Review Article

Skin grafts in cutaneous oncology*
*Enxertia de pele em oncologia cutânea**

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Abstract: In cutaneous oncology, there are many situations in which skin grafts could be a good alternative for closing surgical defect. Dermatological surgeons should have enough knowledge about graft integration and contraction in order to not contradict the basic principles of skin transplantation. The authors review skin graft classification and physiology and make some surgical considerations on successful procedures.
Keywords: Skin neoplasms; Skin transplantation; Transplantation, homologous

Resumo: *Em oncologia cutânea depara-se freqüentemente com situações em que a confecção de um enxerto é uma boa alternativa para o fechamento do defeito cirúrgico. Conhecer aspectos referentes à integração e contração dos enxertos é fundamental para que os cirurgiões dermatológicos procedam de maneira a não contrariar princípios básicos do transplante de pele. Os autores fazem uma revisão da classificação e fisiologia dos enxertos de pele, acrescendo considerações cirúrgicas determinantes para o sucesso do procedimento.*
Palavras-chave: Neoplasias cutâneas; Transplante de pele; Transplante homólogo

INTRODUCTION

A skin graft is a patch of a live tissue that is transplanted from one area to another on the same or a different body.[1] Nevertheless, the use of the term skin graft to describe the surgical procedure, even though misleading, has become colloquial. The appropriate terms to describe the surgical procedure to transfer skin from one area to another, losing complete continuity with the donor area, are skin grafting or transplantation.

There are four different graft classifications. One is based on its histological composition. They are classified as simple/free when comprised of a single type of tissue and composite when composed of two or more types of tissue. In cutaneous oncology, a composite graft is used when the surgical defect to be covered requires more internal support as in the case of ear and nasal ala flap reconstructions.[2,3] In these

* Study promoted by the Graduate Course in Dermatology at the Dermatologia at UFRJ and carried out at the Hospital Geral de Bonsucesso, Hospital de Força Aérea do Galeão and Universidade Federal do Rio de Janeiro - (UFRJ) - Rio de Janeiro (RJ), Brazil.
Conflict of interests: None

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three-dimensional reconstructions, the auricular cartilage is included in order to improve the graft performance.

Depending on the donor source, grafts can also be classified as autologous, when the donor and recipient are the same individual; allogeneic or homologous when the donor and recipient are different but from the same species; and heterologous or xenografts, when the donor and recipient are from different species.[4,5] In dermatological practice, autografts are used more often since allografts and xenografts are temporary and only act as biological dressings to stimulate healing.[6,7]

A third classification is based on thickness. Full-thickness skin grafts contain epidermis and all the dermis including the adnexal structures. Split-thickness skin grafts contain epidermis and a portion of the dermis, and are further subdivided into thin, intermediate and thick, according to the amount of dermis included in the graft[8] (Table 1).

Lastly, skin grafts can be classified according to how they were processed. After harvesting, grafts can be processed to enlarge their size. This can be accomplished in the operating room using an expansor that transforms them into an expanded grid similar to a net (mesh grafts), or in a laboratory, using cell cultures. The cultivated keratinocytes can be autologous or allogeneic and can be applied with or without a dermal substitute.[9]

The clinical situation determines the type of graft to be used.

AUTOGRAFT PHYSIOLOGY

After skin grafting, the wound healing process is marked by two characteristic and sequential events.

A - Integration

The clinical characteristics of autologous graft integration are adherence, perfusion and viability of the transferred skin segment which depends exclusively on its vascularization.

During the first 24 hours after grafting, the plasma exuded from the recipient area is absorbed by the graft forming a fibrin mesh that attaches and nourishes the graft (plasmatic imbibition phase). Next, the anastomosis of small capillaries unites the graft surface with the recipient bed (inosculation phase). The attachment of the graft is still fragile and could be cyanotic. The emergence and proliferation of new vessels guarantees the survival of the transplanted skin. Actual blood flow occurs between the fifth and seventh postoperative day (revascularization phase).[4,5]

Yamagushi et al.[10] studied the involvement of a fourth phase, the keratinocyte activation phase in cutaneous graft healing. In an experimental study the activation of keratinocytes was evaluated by the Ki-67 cellular proliferation marker and cell-matrix adhesion by B1 integrin expression. The Ki-67 and B1 integrin expression was only observed in split-thickness grafts. Since they are thinner, they allow better imbibition in the initial grafting phase and require less blood supply from the adjacent bed. Nevertheless, keratinocyte activation could represent an additional factor to facilitate split-thickness graft integration in comparison to full-thickness grafts.

The preparation of the anesthetic solution used for skin grafting usually contains a vasoconstriction substance in varying concentrations. A 1:100,000 epinephrine anesthetic solution seems to slightly increase the risk of complications, such as partial graft loss and epidermal necrosis during the first week after grafting.11 The risk/benefit ratio related to the use of epinephrine should be evaluated on a case by case basis. In circumstances where the vascularization in the recipient bed is compromised or in smokers, the isolated use of lidocaine seems to be advantageous in reference to integration.

TABLE 1: Measurement table for split-thickness skin graft thicknesses. These references are useful for regulating the dermatome before graft harvesting

Graft thickness	Inches	Millimeters
Thin	0.005 to 0.012	0.12 to 0.30
Intermediate	0.012 to 0.018	0.30 to 0.45
Thick	0.018 to 0.030	0.45 to 0.76

B - Contraction

Once the graft is integrated to the recipient bed and after the 10th day, the action of contractible myofibroblasts and proteins promote graft contraction. This process could last for six months and jeopardize the cosmetic appearance.

Myofibroblasts (granulation tissue fibroblasts) develop biochemical and ultrastructural characteristics of smooth muscle cells including the presence of microfilaments and the alpha actine expression of smooth muscle. In addition to wound contraction, the synthesis of extracellular matrix components is attributed to the myofibroblasts.[12] The grafts can affect the myofibroblast population in the wound, depending on the percentage of dermis grafted. In thick grafts, lower proportions of myofibroblasts are found and the tissue contraction is less evident.[13]

Fibronectin, an anchoring element for the tem-

porary matrix, disappears when the collagen fibers are established. In full-thickness grafts, their intensity and distribution is less evident and they disappear earlier than in split-thickness grafts.[14] These observations reveal an association between the presence of fibronectin and myofibroblasts as well as myofibroblasts with graft contraction.

Stephenson et al.[15] conducted a study aiming to evaluate the assumption that the contraction of full-thickness human skin grafts is minimal. Until that time, the contraction of full-thickness grafts in humans had never been measured. The degree of contraction in fifty grafts was measured using photographs over a period of eight months. The parameters evaluated, such as age, graft donor area and initial size of the defect did not reveal any significant difference in regard to contraction. In case of infection, the contraction represented almost half of the initial area, whereas in the absence of infection the contraction of the graft/recipient bed represented one third of the initial area.

Yamagushi et al.[10] also evaluated contraction using grafts of different thicknesses in wounds with varying depths. Superficial wounds covered with full-thickness skin contracted more than those covered with split-thickness skin. Wounds that reach the muscular fascia, when covered with pure epidermis or a split-thickness skin graft presented greater contraction than those covered with full-thickness skin grafts. These results indicate the necessity to adjust the graft thickness to the depth of the wound.

SKIN GRAFTING AS A TEMPORARY DRESSING

The value of temporary wound coverage with fresh or stored cadaveric skin or even animal skin is recognized for large burns,[6] and can also be used successfully for dermatologic and reconstructive surgery.[7] Its application promotes wound occlusion, keeps the area moist and as a consequence accelerates granulation, neovascularization and healing. Since they are highly immunogenic, they are rejected after a few days.

When allogeneic skin is grafted it is revascularized for a short timeframe. The presence of donor antigens causes an immunological reaction.[16] Its rejection is indicated by vasodilation followed by sluggish circulation. Complete blood flow cessation occurs in the majority of viable human skin allografts within seven to ten days. It then becomes dry and spontaneously detaches from the implantation area.[1] The use of cadaveric allografts is safer and more economically viable than other temporary biological dressings such as porcine xenografts or amniotic membrane. They present quick adherence and less chance of antigenicity when compared to other alternatives.[17]

These temporary dressings are often used to prepare the wound bed for a permanent covering. For nonvascular areas, such as defects over bones and cartilage, these grafts dramatically increase the formation of granulation tissue increasing the integration possibilities of an autologous graft to be placed later.

Various studies demonstrate the safety of using cadaveric skin, excluding the risk of transmitting viable infectious agents.[18,19] To minimize the risk of transferring diseases, the skin banks follow protocols submitting the donor cadaver to a thorough serological analysis.

Another concern is bacterial contamination of the graft. A microbiological study conducted by Obeng et al.[17] involving the skin of 1112 donors, demonstrated a contamination rate of 4.9%. Despite the cleaning performed on the skin before harvesting with antiseptics and further skin incubation in a recipient with antibiotics, microbiological control of the grafts should be made routinely and when contamination of the material is detected, it should be disposed of.

In the dermatological practice, autografts are used more frequently owing to their efficacy, safety, low cost and ability to act as a permanent covering.

GRAFT SELECTION

Skin grafting is often used in reconstructions after the removal of malignant cutaneous neoplasms. Nevertheless, it is also indicated to substitute lost tissue as a result of burns and for covering chronic ulcers that do not heal. Other treatment indications include treatment of alopecia and vitiligo, where the transfer of mini grafts restore hair and pigmentation to the affected areas.

A - Full-thickness autologous grafts

We rarely encounter circumstances of surgical defects that are so extensive that coverage with full-thickness grafts is impossible. These grafts offer, in most cases, the best cosmetic results – hence, they are preferred in face reconstructions.

The selection of full-thickness grafts is not only based on the size of the recipient area. It is necessary to select a donor area that matches the color and texture of the recipient area, or in other words, the anatomical characteristics of the two areas should be as close as possible.

The recipient area should be well-vascularized. Good quality muscles, aponeurosis and granulation are desirable. The subcutaneous, as it is a poorly vascularized tissue, should be removed from the recipient bed. Residual fat on the inner face of the graft should also be eliminated using scissors

before grafting.

The partial closing of large surgical defects, preferably in the cosmetic facilities, reduces the size of the graft required to cover the remaining part of the wound.[20] In circular defects, a suture placed at the edge of the defect – purse string suture – reduces its size. The surrounding skin becomes wrinkled however this does not jeopardize graft adherence.[21]

B - Split-thickness autologous grafts

The greatest advantage of split-thickness skin grafting is the larger availability of donor areas since they repair spontaneously. They are harvested using a dermatome or Blair knife that can be regulated in order to obtain the desired thickness even though thickness irregularities could occur depending on the operator's steadiness during the procedure. Lubrication of the donor area with mineral oil before harvesting facilitates the movements of the dermatome.[22]

When selecting the donor area, preference should be given to areas normally covered by clothing, since differences in thickness and/or pigmentation are common. The rapid re-epithelialization in the donor area occurs since the cutaneous appendages are preserved. On the other hand, there is no regrowth of hair on the grafted area which can cause contrasts when the neighboring graft region presents developed hair. Full-thickness grafting can present the opposite effect, that is, hair begins to grow in glabrous areas.

Donor areas for split-thickness grafts should be kept moist. The moist environment promotes and stimulates the synthesis of cellular growth factors. Likewise, epithelial migration becomes easier.[23] Other advantages of occlusive dressings include less pain and a lower risk of infection. Reduced inflammation is also observed and leads to less fibrosis and therefore better final healing results.[24] Among the auxiliary healing resources that produce good results, semi-occlusive adhesive films made from a layer of transparent polyurethane produce good results.[25]

For extensive lesions, enlarged skin grafts can be used where the graft is transformed into a type of mesh that enables its expansion. The expansion index results vary from 3:1 to 9:1. The open area of the mesh can cause poor cosmetic and functional results as heals by second intention.[26,27] These grafts tend to present greater secondary contraction and are indicated in selected cases. Consideration of this method is worthwhile in case of large burns; however its use is very limited in cutaneous oncology surgery.

C - Cultivated keratinocyte grafts

The first successful keratinocyte cultivation experiences took place more than 25 years ago. In 1979, Green et al. demonstrated that a great amount of cultivated epithelium could be produced from a small fragment of epidermis in a short timeframe, making it possible to use epithelial cell cultures to restore epidermal defects in the same individual.[28]

The cultivated keratinocyte autograft has been commercially available since 1988 (Epicel®). However, it requires a skin biopsy from the patient and an interval of two to three weeks to expand the keratinocytes to the diameter required to cover the desired area.

Epithelial culture slides do not present good integration when applied directly over bloody, irregular skin surface areas with no dermis. The isolated use of epidermis should be restricted to bloody areas that contain dermis. Good integration occurs over the dermal surface of split-thickness donor areas, promoting rapid epithelialization as well as eliminating pain and wound exudation.[29]

Cultivation and grafting of allogeneic keratinocytes can only be used to stimulate healing. They act as a temporary dressing that is gradually replaced by epithelium of the host.[30]

Blight et al.[31] studied the effect of allogeneic keratinocyte grafts in split-thickness skin graft donor areas in patients aged over 60 years. These cells are not incorporated in the wound but produce factors that stimulate the remaining autologous cells to proliferate. It may seem inappropriate to graft an area that was just used as a donor area, but elderly patients with known healing difficulties benefit from this technique.

SURGICAL CONSIDERATIONS

In cutaneous oncology, skin grafting should be considered in the case of wounds whose size makes flap and primary closure impossible. In regions with limited skin elasticity, such as the nose and distal leg, covering even small defects with a graft is recommended.

Familiarity with the distinct physiology of skin grafting is mandatory in order to not contradict the basic principles. As in any surgery, adequate planning of the steps before, during and after the surgery is the key to a successful procedure.

Often, attention is directed to the graft recipient area, underestimating the importance of selecting an adequate donor area. The donor area, as mentioned earlier, should match the skin adjacent to the recipient area. However, other considerations are pertinent. The donor area should be free

from preneoplastic lesions – very common in patients that have already presented a malignant cutaneous neoplasia/skin tumor/malignancy. When a donor area close to the lesion is selected, the area may require treatment with either 5-fluoracil or imiquimod before the graft is harvested, to minimize the risk of early onset of a new tumor in the operated area that could lead to a false impression of relapse.[32] On the other hand, this treatment involves additional costs and delays the surgical procedure. The selection of a covered donor area, free from lesions, is the usual alternative and even though it may not be as cosmetically pleasing, it is safer (Figures 1 and 2).

Another important observation before graft harvesting refers to the closure of the defect to be created. Part of the surgical planning involves thorough analysis of the skin elasticity, in order to eliminate excessive tension on the suture and all consequent morbidity arising from the use of this bad technique. Although rare, the unpleasant situation of having to harvest a second graft to close the donor area is possible.

The upper eyelid is a donor site that does not usually receive much attention or clinical use. Facial surgical defect reconstruction using eyelid grafts demonstrated contraction rates of less than 8%.[33] It is possible that the large amount of elastic fibers in the eyelid is responsible for this low contraction percentage. One disadvantage associated with its use, is the insufficient thickness to cover deep defects. The patient's age is also a limiting factor.

The recipient area also should be analyzed and prepared, to verify whether it has sufficient vascularization to nourish the graft. Grafting over bones with

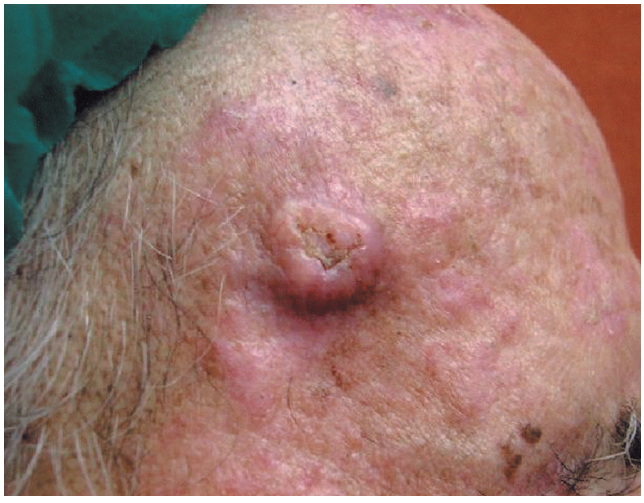

Figure 1: Actinic keratosis adjacent to a tumor making flap preparation unviable

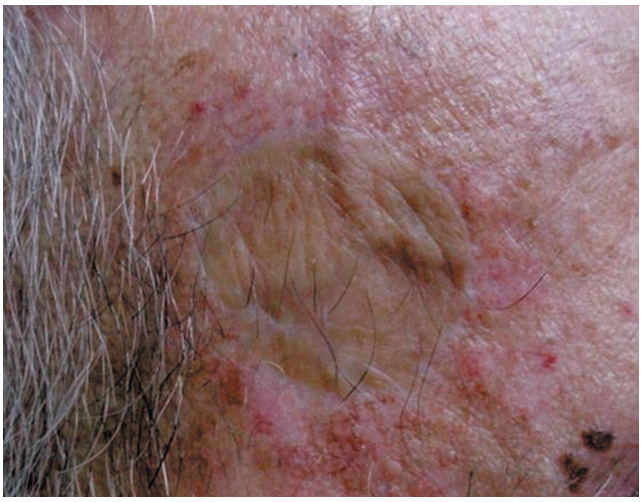

Figure 2: Grafting of healthy skin associated with topical 5-fluoracil treatment of preneoplastic lesions

no periosteum, cartilage with no perichondrium and directly over adipose tissue should be avoided. The recipient bed cannot be bleeding, should have an even surface and the lowest possible number of cauterized areas.

Blood supply to the legs is usually poor, particularly in elderly people. Even split-thickness grafts placed immediately after surgical tumor removal are frequently unsuccessful. Delaying the grafting procedure is particularly useful in this region. The presence of granulation tissue makes the bed more receptive for graft placement with the additional advantages of reduced defect depth and possibility of seroma or hematoma formation.[34]

According to the inherent physiology of graft integration, revascularization occurs between the fourth and fifth postoperative day. Therefore, intimate contact and immobility between the graft and the recipient bed for a minimum period of five days is essential. To ensure this, a special type of dressing is used: an even number of sutures with the same orientation that are long enough to tie something over the graft to apply pressure to the wound bed. The mould placed over the wound could be adequately wrapped moistened gauze or a surgical sponge.[35,36] A second layer of gauze secured with adhesive tape ensures graft immobility.

Fibrin glue and flexible synthetic tissue adhesives can be used to secure the grafts. They promote immediate hemostasis, good graft adherence to the wound bed and reduced surgical time.[37] They are particularly useful in areas where graft attachment is difficult such as axilla, perineum and gluteal creases.[38] They eliminate the need for sutures or compressive dressings immediately following surgery.[39]

The initial dressing should be left in place for

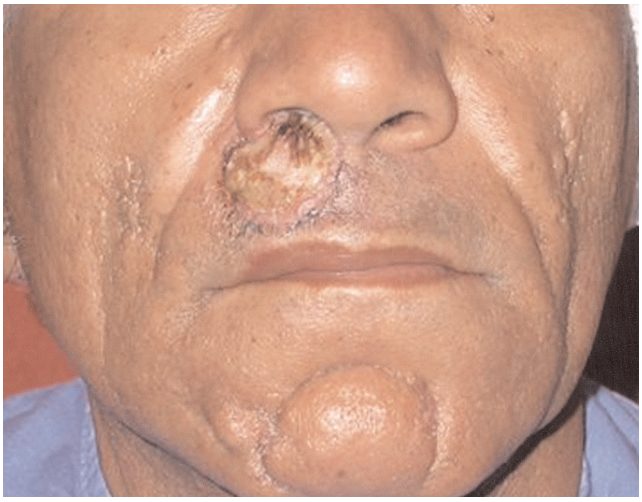

Figure 3: Grafting performed in a risk area, close to the free margin, which developed infection

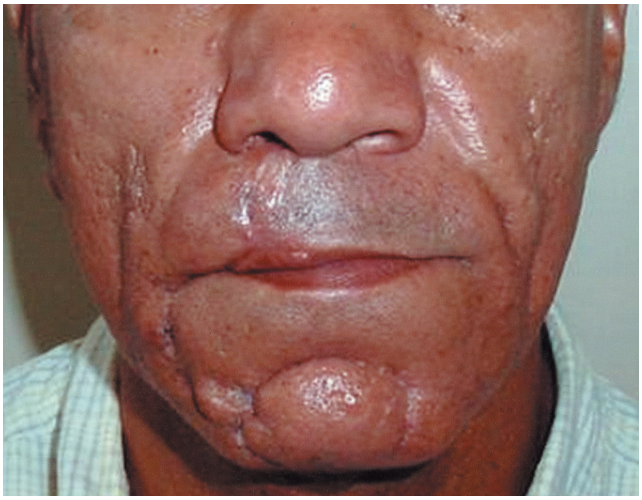

Figure 5: Final result after lip retraction correction

five to seven days, unless there is secretion or erythema along the edges, indicating infection. When infection is suspected the dressing should be removed to assess whether the necrotic areas require debridement or if the accumulated secretions require draining. After this initial timeframe, the region can be cleansed on a daily basis and covered with a light dressing.

Once the graft integration is guaranteed, the concern is its contraction. When control measures are taken, this phase becomes safer. The application of a graft slightly larger than the defect reduces contraction.[15] The presence of infection completely modifies skin graft behavior. The presence of infection should be monitored and if it occurs, early control is essential. It is wise to evaluate the benefits of antibiotic therapy on a case by case basis even when dealing with a clean surgery.

It is standard to not perform grafting close to free margins so that contraction does not promote lip or eyelid retraction. Another rule is to avoid grafting in depressions such as the neck and axillae, since contraction in these areas could reduce movement range (Figures 3, 4 and 5).

CONCLUSION

According to graft physiology, chronologically the first complication expected would be non-integration and the second, more feared, excessive contraction with tissue distortion. Whenever possible, planning and performance of the surgical team should minimize the possibility of such complications. ❑

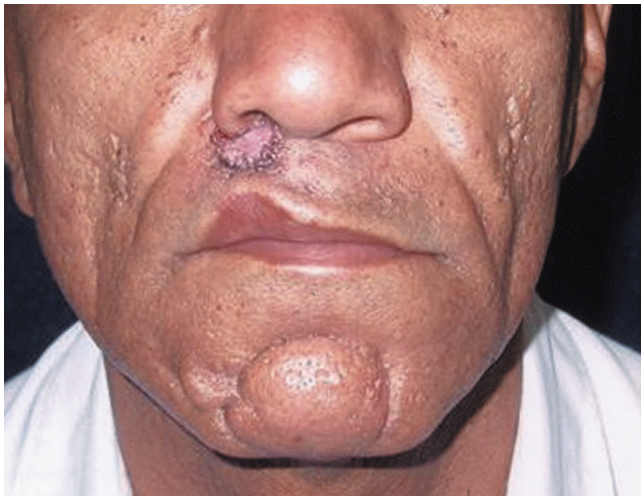

Figure 4: Excessive contraction resulting from infection followed by graft loss causing lip retraction

REFERENCES

1. Andrew B, Lam PK, Lau H. Allogenic skin: transplant or dressing? Burns. 2002;28:358-66.
2. Chang JS, Becker SS, Park SS. Nasal reconstruction: the state of the art. Curr Opin Otolaryngol Head Neck Surg. 2004;12:336-43.
3. Keck T, Lindemann J, Kuhnemann S, Sigg O. Healing of composite chondrocutaneous auricular grafts covered by skin flaps in nasal reconstructive surgery. Laryngoscope. 2003;113:248-53.
4. Franco D, Cláudio-da-Silva CS. Enxertos, retalhos e implantes. In: Franco T. Princípios de cirurgia plástica. São Paulo: Ateneu; 2002. p.87-106.
5. Golcman B, Golcman R. Principais tipos e indicações de enxertos. In: Gadelha AR, Costa IM, editores. Cirurgia dermatológica em consultório. São Paulo: Atheneu; 2002. p.285-91.
6. Kreis RW, Hoekstra MJ, Mackie DP, Vloemans AF, Hermans RP. Historical appraisal of the use of skin allografts in the treatment of extensive full skin thickness burns at the Red Cross Hospital Burns Centre, Beverwijk, The Netherlands. Burns. 1992;18(Suppl 2): S19-22.
7. Davis DA, Arpey CJ. Porcine heterografts in dermatologic surgery and reconstruction. Dermatol Surg. 2000;26:76-80.
8. Ratner D. Skin Grafting: from here to there. Dermatol Clin. 1998;16:75-90.
9. Trent JT, Kirsner RS. Skin grafting. In: Nouri K, Leal-khouri S, editors. Técnicas em Cirurgia Dermatológica. Rio de Janeiro: Di-Livros; 2005. p.153-62.
10. Yamagushi Y, Hosokawa K, Kawai K, Inoue K, Mizuno K, Takagi S, et al. Involvement of Keratinocyte activation phase in cutaneous graft healing: Comparison of full-thickness and split-thickness skin Grafts. Dermatol Surg. 2000;26:463-8.
11. Fazio MJ, Zitelli JA. Clinical observation on the impact of using epinephrine in local anesthesia of the donor site. Arch Dermatol. 1995;131:691-4.
12. Lorena D, Uchio K, Costa AMA, Desmouliere A. Normal scarring: importance of myofibroblasts. Wound Repair Regen. 2002;10:86-92.
13. Rudolph R. Inhibition of myofibroblasts by skin grafts. Plast Reconstr Surg. 1979;63:473.
14. Vande Berg JS, Rudolph R. Immunohistochemistry of fibronectin and actin in ungrafted wounds and wounds covered with full- and split-thickness skin grafts. Plast Reconstr Surg. 1993;91:684-92.
15. Stephenson AJ, Griffiths WR, La Hausse-Brown TP. Patterns of contraction in human full thickness skin grafts. Br J Plast Surg. 2000;53:397-402.
16. Lee KH. Tissue-engineered human living skin substitutes: development and clinical application. Yonsei Med J. 2000;41:774-9.
17. Obeng MD, McCauley RL, Barnett JR, Heggers JP, Sheridan K, Schutzler SS. Cadaveric allograft discards as a result of positive skin cultures. Burns. 2001;27:267-71.
18. Laurence JC. Allografts as vectors of infection. Lancet. 1987;1:1318.
19. Kealey GP. Disease transmission by means of allograft. J Burn Care Rehabil. 1997;18:10-1.
20. Kaufman AJ. Adjacent-tissueskin grafts for reconstruction. Dermatol Surg. 2004;30:1349-53.
21. Hill TG. Contouring of donor skin in full-thickness skin grafting. J Dermatol Surg Oncol. 1987;13:883-8.
22. Sams HH, McDonald MA, Stasko T. Useful adjuncts to harvest split-thickness skin grafts. Dermatol Surg. 2004;301:591-2.
23. Katz MH, Alvarez AF, Kirsner RS, Eaglstein WH, Falanga V. Human wound fluid from acute wounds stimulates fibroblast and endothelial cell growth. J Am Acad Dermatol. 1991;25:1054-8.
24. Eaglstein WH. Moist wound healing with occlusive dressings: a clinical focus. Dermatol Surg. 2001;27:175-81.
25. Mandelbaum SH, Di Santis EP, Mandelbaum MHS. Cicatrização: conceitos atuais e recursos auxiliares - Parte II. An Bras Dermatol. 2003;78:525-40.
26. Waymack P, Duff RG, Sabolinski M. The effect of a tissue engineered bilayered living skin analg, over meshed split-thickness autografts on the healing of excised burn wounds. Burns. 2000;26:609-19.
27. Davison PM, Batchelor AG, Lewis-Smith PA. The properties and uses of non-expanded machine-meshed skin grafts. Br J Plast Surg. 1986;39:462-8.
28. Green H, Kehinde O, Thomas J. Growth of cultured human epidermal cells into multiple epithelia suitable for grafting. Proc Natl Acad Sci USA. 1979;76:5665-8.
29. Franco T, Branco PS, Franco D, Gonçalves LF, Borojevic R. Enxerto autólogo de epiderme cultivada. Rev Soc Bras Cir Plast. 2000;15:63-78.
30. Phillips TJ, Kehinde O, Green H, Gilchrest BA. Treatment of skin ulcers with epidermal allografts. J Am Acad Dermatol. 1989;21:191-9.
31. Blight A, Fatah F, Datubo-Brown D, Mountford M, Cheshire LM. The treatment of donor sites with culture epithelial grafts. Br J Plast Surg. 1991;44:12-4.
32. Persaud AN, Shamuelova E, Sherer D, Lou W, Singer G, Cervera C, et al. Clinical effect of imiquimod 5% cream in the treatment of actinic keratosis. J Am Acad Dermatol. 2002;47:553-6.
33. Tuncali D, Ates L, Aslan G. Upper eyelid full-thickness skin graft in facial recontruction. Dermatol Surg. 2005;31:65-70.
34. Coldiron BM, Rivera E. Dalayed full-thickness grafting of lower leg defects following removal of skin malignancies. Dermatol Surg. 1996;22:23-6.
35. Dunst KM, Huemer GM, Zelger B. Wet cotton as a dressing for split-thickness skin grafts. Dermatol Surg. 2004;30:477-8.
36. Zanini M, Machado Filho CDS, Timoner F. Uso de esponja cirúrgica para curativo compressivo de enxerto cutâneo. An Bras Dermatol. 2004;79:359-62.
37. De Moraes AM, Annichino-Bizzacchi JM, Rossi AB. Use of autologous fibrin glue in dermatologic surgery: application of skin graft and second intention healing. Sao Paulo Med J. 1998;116:1747-52.

38. Vedung S, Hedlung A. Fibrin glue: its use for skin grafting of contaminated burn wounds in areas difficult to immobilize. J Burn Care Rehabil. 1993;14:356-8.
39. Saltz R, Dimick A, Harris C, Grotting JC, Psillakis J, Vasconez LO. Application of autologous fibrin glue in burn wounds. J Burn Care Rehabil. 1989;10:504-7.

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