Decellularized Dermal Grafting in Cleft Palate Repair

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Objective: To assess the efficacy of decellularized dermal grafting used as an adjunct to the performance of primary repair of wide cleft palates.

Design: Retrospective review.

Setting: Tertiary referral center for large managed care organization.

Methods: Seven consecutive patients with clefts of the hard and soft palates wider than 15 mm as measured at the posterior edge of the hard palate. Palates were repaired in the standard 2-flap approach with intravelar veloplasty. The decellularized dermal graft (AlloDerm) was applied immediately deep to the oral mucosal closure. Patients were followed up with serial postoperative examination. Palates were assessed for dehiscence, fistula, infection, rejection, scarring, and contracture.

Results: There were no fistulas. In 2 patients, the oral mucosa dehisced, exposing the dermal graft. In 2 other cases, nasal mucosal tears were inadvertently created during closure of the nasal layer. In all cases, the decellularized dermal graft mucosalized and, by clinical examination, became incorporated into the wound. There were no cases of local inflammation or infection. The degree of scarring and contracture was indistinguishable from the adjacent scar.

Conclusions: Decellularized dermal graft is safe and effective for use in primary closure of wide clefts involving the hard and soft palates. Its application to wide clefts otherwise at risk of fistula is justified. Its use in repair of an existing fistula is also promising.

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The management of patients with cleft palate has improved significantly over the past 20 years. Important surgical advances have accompanied a multidisciplinary approach to patient care. Technical innovations have become focused on improving functional results. Despite this, however, palatal fistulas remain a challenge. Reports of the incidence of postoperative fistula following palate repair range from 11% to 23%. The site most likely to fistulize is at the junction of the hard and soft palates. A defect at this location is frequently associated with hypernasality of speech, depending on its size. Nasal exposure to oral contents and food trapping may be seen as well.

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The importance of fistula prevention is highlighted by the difficulty in attempts at repair. Due to fibrosis and poor vascularity of adjacent tissues, high recurrence rates are typical. Closure of wider clefts is particularly tenuous at the hard palate–soft palate junction. Despite wide undermining of palatal flaps and skeletonization of the greater palatine pedicle, this site represents the area of least mobility and greatest tension. These factors, compounded by the atrophic nature of the mucosa, the inadequate muscular layer centrally at the hard palate–soft palate junction, and the constant motion of the soft palate against the hard palate, further challenge successful closure.

Beyond the issue of fistulization, theoretical concerns relate to scar formation and wound contraction. Closure techniques that cause tension at the level of the soft palate may ultimately lead to contracture-related shortening of the palate and worse functional outcomes.

Techniques have been advocated to gain tissue for closure in this area, including hamulus fracture and distal dissection of the vascular pedicle. These techniques, however, may only provide 1 to 2 mm of additional length. For larger de-
fects, local flaps may be used. The buccal fat pad flap,4
buccinator musculomucosal flap,5 and tongue flaps6 have
been advocated. These flaps, however, can be bulky and
usually require a second-stage procedure. They are gen-
erally reserved for use once a fistula has occurred.

An ideal approach would use readily available tis-
sue, prevent scarring and contracture, and be associated
with a low incidence of complications. In the present
study, we retrospectively reviewed patients who under-
grew repair of wide cleft palates (Figure 1) using de-
cellularized dermal allograft (AlloDerm; LifeCell Cor-
novation, Branchburg, NJ).

METHODS

SUBJECTS

The first case that led to the use of the decellularized dermal
graft was a patient with an 18-mm-wide unilateral cleft palate
(Table). The palate was repaired using a 2-flap palatoplasty
technique. At 1 week postoperatively a fistula was noted at the
hard palate–soft palate junction. The senior author (J.M.I.) de-
cided to use decellularized dergraft on the subsequent fis-
tula repair, which healed after exposure of the decellularized
dermal graft on the oral side, noted at the 1-week postopera-
tive clinic visit. The oral mucosa was completely healed at the
1-month postoperative clinic visit. From then on, it was de-
cided that repairs of palatal clefts measuring 15 mm and greater
would use decellularized dergrafting adjunctively to re-
duce the risk of primary fistulization.

Consecutive patients undergoing repair of combined hard
and soft cleft palates were then reviewed. Patients whose pala-
tal defects were less than 15 mm were treated with standard
2-flap palatoplasty with intravelar veloplasty using previously
described techniques to allow for a tension-free closure. Pa-
ients whose defect equaled or exceeded 15 mm were treated
using a decellularized dergraft, and are included for re-
view. The width of the palatal defect was measured at the pos-
terior margin of the hard palate, at its junction with the soft
palate (Figure 2). The age range for surgery on cleft palates
in our clinic is 12 to 18 months. The first patient in the series
(Table) had Down syndrome and was not medically stable for
surgery until 20 months of age. Another child came to our clinic
with an unrepaired cleft at 24 months of age.

TECHNIQUE

AlloDerm is prepared as follows: fresh cadaveric skin is ob-
tained from an approved tissue bank. The donors of the sup-
plied skin have been screened serologically for hepatitis B and
C viruses, human immunodeficiency virus, human T-
lymphotropic virus, and syphilis. The skin is incubated over-
night in a salt solution to release the epidermis. The dermal
tissue is then treated with a detergent to free it of all remain-
ing cellular elements. The resulting product is then cryop-
ected and freeze-dried.

Decellularized dergraft was incorporated into palatal
closure in the following manner: full-thickness flaps were raised
from the palatal shelves. Nasal mucosal flaps were raised as well.
At the level of the soft palate, oral mucosal flaps were dis-
sected from the muscular layer. The nasal mucosa was closed
(Figure 3). Next, the muscular layer was apposed, after free-
ing it from its attachment to the posterior edge of the hard pal-
ate. The oral mucosal flaps were then inspected. After rehy-
dratation with 2 consecutive saline baths, a piece of decellular-
dized dergraft was cut to size, secured to the muscular bed pos-
teriorly, and draped over the posterior aspect of the hard pal-
ate anteriorly (Figure 4). The decellularized dergraft was posi-
tioned such that the basement membrane complex was ori-
ented toward the side of greatest tension (Figure 5). The oral
mucosa was then closed over the dergraft (Figure 6). In the
cases where excess tension on the oral mucosa was noted,
it was believed that a gap of 1 to 2 mm could be left at time of
closure with less concern for fistulization.

FOLLOW-UP

The surgical sites were followed closely postoperatively, at 10
days, 4 weeks, 3 months, 6 months, and 1 year. Evaluation was
made for the presence of inflammation, infection, dehiscence,
fistula, scarring, and wound contraction. Family members were
queried for evidence of leakage of oral contents into the nose.

RESULTS

All patients were found to heal without fistulization. There
were 2 patients whose oral mucosal closure dehisced. At
such a point, the decellularized dergraft was visible
within the wound. In these cases, at postoperative day
10, the graft appeared pale and without obvious vascu-
larity. Continued observation, however, demonstrated
mucosalization of the graft, and by 4 weeks' follow-up,
the wound was visibly indistinguishable from the adja-
cent palatal closure. There were 2 additional known cases
of nasal mucosal dehiscence. It is presumed that the ex-
posed decellularized dergraft (to the nasal cavity) re-
mucosalized, similar to that observed in the patients with
dehiscences on the oral side.

It has been suggested that fibroblasts within a dergal
autograft may function as pluripotential cells ca-
ble of generating epithelium of a dergal origin. The
pattern observed in the palatal repairs with decellular-
dized dergraft, however, was of peripheral ingrowth.
The palates healed without evidence of contracture or

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palatal shortening. Over time, there were no identified functional difficulties relating to length or pliability of the palate.

**COMMENT**

AlloDerm is a cadaveric dermal graft. Its processing involves deepithelialization and dermal decellularization to produce a completely acellular dermal matrix. It is believed to act as a scaffold for migration of host fibroblasts and retains its basement membrane complex to facilitate attachment of surface epithelium.

Decellularized dermal graft was developed for use in treatment of full-thickness burns. Usual management of these burn patients is made difficult by a lack of donor skin as well as the extensive scarring seen after split-thickness skin grafts. Initially in a porcine model and then as applied to humans, the decellularized dermis was ap-

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**Patient Summary**

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Date of Surgery</th>
<th>Age at Repair, mo</th>
<th>Type of Cleft</th>
<th>Width of Cleft, mm</th>
<th>Comments</th>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>8/6/99</td>
<td>20</td>
<td>Unilateral CL/P</td>
<td>18</td>
<td>Postoperative dehiscence of repair; this was the case that led to use of AlloDerm*</td>
</tr>
<tr>
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<td>1/13/00</td>
<td>25</td>
<td>Unilateral CL/P</td>
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<td>Fistula repair; postoperative dehiscence of oral side with AlloDerm exposure; 100% closure</td>
</tr>
<tr>
<td>2</td>
<td>1/13/00</td>
<td>16</td>
<td>Cleft sec palate</td>
<td>20</td>
<td>Postoperative dehiscence of oral side with AlloDerm exposure; 100% closure</td>
</tr>
<tr>
<td>3</td>
<td>5/5/00</td>
<td>24</td>
<td>Unilateral CL/P</td>
<td>18</td>
<td>100% Closure</td>
</tr>
<tr>
<td>4</td>
<td>7/6/00</td>
<td>13</td>
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<td>100% Closure</td>
</tr>
<tr>
<td>5</td>
<td>7/13/00</td>
<td>15</td>
<td>Bilateral CL/P</td>
<td>17</td>
<td>Nasal side perforation at time of repair; 100% closure</td>
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<tr>
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<td>15</td>
<td>100% Closure</td>
</tr>
<tr>
<td>7</td>
<td>12/7/00</td>
<td>15</td>
<td>Cleft sec palate</td>
<td>15</td>
<td>Nasal side perforation at time of repair; 100% closure</td>
</tr>
</tbody>
</table>

Abbreviations: CL/P, cleft lip and palate; sec, secondary.

*AlloDerm is the trade name for decellularized dermal allograft manufactured by LifeCell Corporation, Branchburg, NJ.

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**Figure 2.** Intraoperative photograph demonstrating the measurement of a wide (15 mm) cleft (patient 7, see Table).

**Figure 3.** Intraoperative photograph. After releasing the flaps, the nasopharyngeal mucosa was under significant tension. A rent in the mucosa is seen to the patient’s left side of the closure adjacent to the medial edge of the hard palate, distal to the vomer flap.

**Figure 4.** Intraoperative photograph demonstrating measurement of the decellularized dermal graft (AlloDerm) to overlap the dehiscence.

**Figure 5.** Intraoperative photograph. After the decellularized dermal graft (AlloDerm) is sutured into place, blood can be seen adhering to the dermal side of the graft.
plied to a full-thickness defect and an ultrathin split-thickness skin graft overlaid. It was found that epithelial ingrowth occurred from the skin graft as well as from the peripheral skin. The retained basement membrane complex is thought to provide the requisite adhesion molecules, particularly laminin and type IV collagen, necessary for epithelialization. The processing of the allogenic graft results in a framework that retains normal collagen organization as well as acellular vascular channels. These conduits have been shown to become rapidly repopulated by the host, and by day 7 after implantation, the endothelium is restored. The collagen scaffold initially contains empty spaces vacated by donor fibroblasts. These spaces can also be seen to repopulate with host fibroblasts over time. This process results in the matrix being turned over and incorporated into the host tissue. By 4 weeks after implantation the graft is unidentifiable as a discrete entity.

The processing of the allograft is critical in preventing immunologic rejection. Use of cellular dermal allografts in burns is limited to use as a temporary dressing. This tissue has an excellent take rate, but, is routinely rejected. This is a cellular mediated immune response and the foreign antigens thought to be responsible are major histocompatibility molecules on keratinocytes, melanocytes, Langerhans cells, and dendritic cells. Immuneologic reaction to endothelium is thought to lead to vascular occlusion, ischemia, and eventual sloughing that characterizes graft rejection. By decellularizing the allograft, an immunologically inert biologic implant is generated. Experimental studies have shown no induction of a specific immune response and only minimal local inflammation. AlloDerm has been used clinically since 1996 in the management of burn patients and has been found to be without rejection problems.

One of the benefits of decellularized dermal graft is its resistance to contraction. Split-thickness skin grafts are ideally limited to applications where significant wound contraction poses no negative functional or cosmetic sequelae. Full-thickness autografts have been shown to be relatively resistant to wound contraction, but donor site morbidity and availability limit their use. A comparison of decellularized to a cellular dermal graft showed significantly less wound contraction and improved cosmetic results with the processed graft. By avoiding tension at closure, less scarring and contracture may be seen at the hard palate–soft palate junction. This could lead to better long-term palate lengthening and improved function.

These findings have led to the use of decellularized dermal grafting in a variety of aesthetic and reconstructive challenges. It has been used successfully for aesthetic facial augmentation, sepal perforations, tympanoplasty, intraoral reconstruction, oculoplastic surgery, and dural repair, and is being explored for use in intra-abdominal applications.

The clinical findings in our small series of patients bear out the early experimental data. The decellularized dermal graft provides a framework for revascularization and mucosal reepithelialization without the expense of donor site morbidity or immunologic rejection. All patients in our series healed without adverse functional sequelae, including fistula formation or tethering of the palate by excessive scarring (Figure 7).

In the years of running our Cleft Palate Clinic since 1985 the fistula rate has been 5% to 6%. Almost all of the fistulas were in palatal clefts greater than 15 mm. This study came out of a difficult re-do case with concern for another fistula after second repair. Decellularized dermal grafting was used as it made sense based on its prior use for the correction of nasal septal perforations. Indeed, in this first case (second surgery) there was a 2-mm gap in the oral mucosa that surely would have again fis-
Decellularized dermal allograft matrix was used successfully to close wide defects involving the hard and soft palates. Closure of large palatal cleft defects may be associated with postoperative fistulization; however, this problem was not seen with this technique. There were no incidences of implant rejection or excessive scarring. The use of decellularized dermal graft also holds promise in the repair of existing palatal fistulas. Although not investigated in this study, there is also potential for improved functional results.

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REFERENCES