the graft donor skin fails to match the recipient area completely. Immediate skin grafting can result in a tissue deficit under the graft, and a noticeable deformity.

Local tissue flaps have been utilized to cover the defect but involves rearrangement of perimeter skin and tissue making margin identification more difficult in the event of a positive margin. Immediate flap closure has the disadvantage of changing the orientation of the margins. Should an involved margin be detected on pathology, deconstruction the flap and re-excision should be performed thus complicating subsequent closure.

Current xenograft extracellular matrix devices differ from previously available xenografts in that processing has been developed to preserve the bioavailability of active elements in the material. First, more diverse and biologically active tissues are used in the development of these devices in order that these factors are present in the material sufficient to provide these molecules in the end product provisional matrix.[16-18] In doing so, new modern day xenografts become incorporated and remodeled in the wound rather than immunologically rejected by the host. The matrix becomes a provisional structural extracellular matrix that will serve as a substrate for orchestrated healing. The matrix becomes actively remodeled and an active part of the process and in a fashion, consumed in healing rather than rejected. The basement membrane of the sheep foregut is used to produce the Myriad™ ECM device (Aroa Biosurgery). This highly active source tissue is rich in the components known to be involved in the healing process.[19] The ECM device has key elements known to impact and direct healing processes. New processing techniques are intended to maintain these bioactive properties of the material that are key to its effectiveness in orchestrating healing.[15,20] The retention of growth factors and other key molecules such as fibroblast growth factor, glycosaminoglycans (GAGS), fibronectin, hyaluronic acid, and laminin are important in healing.[19] The ECM device promotes granulation tissue formation in the wound providing structure for remodeling filling the defect.[16] With the ECM architectural structure intact, structural ligands are present that when fibroblasts attach to the ECM through these ligands, that interaction signals intracellular phenotypic programed change bringing about new sequenced cellular functions in fibroblasts. These new next step processes allow orderly healing and tissue remodeling to continue. Healing is further enhanced by the recruitment of stem cells to the surgical site.[16] The recent discovery of ECM-derived bioactive homing factors such as the May-Day protein attract stem cells to the site as the provisional matrix is remodeled by macrophages.[16] Attracting stem cells to the site through homing lends support to the effectiveness of these materials to impact on healing.[16]

The surgical excision site defects heal quickly and with minimal deformity and acceptable cosmetic results. The ECM tissue device graft does generate granulation tissue in the excision site. The granulated excision site does epithelialize with nearby cells which may ultimately better match surrounding skin as seen in the figures provided. Using an ECM device such as Myriad™ (Aroa Biosurgery) has advantages over immediate closure with flap or skin graft techniques by allowing permanent section evaluation of the margins of resection. In the event a positive margin is determined on permanent section, the specific quadrant can be resected and examined specific to that portion without significant disruption of the healing site. More directed re-excision can be undertaken avoiding disruption to the graft area. Once granulated, the site can be skin grafted if need be or in the case of appropriately sized sites, allowed to heal and epithelialize.[4,15] We have found that the healed result provides for acceptable cosmetic result and match to surrounding skin. Further development of ECM devices will bring about opportunities for use in surgical application. The healing potential of an ECM device that can actively participate in normal physiological processes opens new opportunities to re-examine even common surgical procedures as excisional treatment of common skin cancers.

CONCLUSION

Through continued healing research, a better understanding of the role a provisional ECM device has provided new opportunities to rethink typical approaches to surgical procedures. Biologically active devices are more commonly used in surgical procedures as an implant or adjunct. As the interactions orchestrated by the structural elements and peptides of an ECM are being better described, their application during surgery may well lead to improved healing outcomes.[21] This manuscript reports a new approach to common skin excisions where margin control is primarily important to the ultimate outcome. With the use of a provisional ECM matrix, attention to initial margin control can be more generous in terms of excision. Additionally, the use of an ECM device allows re-excision of an involved margin without the concern of disturbing a skin graft of more complex flap closure. STI

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AUTHORS' DISCLOSURES

Dr. Bohn is a Medical Consultant for Aroa Biosurgery Ltd (Auckland, New Zealand).

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