Clinical applications of acellular dermal matrices: A review

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Abstract

Introduction: The extracellular matrix (ECM) plays an integral role in wound healing. It provides both structure and growth factors that allow for the organised cell proliferation. Large or complex tissue defects may compromise host ECM, creating an environment that is unfavourable for the recovery of anatomical function and appearance. Acellular dermal matrices (ADMs) have been developed from a variety of sources, including human (HADM), porcine (PADM) and bovine (BADM), with multiple different processing protocols. The objective of this report is to provide an overview of current literature assessing the clinical utility of ADMs across a broad spectrum of applications.

Methods: PubMed, MEDLINE, EMBASE, Scopus, Cochrane and Web of Science were searched using keywords 'acellular dermal matrix', 'acellular dermal matrices' and brand names for commercially available ADMs. Our search was limited to English language articles published from 1999 to 2020 and focused on clinical data.

Results: A total of 2443 records underwent screening. After removing non-clinical studies and correspondence, 222 were assessed for eligibility. Of these, 170 were included in our synthesis of the literature. While the earliest ADMs were used in severe burn injuries, usage has expanded to a number of surgical subspecialties and procedures, including orthopaedic surgery (e.g. tendon and ligament reconstructions), otolaryngology, oral surgery (e.g. treating gingival recession), abdominal wall surgery (e.g. hernia repair), plastic surgery (e.g. breast reconstruction and penile augmentation), and chronic wounds (e.g. diabetic ulcers).

Conclusion: Our understanding of ADM's clinical utility continues to evolve. More research is needed to determine which ADM has the best outcomes for each clinical scenario.

Keywords

Acellular dermal matrix, complex wound, soft-tissue defects, wound closure, wound healing, breast reconstruction, hernia repair, skin substitute

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Lay Summary

Large or complex wounds present unique reconstructive and healing challenges. In normal healing, the extracellular matrix (ECM) provides both structural and growth factors that allow tissue to regenerate in an organised fashion to close the wound. In difficult or large soft-tissue defects, however, the ECM is often compromised. Acellular dermal matrix (ADM) products have been developed to mimic the benefits of host ECM, allowing for improved outcomes in a variety of clinical scenarios. This review summarises the current clinical evidence regarding commercially available ADMs in a wide variety of clinical contexts.

Introduction

Historically, large and/or complex soft-tissue defects have been treated with techniques including full and split-thickness skin grafts (FTSG and STSG), local flap coverage and free tissue transfer. Each of these has disadvantages such as donor site morbidity, risk of flap/graft complications or even failure.[1] In some cases, such as excessive wound depth or specialised function of tissue needing repair, patient and/or wound characteristics may preclude the use of traditional techniques for soft-tissue coverage.[1]

Successful wound healing depends largely on the interactions of proliferating cells with the extracellular matrix (ECM) in a process known as dynamic reciprocity.[2] The ECM—composed of proteoglycans, hyaluronic acid, collagen and elastin—directs tissue regeneration and differentiation via mechanical cues and signalling molecules.[2] In traumatic or chronic wounds, the ECM is often damaged to the extent that it no longer adequately supports healing. Acellular dermal matrices (ADMs) were developed in an attempt to capitalise on the properties of native ECM and promote organised regeneration of host tissue in a wide variety of clinical contexts.[2]

When ADMs are placed, host cells are incorporated into the matrix and directed by preserved growth factors and mechanical cues in the matrix structure.[2,3] A variety of cells invade the ADM, including fibroblasts, myofibroblasts, lymphocytes, macrophages, granulocytes, mast cells and others.[3,4] After inflammatory cell infiltration, the matrix undergoes remodelling, collagen and elastin levels increase, and revascularisation is initiated.[3,5–7] Lymphangiogenesis is possible, but is slower.[3] Essentially, the ADM acts as a scaffold to promote host tissue growth.[1]

ADMs were initially used to treat burn wounds in the 1990s and have since become a valuable addition to reconstructive algorithms as they are available off the shelf and have superior biocompatibility compared to synthetic soft-tissue grafts.[8,9] All ADMs are decellularised and antigenic components have been removed to prevent immune rejection[4] (Figure 1).
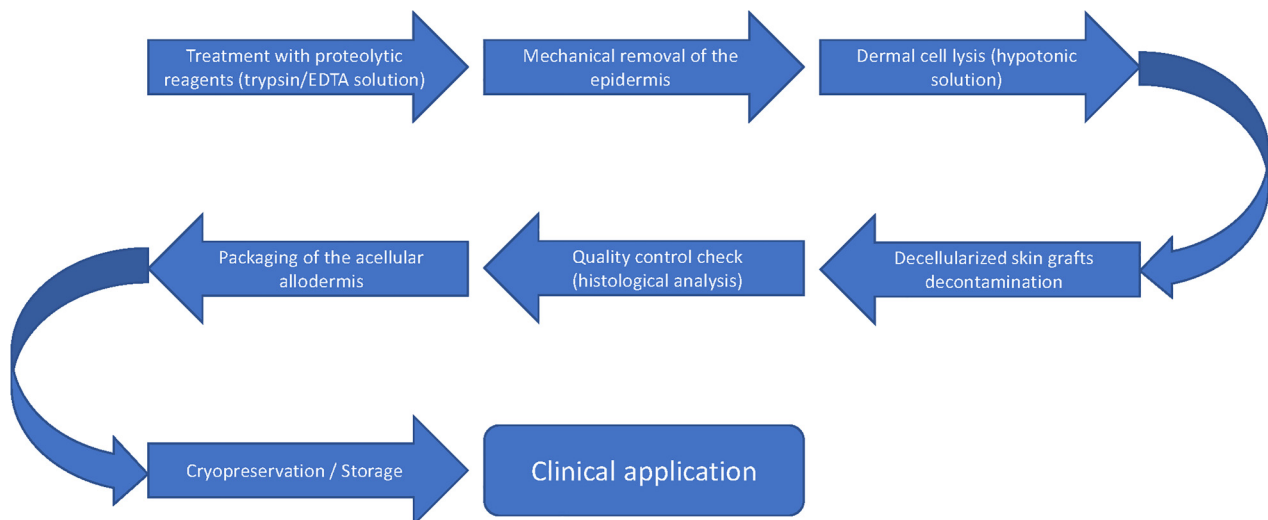

Figure 1. Schematic representation of ADM preparation. ADM, acellular dermal matrix.

Table 1. Common commercially available ADMs.

Product	Description
AlloDerm® (LifeCell Corp., Bridgewater, NJ, USA)	Human, non-cross-linked
AlloMax® (CR Bard/Davol Inc., Cranston, RI, USA)	Human, non-cross-linked
DermACELL® (LifeNet Health Inc., Virginia Beach, VA, USA)	Human, non-cross-linked
FlexHD® (Ethicon, Inc., Somerville, NJ, USA)	Human, non-cross-linked
Cortiva® (RTI Surgical, Alachua, FL, USA)	Human, non-cross-linked
Integra™ (Integra Life Sciences, Princeton, NJ, USA)	Bovine, cross-linked
MatriDerm® (Dr Suwelack AG, Billerbeck, Germany)	Bovine, non-cross-linked
SurgiMend® (Integra Life Sciences, Princeton, NJ, USA)	Bovine, non-cross-linked
Strattice® (Allergan, Madison, NJ, USA)	Porcine, non-cross-linked
Permacol™ (Medtronic, Minneapolis, MN, USA)	Porcine, cross-linked
CollaMend™ (CR Bard/Davol Inc., Cranston, RI, USA)	Porcine, cross-linked

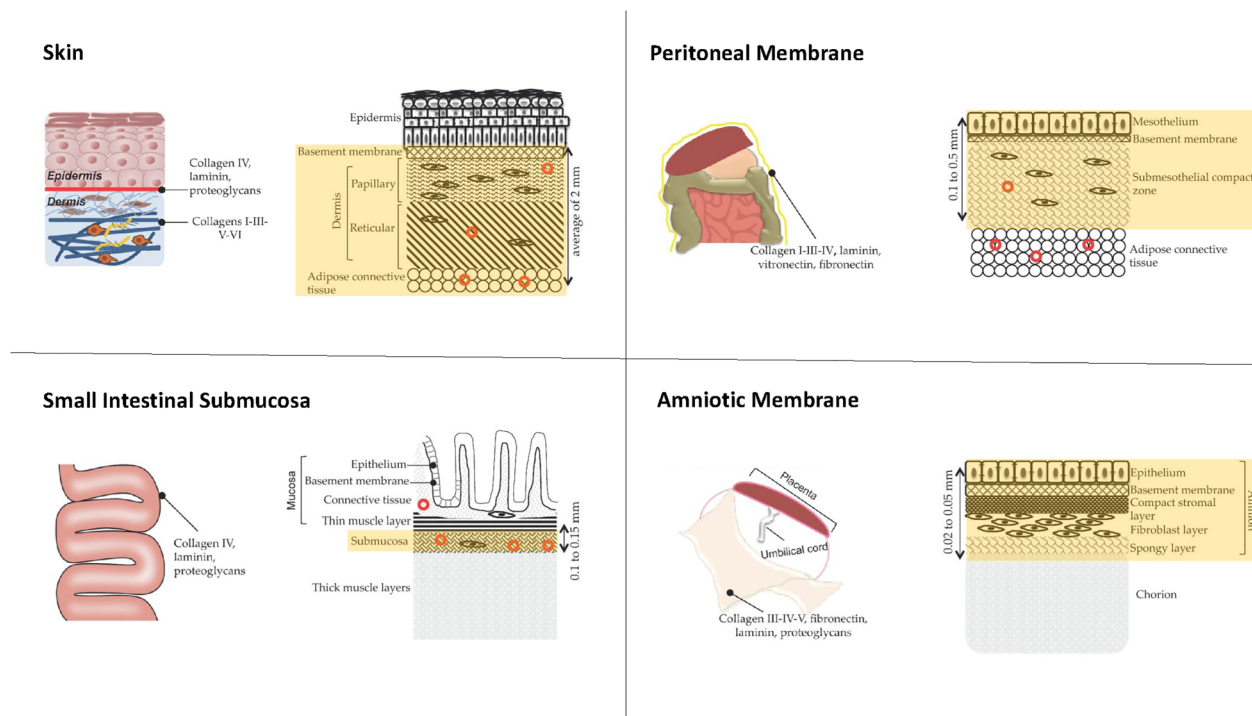ADM, acellular dermal matrix.

Figure 2. Diagrams showing common sources of ADM tissue. Yellow highlighted portions represent the area harvested for processing. ADM, acellular dermal matrix.

Given the success of early ADM applications, interest has evolved to include a variety of procedures spanning multiple surgical subspecialties.[10] Over the past two decades, a number of commercially available ADMs have been developed that vary both in origin of tissue and level of processing (Table 1, Figure 2).[11] Human cadaver (HADM), bovine (BADM) and porcine (PADM) tissues have been used in a variety of different clinical contexts, with results differing by

product and application.[11] Products are further distinguished by tissue type (Figure 2), additives (e.g. antibiotics or surfactants) and preparation regulations.[12] In this article, we review the current literature assessing the clinical utility of ADM across a broad spectrum of applications.

Methods

The authors performed a review of the PubMed, MEDLINE, EMBASE, Scopus, Cochrane and Web of Science databases using keywords 'acellular dermal matrix', 'acellular dermal matrices' and brand names for commercially available ADMs shown in Table 1. Articles were screened by title and abstract, then by full text for inclusion. Our search was limited to English language articles (or those with available English translations) published from January 1999 to September 2020. This review is focused on recent clinical data with special attention to studies comparing different ADMS.

Summary findings of included studies are presented in tables divided by clinical context (Tables 2–9). Within each table, articles are grouped by level of evidence (e.g. case report/ series, retrospective study, prospective study, meta-analysis).

Results

After duplicates were removed, there were 2443 records identified that underwent screening. After screening, 170 articles were included in our synthesis of the literature. A total of 19 articles were included in *Burn*, 18 in *Wound Care*, 30 in *Breast Reconstruction*, 9 in *Andrology*, 11 in *Gynecology and Gynecological Oncology*, 26 in *Orthopaedic Surgery*, 18 in *Oral and Maxillofacial Surgery*, 9 in *Craniofacial Surgery*, 16 in *Abdominal Wall / Hernia* and 7 in *Otolaryngology/Ear, Nose, and Throat (ENT)*.

Plastic and reconstructive surgery—burn

ADMs have been used as an adjunct for tissue modification and enhancement following severe burns (Table 2).[13–16] ADM application to self-assembled skin substitute (SASS) has been shown to increase cell proliferation, preserve intrinsic properties and reduce likelihood of rejection.[13]

Researchers have manipulated the biological signalling pathway via either direct application of signalling cells to an ADM or by combining a deep-degree burned dermal matrix (DDBDM) harvested from the host with an ADM.[14,17] ADMs impregnated with signalling cells or DDBDMs had higher probability of maintaining integrity, histocompatibility and stability.[14]

Integra™ (BADM) is the most commonly used ADM for treating severe burns.[18,19] In a large, multicentre study, Integra™ showed improvements in hypertrophic scarring compared to controls.[20] While subsequent studies have confirmed its efficacy in improving appearance, elasticity and functional outcomes,[21] infection rates remain a concern.[22,23] The use of antimicrobial dressings and/or negative pressure wound therapy (NPWT) in conjunction with Integra™ has led to improved infection rates.[19,24] Recently, MatriDerm (BADM) has been used in pediatric[25] and adult populations[26–28] to treat burns via a single staged procedure.[19] Compared to Integra™, MatriDerm has demonstrated increased neovascularisation and higher degradation rates.[19] The concurrent use of NPWT with MatriDerm has improved clinical outcomes.[18] While early clinical data on MatriDerm are promising, the literature lacks direct clinical comparisons of MatriDerm and Integra™.[18]

One case study described HADM application to infant calvarial burns involving the brain.[29] Recommended treatments typically involve high speed drilling for massive calvarial exposure or coverage with adjacent vascularised scalp tissue,[30,31] but these techniques prove challenging with immature cranial development. However, in this case, HADM (AlloDerm) was used to reconstruct a large dural defect and calvarial burn, which successfully prevented cerebrospinal fluid leakage, facilitating dural reconstruction and efficient revascularisation of tissues.[29] *Candida parapsilosis*, a common exogenous yeast that resides in burn wounds, has been observed proliferating on HADM (Pelnac®) after seven days of incubation as well as penetrating and crossing the ADM within three days.[16]

While existing literature is limited, PADM has been used in treating burn wounds due to its ability to support proliferation and enhanced epidermal cell attachment given the partial conservation of basement membra. Dermabrasion used in conjunction with PADM resulted in wound healing duration of 22.5 days, whereas those treated conservatively without PADM required 30.3 days.[15] Limited use of PADM in this context may be attributed to high cost and/or concern for transmitting infection from source tissue.[19]

Wound care. Lower limb skin and tissue are extremely thin, especially from the foot and ankle, which poses a challenge for obtaining wound closure (Table 3). Reverse sural

Table 2. Clinical evidence for ADMs in burn wounds.

Authors	Product name(s), Material	Usage, Population	Summary findings
Retrospective studies			
Guo et al. (2016)	Unspecified PADM	Deep dermal burn wound treatment 60 adult burned patients Excluded: older than 65 years, those with naturally occurring musculoskeletal or visceral injuries, and those already admitted into hospital 3 + days after injury	• Early dermabrasion + PADM mean healing time was 22.50 ± 4.72 days, whereas early dermabrasion and nano-silver dressings only needed up to 6.0 days longer • Early dermabrasion and PADM mean time in hospital was 28.3 ± 7.2 days, whereas only early dermabrasion and nano-silver dressing treatment needed 36.5 ± 8.3 days • 3 months after injury: the mVSS-TBSA shows significant improvement of vascularity, pliability, pigmentation and height in the patients treated by early dermabrasion and PADM
Prospective studies			
Heimbach et al. (2003)	Integra™, BADM	216 burn injury patients who were treated at 13 burn care facilities in the USA. The mean TBSA burned was 36.5% (range = 1%–95%). Integra™ was applied to fresh, clean, surgically excised burn wounds	• The incidence of invasive infection at Integra™-treated sites was 3.1% (95% CI = 2.0%–4.5%) and that of superficial infection 13.2% (95% CI = 11.0%–15.7%). Mean take rate of Integra™ was 76.2%; the median take rate was 95%. The mean take rate of epidermal autograft was 87.7%; the median take rate was 98%
Nguyen et al. (2010)	Integra™, BADM	6 adult patients who had been successfully treated with Integra™ ± STSG	• Integra™ sites correlated well with normal skin as measured by Cutometer • Statistically significant correlation between Integra™ sites and normal skin for the elastic function and gross elasticity • No correlations found between STSG and normal skin
Moiemen et al. (2010)	Integra™, BADM	8 patients (9 reconstruction sites) had unmeshed Integra™ with TNP therapy between the 1st and the 2nd stages. Patients underwent serial biopsies on days 7, 14, 21 and 28 after application	• Application of TNP dressings reduced shearing forces and seroma and hematoma formation
Angspatt et al. (2017)	PoreSkin®, HADM	Burn scar treatment 8 patients, 11 hypertrophic burn scars	• Graft take of PoreSkin was 97.7% at day 21. Autologous skin graft placed over PoreSkin was 91.8% • VSS shows statistically significant improvement in scar quality with PoreSkin • No major complications or rejection

(Continued)

Table 2. (Continued)

Authors	Product name(s), Material	Usage, Population	Summary findings
Demircan et al. (2015)	Matriderm®, BADM	15 paediatric patients with full-thickness facial burns. In all patients, TBSA burnt was >50%	• Average TBSA of patients was 72% (range = 50–90%) • VSS of the first 10 of 15 patients at 6 months: average 2.55 ± 1.42 (range = 1–6) • Mean vascularity, pigmentation, pliability and height: 0.1, 0.3, 0.7 and 1.2, respectively
Bloemen et al. (2010)	Matriderm®, BADM	46 patients, 69 pairs of BADM and conventionally treated (no BADM) sites	• 12 years follow-up • Reconstructive scars: 1 surface roughness parameter better in BADM scars • Subjective assessment showed several statistically significant differences in favour of BADM scars with pliability, relief and the general observer score • Higher elasticity scores for BADM scars, though not statistically significant • For scars treated with a largely expanded meshed skin graft, significantly higher elasticity was found with BADM
Okuno et al. (2018)	PELNAC®, HADM	Studying yeast culture properties isolated from burn wounds in vitro 36 of 273 patients fulfilled inclusion criteria to isolate burn wounds tissue for analysis	• Yeast was isolated from 7 patients: *Candida parapsilosis* (4/7), *C. albicans* (2/7) and *C. glabrata* (1/7) • *C. parapsilosis* penetrated ADM in 3 days and more efficiently in 7 days • *C. parapsilosis* grew, crossed the ADM and formed a biofilm in 7 days

ADM, acellular dermal matrix; BADM, bovine acellular dermal matrix; CI, confidence interval; HADM, human acellular dermal matrix; mVSS, modified Vancouver Scar Scale; PADM, porcine acellular dermal matrix; STSG, split-thickness skin graft; TBSA, total body surface area; TNP, topical negative pressure; VSS, Vancouver Scar Scale.

adipofascial flaps (RSAF) are commonly used to achieve coverage, but when used in conjunction with STSG, healing is prolonged.[32,33] One report detailed a method of RSAF application in which ADM was successfully (25% faster healing) used in concert with NPWT.[34] ADMs may be a useful adjunct to RSAF as they increase tissue vascularisation and support early fibroblast and endothelial cell growth.[22,35] A retrospective study of eight patients with foot and ankle wounds reported healing in an average of 104.5 days when treated with ADM and NPWT before STSG and RSAF compared to 141.2 days with STSG and RSAF alone.[34] Other reports have shown that patients treated conservatively (nano-silver dressing alone) or with dermabrasion + nano-silver dressing had a longer average hospital stay than those treated with dermabrasion + PADM.[15]

ADM application for upper-limb wounds has resulted in improved elasticity and range of motion (ROM) compared to wounds treated with skin graft alone.[36] Axillary and cubital joint dermis wounds are associated with high rates of contracture and severe scarring.[37] However, with ADM application, one retrospective study of 89 patients reported patient satisfaction with pain relief, ROM and aesthetic outcome in 82%, and 75% had good-excellent physician-reported functionality and ROM.[38]

Table 3. Clinical evidence for ADMs in wound care and ulcers.

Authors	Product name(s), Material	Usage, Population	Summary findings
Case series and case reports			
Pontell et al. (2018)	Integra™, BADM	Lower-extremity wound reconstruction 8 patients: 4 with all components and 4 with only RSAF and STSG	• RSAF and immediate STSG group time of healing was 141.2 days on average and 2 required reoperation • ADM, STSG, NPWT and RSAF group time of healing was 104.5 days and 1 patient required reoperation (reduction in about 36.7 days, or 25%) • All patients achieved complete wound closure
Retrospective studies			
Paredes et al. (2017)	PriMatrix®, FBADM	Chronic, large venous leg ulcers 33 patients, 40 total wounds Excluded: Those with non-CEAP class 6 wounds	• 45% of wounds had been open for $\geq$12 months • Wound sizes are in the range of 0.24–131.35 cm^2, mean = 21.1 $\pm$ 27.4 cm^2 • 4 weeks after treatment: 23.5% median area of reduction for all wounds • Average VLU closure rate of 1.96 cm^2/week after 4 weeks • Those that required reapplication of FBADM (14/40 wounds): $\geq$40% reduction in wound size after 4 weeks
Prospective studies			
Cazzell et al. (2019)	DermACELL®, HADM	VLUs 28 patients: 18 utilising D-ADM and 10 without	• Average reduction in percent wound area of 59.6% at 24 weeks in the D-ADM group vs. 8.1% at 24 weeks • Substantial wound area reduction was seen in wounds present for <1 year in the D-ADM arm (74.1%) compared with conventional care (2.0%) • 1 application of D-ADM had a substantial increase in the healing rate over the control (44.4% vs. 33.3%, respectively) after 24 weeks • D-ADM wounds remained closed at higher rate than non-D-ADM
Kavros et al. (2014)	PriMatrix®, FBADM	DFUs 46 patients completed (out of 55) Mean age: 61 $\pm$ 14 years Mean BMI: 28.9 $\pm$ 4.3 BMI of 38 or less Those with comorbidities were excluded	• 76% of the completed treatment population achieved complete wound closure by week 12 post-operation, with a mean time of 53.1 $\pm$ 21.9 days to close • 57.1% used only 1 round PriMatrix, and 22.9% required 2 • 23 $\pm$ 13.5 days on average in between each application • For those that did not completely heal, wound reduction area by 12 weeks was 71.4% $\pm$ 27.0%

ADM, acellular dermal matrix; BADM, bovine acellular dermal matrix; CEAP, clinical aetiology anatomy pathophysiology; DFU, diabetic foot ulcer; FBADM, fetal bovine acellular dermal matrix; HADM, human acellular dermal matrix; NPWT, negative pressure wound therapy; RSAF, reverse sural adipofascial flap; STSG, split-thickness skin graft; TBSA, total body surface area; VLU, venous leg ulcer.

Table 4. Clinical evidence for ADMs in breast reconstruction.

Authors	Product name(s), Material	Usage, Population	Summary findings
Case series and case reports			
Knabben et al. (2016)	Permacol®, PADM	Breast reconstruction post skin-sparing mastectomy in those with breast cancer 10 patients Mean age: 50.9 years (range = 37–64 years) Mean BMI: 21.1 kg/m^2 (17.6–26.5 kg/m^2) 2 had a history of smoking, 1 had history of diabetes mellitus	• No intraoperative complications • 1 patient required removal due to necrosis after 3 months, half underwent a corrective surgery • Lower BMI and patient satisfaction positive correlation • Permacol can physically change implant shape and improve cosmetic outcome
Kornstein A (2013)	Strattice®, PADM	Case 1: 40-year-old white female, postpartum soft-tissue laxity and grade II ptosis Case 2: 30-year-old white woman, congenital soft-tissue laxity and grade 1 ptosis Case 3: 49-year-old white woman, postpartum and post-weight-loss induced laxity and grade III ptosis	• All 3 patients had no complications (infection, haematoma, seroma, rippling, malposition or capsular contracture) and were pleased with the outcome
Retrospective studies			
Butterfield (2013)	SurgiMend®, FBADM AlloDerm®, HADM	Breast reconstruction 440 reconstructions SurgiMend® (79%) AlloDerm® (21%)	• No significant differences in complication rates were observed between SurgiMend and AlloDerm for haematoma, infection, major skin necrosis or breast implant removal • Seroma rate for AlloDerm (15.7%) was significantly greater than that for SurgiMend (8.3%) • SurgiMend costs less than AlloDerm
Ricci et al. (2016)	SurgiMend®, FBADM AlloDerm®, HADM	Breast reconstruction 952 reconstructions SurgiMend® (39%) AlloDerm® (61%)	• Mean follow-up: 587 days • Type of matrix was not an independent risk factor for complications • Smoking, age, radiotherapy and initial expander fill volume were associated with increased risk of complications
Mazari et al. (2018)	SurgiMend®, FBADM Strattice®, PADM, non-cross-linked	Breast reconstruction 97 reconstructions SurgiMend® (56%) AlloDerm® (44%)	• No differences by age, co-morbidities, specimen weight or implant volume • Drains were used in all cases of Strattice and 36 cases of (84%) SurgiMend • Implant loss rate: higher for Strattice (20%) compared with SurgiMend (7%) but not significant ($P = 0.077$) • ADM loss rate: significantly higher (Fisher's exact test, $P = 0.014$) in the Strattice group (n = 7, 14%), zero loss with SurgiMend

Table 4. (Continued)

Authors	Product name(s), Material	Usage, Population	Summary findings
			• Reoperation rate: significantly higher (chi-square test, $P = 0.002$) in the Strattice group (33% vs. 7%) • Incidence of red breast: significantly higher ($P = 0.022$) in the SurgiMend group (21% vs. 6%) • Seroma, wound problems and infection rates were similar
Gabriel et al. (2018)	Alloderm RTU® (ready to use) Sterile version of AlloDerm®, HADM	Breast reconstruction 68 patients, 116 biopsy specimens Mean age: 53 years Mean BMI: 26 kg/m² 43% of patients having had chemotherapy and 17% radiotherapy	• Short-term postoperative complications: skin necrosis (10.3%), seroma (4.3%) and infection (2.6%) • Long-term postoperative complication: capsular contracture (grade 3) (5.2%) • Mild-to-moderate neovascularisation and cellular repopulation with no inflammatory cell up to at least 5 years follow-up
Ranganathan et al. (2016)	FlexHD®, HADM AlloDerm®, HADM	Breast reconstruction 309 patients FlexHD (60.2%) AlloDerm (39.8%)	• Mean follow-up: 20.0 months • Patients with AlloDerm were half as likely to have major infections compared with FlexHD (OR = 0.50; 95% CI = 0.16–1.00; $P < 0.05$) • Rates of other complications were similar between the two groups
Keifer et al. (2016)	AlloDerm®, HADM (58.4%) Cortiva®, HADM (41.6%)	Prosthetic-based breast reconstruction 166 patients, 298 total breast reconstructions Cortiva patients, on average, weighed 1.7 kg more and were 1.6 years older	• 34 complications: 16 in AlloDerm group and 18 in Cortiva group, not significantly different ($P = 0.195$) • Cortiva group: significantly higher incidence of mastectomy flap necrosis (6 vs. 1; $P = 0.022$), due to BMI differences, though • Only current tobacco use ($P = 0.033$) was a significant predictor for a complication • Trending predictors: BMI ($P = 0.074$) and age ($P = 0.093$) • ADM type: not a significant predictor for any recorded complication ($P = 0.160$)
Qureshi et al. (2016)	AlloDerm®, HADM	Breast reconstruction 367 patients (265 ADM and 102 non-ADM) Mean age: 50 years for both groups BMI: 28.2 kg/m²	• Average hospital 2-year direct cost per reconstruction patient: ADM group = $11,862; average cost for non-ADM group = $12,319 • Initial reconstructions more costly in ADM group ($6868 vs. $5615) • 2 years later: ADM ($5176) costed less than non-ADM ($6704)
Rose et al. (2016)	AlloDerm®, HADM	Expander-based breast reconstruction 55 patients, 77 ADM-based tissue expander reconstruction	• Increased complication rates seen as ADM thickness increased • Significant associations between smokers and skin necrosis ($P < 0.0001$), seroma and prolonged JP drainage ($P = 0.0004$) and radiated reconstructed breasts and infections ($P = 0.0085$)

Table 4. (Continued)

Authors	Product name(s), Material	Usage, Population	Summary findings
			• Elevated BMI is a significant predictor for increased infection rate (P = 0.0037)
Salzberg et al. (2016)	AlloDerm®, HADM (93%) Strattice®, non-cross-linked PADM (6.9%) FlexHD®, HADM (0.1%)	Breast reconstruction 863 patients, 1584 total reconstructions Mean age: 47.0 years 14% current/former smokers, 10% other co-morbidities, 25% using chemotherapy, 10% using radiotherapy	• Capsular contracture incidence was 0.8% and 1.9% in irradiated breasts • All contractures occurred within 2 years • <400 mL implants and postoperative radiotherapy increased risk
Prospective studies			
Bullocks et al. (2014)	DermACELL®, HADM	Two-stage breast reconstruction 10 female patients, 18 total breasts Age range: 33–59 years 2 smokers	• 8 completed reconstruction while two patients failed reconstruction (both smokers) due to seromas and infection • A few patients required postoperative chemotherapy and radiation • 4 breasts developed seromas, 2 surgical site infections, 4 delayed healing and 3 flap necrosis • Histology confirms rapid integration of mesenchymal cells into the matrix (compared to non-ADM)
Vu et al. (2015)	FlexHD Pliable®, HADM	Breast reconstruction 41 patients, 72 breasts Age: at least 18 years No patients who experienced complications from previous surgeries or previously underwent reconstruction with tissue expander No patients with BMI >40 kg/m² or who had previous radiation treatment	• No cases of infection, seroma, or implant extrusion or malposition • BREAST-Q scores: outcome satisfaction (70.13 ± 23.87), breast satisfaction (58.53 ± 20.00), psychosocial wellbeing (67.97 ± 20.93), sexual wellbeing (54.11 ± 27.72) and physical wellbeing (70.45 ± 15.44). • 12.5% complication rate
Systematic reviews and meta-analyses			
Adetayo et al. (2016)	Alloderm®, HADM	Breast reconstruction and abdominal wall	• 53 studies for meta-analysis. Majority (68.6%) were retrospective. Mean follow-up in the breast group was 16.8 ± 13.2 months • Breast complication rates: 4.4% cellulitis, 6.1% implant failure, 4.1% seroma formation, 2.0% wound dehiscence, 5.1% wound infection

ADM, acellular dermal matrix; BADM, bovine acellular dermal matrix; BMI, body mass index; FBADM, fetal bovine acellular dermal matrix; HADM, human acellular dermal matrix; JP, Jackson Pratt; OR, odds ratio; PADM, porcine acellular dermal matrix.

Table 5. Clinical evidence for ADM in andrology.

Authors	Product name(s), Material	Usage, Population	Summary findings
Retrospective studies			
Xu et al. (2019)	Unspecified PADM	Penile girth enhancement 78 patients Mean age: 31.14 years (age range = 21–66 years) Exclusion: patients aged 70+ years, history of mental illness, coagulopathy or type I/II diabetes	• 3-month postoperatively: penile circumference increased by 1.1 cm (range = 0.5–2.1 cm) on average • Complications noted: 47 patients with erectile discomfort, 12 patients delayed healing, 10 unobvious augmentation effect, 8 wound haematoma, 7 prepuce oedema, 4 wound infection and 3 with skin necrosis of the dorsal side • 7 patients eventually underwent ADM removal
Prospective studies			
Alei et al. (2012)	Unspecified PADM	Penile girth augmentation 69 patients	• Postoperatively at 6 and 12 months: mean flaccid penis circumference was 11.3 cm (range = 8.2–13.2 cm), a 3.1-cm mean increase, and erect mean circumference was 13.2 cm (range = 8.8–14.5 cm), a 2.4-cm increase • Psychosexual impact of operation was beneficial in the majority • Minor complications resolved with conservative treatment within 3 weeks, no major complications noted
Tealab et al. (2013)	Pelvicol™, PADM	Penile augmentation 18 patients Mean age: 24 years (age range = 19–38 years)	• Pelvicol is not an ideal option for enhancing penile girth • In total after 1 year: 2 patients highly satisfied, 7 patients moderately satisfied and 9 unsatisfied • 8 total complications resulting in severe penile oedema and ischemic shaft ulcers • 4 total patients required total graft removal • Group 1: mean increase in girth was 2.8 cm (range = 2–3.2 cm); Group 2: mean girth increase was 1.7 cm (range = 1.2–2 cm)
Zhang J et al. (2004)	Unspecified PADM	Penile augmentation 12 patients	• Postoperative: mean increase in flaccid penile girth was 2.6 cm (1.3–3.1 cm) • All patients regained sexual ability within 3 months postoperatively • 1 patient: delayed wound healing (due to tight dressing), repaired with a scrotal skin flap • Aesthetically normal results without contour deformities

(Continued)

Table 5. (Continued)

Authors	Product name(s), Material	Usage, Population	Summary findings
Zhang X et al. (2018)	Unspecified PADM	Penile augmentation for improvements in premature ejaculation 39 patients Mean age at the time of operation: 29 years (age range = 24–37) Excluded: those with penis deformities, bleeding disorders, keloid formation; those who were on medication for ejaculatory function	• Baseline data: 6.93 ± 1.00 cm flaccid girth, 10.59 ± 1.15 cm erect girth, 225.6 ± 120.4 s IELT (self-estimated) • 6-month follow-up: 8.07 ± 1.06 cm flaccid girth, 12.79 ± 1.22 cm erect girth, 424.3 ± 123.8 s IELT (self-estimated) • 2-year follow-up: 7.89 ± 1.04 cm flaccid girth, 11.53 ± 1.19 cm erect girth, 412.8 ± 123.1 s IELT (self-estimated) • Minor complications were resolved with conservative treatment within 3 weeks
Zhang Z et al. (2015)	Unspecified PADM	Wound healing of Fournier gangrene 36 total patients, 17 experimental (those with XADM) and 19 controls	• Hospitalisation period: experimental group 26.06 ± 0.83 days and control group 38.11 ± 5.60 days • Wound preparation time: experimental group 13.64 ± 1.46 days and control group 22.37 ± 1.38 days • Interecological organisation protection, granulation tissue growth promotion, and penile function and morphology retained all observed

ADM, acellular dermal matrix; IELT, intravaginal ejaculation latency time; PADM, porcine acellular dermal matrix; XADM, xenographic acellular dermal matrix.

ADMs are particularly useful when treating exposed tendons and bones that may be unsuitable for skin graft coverage.[37,39] In radial forearm flap donor site closure, ADM application has led to minimal scar contracture and complications, as well as normal ROM, grip and pinch.[37,40,41] In tumour resection surgery, skin contracture is a common complication; however, application of ADM rather than skin grafts alone has improved final ROM.[42]

Skin grafting can be difficult in lower-limb wounds as limited available tissue may lead to dermal tension. However, one study of 30 lower-limb injuries treated with combination ADM and STSG reported successful grafting in 29 wounds and an average of 56.4 days to complete healing.[43] Success in these patients may be attributed to ADM's ability to maintain elasticity and tensile strength while promoting vascularisation and preventing infection.

ADMs have shown efficacy as an adjunct in lower limb ulcers treatment.[2,44–46] One randomised controlled trial showed that HADM resulted in greater reduction in wound size at 24 weeks (59.6% HADM vs. 8.1% control).[44] In the same study, 100% of HADM-treated wounds remained closed at four weeks postoperatively and 75% remained closed at 12 weeks compared to 66.7% at four weeks and 33.3% at 12 weeks in the control group.[44] Fetal BADM has been used in treatments for diabetic foot ulcers (DFUs) and venous leg ulcers (VLUs).[45,46] BADM has improved DFU healing outcomes by 40% and led to a wound closure of 76% in 53.1 ± 21.9 days in one cohort.[45] In VLUs, BADM application resulted in a median reduction of 23.5% in the wound area at four weeks postoperatively.[46] When compared to advanced moist wound therapy (AMWT), such as foams and gels, HADM application in DFUs resulted in complete closure in 69.6% compared to 46.2% with AMWT.[2]

In addition to wound closure, ADMs have been shown to improve the aesthetic properties of skin. In burn scars, HADM has been used to achieve significant improvement of burn scar quality as measured by the Vancouver Scar Scale.[47]

ADMs have been associated with complications, including the following: hypopigmentation; lack of vascularisation and lymphatics; absence of hair follicles, sweat and sebaceous glands; and incomplete

Table 6. Clinical evidence for ADMs in orthopaedic surgery.

Authors	Product name(s), Material	Usage, Population	Summary findings
(A) Achilles tendon repair			
Case series and case reports			
Bertasi et al. (2017)	DermACELL®, M-ADM	Achilles tendon repair 35-year-old fell and re-ruptured native tendon 2 months after repair with M-ADM. Histology specimens were obtained 1 month after re-rupture	• Alcian Blue and PAS stains showed excellent attachment of paratenon to M-ADM without evidence inflammatory response • Active infiltration of mesenchymal (likely synovial based on morphology) cells from paratenon into graft • Neovascularisation in infiltrated areas with robust vascularisation at graft–paratenon interface • 60% of graft depth vitalised with new cells
Retrospective studies			
Cole et al. (2018)	ArthroFlex®, M-ADM	Achilles tendon repair 9 patients Mean age: 58.3 years Mean follow-up: 14.4 months	• 4/9 (44.4%) traumatic injuries, 5/9 (55.6%) 'wear and tear' • Mean FFI-R at final follow-up: 33.0
(B) Foot/Ankle arthroplasty			
Case series and case reports			
Carpenter et al. (2017)	Arthroflex®	Interpositional ankle arthroplasty 4 patients (age range = 32–42 years)	• Pain relief, ROM improvement in tibiotalar joint (from a mean of 16.5° preoperatively to 31° postoperatively. • Mean preoperative AOFAS hind-foot ankle scores was 35 and increased to 88.5 postoperatively
Retrospective studies			
Berlet et al. (2008)	??	Interpositional arthroplasty of first MTP joint 9 patients, 5 female Mean age: 53.3 years	• Mean length of follow-up was 12.7 months; no complications or failures • Mean AOFAS score and pain sub-score increased from 63.9 and 17.8 preoperatively to 87.9 and 34.4 postoperatively
(C) Foot/Ankle			
Prospective studies			
Pontell et al. (2018)	ADM, Integra™; Ethicon Inc	RSAFs 8 patients, 4 with an immediate STSG and 4 with a delayed STSG	• Patients with the immediate STSG had a mean time to heal of 141.2 days, with 2 patients needing another operation • Patients with the delayed STSG had a mean time to heal of 104.5 days, with 1 patient needing another operation

Table 6. (Continued)

Authors	Product name(s), Material	Usage, Population	Summary findings
(D) Rotator cuff repair			
Case studies and case series			
Neumann et al. (2017)	Porcine dermal matrix xenograft	60 patients (61 shoulders) were observed for an average of 50.3 months	• Average VAS pain score decreased from 4 to 1 postoperatively • Average active forward flexion, external rotation at 0°, internal rotation at 0°, supraspinatus strength, infraspinatus strength all increased postoperatively • MASES score was 87.8 on average postoperatively • Postoperative ultrasound showed 91.8% of repairs were intact
Mirzayan et al. (2019)		25 shoulders (during 2006–2016) with massive rotator cuff tears underwent a procedure with an ADM Mean patient age: 61 years	• Significant improvements in VAS and ASES scores for type I and II grafts • No difference between VAS and ASES scores postoperatively in type I and II grafts • No improvements in VAS and ASES for type III grafts
Retrospective studies			
Hohn et al. (2018)	??	From 2008 to 2014, 23 patients who received a revision RC repair augmented with ADM with >2 years of follow-up Mean age: 60.1 years	• Improved ASES and SANE scores postoperatively
(E) Glenoid resurfacing			
Case study and case series			
Namdari et al. (2013)	Graftjacket®	2 patients who had hemi-arthroplasty and biologic glenoid resurfacing	• Both patients had a foreign body reaction that necessitated a revision surgery
(F) Forearm/Hand/Wrist			
Laboratory study			
Ehsan et al. (2012)	Arthroflex, LifeNet Health	Scaphoid and lunate with the scapholunate ligament were taken from 15 cadaveric specimens 5 specimens were kept intact, 5 were reconstructed with a 1.0-mm-thick dermal matrix, and 5 were reconstructed with a 1.5-mm-thick dermal matrix	• The intact specimens failed at an average of 172 N and failed mid-scapholunate ligament • The specimens with 1.0-mm dermal matrix failed at an average of 77 N and failed at the suture–matrix interface • The specimens with 1.5-mm dermal matrix failed at an average of 111 N and failed at the bone–suture anchor interface

(Continued)

Table 6. (Continued)

Authors	Product name(s), Material	Usage, Population	Summary findings
Case study and case series			
Gould et al. (2019)		2 female patients treated to prevent recurrence of distal radioulnar heterotopic ossification	• Improvements in ROM, supination and pronation postoperatively • No postoperative complications or recurrence of heterotopic ossification
Peterson and Adham (2006)	ADM (AlloDerm)	5 patients with postoperative and 5 patients with post-traumatic neuropathic pain at the wrist had a neuroma excision and/or neurolysis with interposition of an ADM between skin and nerve	• Patients were followed for 12–25 months and had improvements in pain • 8 patients returned to work
Retrospective studies			
Terry et al. (2014)	Alloderm; LifeCell, Bridgewater, NJ, USA	43 patients who had open fasciotomies between 2005 and 2012. 23 treated with ADM Median age: 66.5 years	• Recurrence was seen in 1 of 23 patients with ADM and 5 of 20 patients without ($P = 0.045$)
Prospective studies			
Hoang et al. (2019)	ADM (FlexHD)	132 patients having an open fasciotomy for Dupuytren's disease. 28 patients were treated with the ADM Median age: 67 years	• In the ADM group, the mean preoperative interphalangeal joint flexion contracture was 66.5° ± 29.9° and was corrected to 9.7° ± 12.4° • In the control group, the mean preoperative interphalangeal joint flexion contracture was 51.4° ± 23.9° and was corrected to 7.8° ± 4.1° ($P < 0.05$) • At follow-up, there was recurrence in 1/28 patients in the ADM group and 9/104 in the control group
Kokkalis et al. (2009)	GraftJacket (ADM)	100 thumbs with trapeziometacarpal osteoarthritis had surgery with ADM instead of the flexor carpi radialis tendon autograft	• All but one patient had significant improvement in pain scale rating, grip and pinch strength • No foreign body reactions or infections
(G) Hip			
Prospective studies			
Rao et al. (2016)	Graft Jacket; Wright Medical Technology, Arlington, TN, USA	12 patients who had a transosseous repair of the gluteus medius and minimus insertions augmented with ADM	• Significant improvements in pain (VAS), limp, gait and abductor strength • Trendelenberg test became negative in 11 patients • At an average follow-up of 22 months, Harris Hip Scores improved from 34.05 to 81.26 ($P < 0.001$)

ADM, acellular dermal matrix; AOFAS, Association of Orthopaedic Foot and Ankle Society; ASES, American Shoulder and Elbow Surgeons; FFI-R, Foot Function Index-Revised; M-ADM, human dermis processed with Matracell®; MTP, metatarsophalangeal; PADM, porcine acellular dermal matrix; PAS, Periodic acid–Schiff; ROM, range of motion; RSAF, reverse sural adipofascial flap; STSG, split-thickness skin graft; VAS, Visual Analogue Scale.

Table 7. Clinical evidence for ADM in oral and maxillofacial surgery.

Authors	Product name(s), Material	Usage, Population	Summary findings
(A) Gingival recessions			
Case series and case reports			
Fickl et al. (2013)	Unspecified PADM	6 patients with 28 gingival recessions had a procedure with a modified tunnelling technique and ADM	• At 6 months postoperatively, mean root coverage was 65.52% • At 12 months postoperatively, mean root coverage was 56.82% • Complete root coverage was achieved in 42.86% of the treated gingival recessions
Prospective studies			
Godavsarthi et al. (2016)	AlloDerm®, HADM	14 patients with Miller Class I or II gingival recessions 3 women Mean age: 41.4 years Randomly assigned to PPG with CAF or ADM with CAF	• Mean recession depth in PPG/CAF decreased from 2.89 ± 0.40 mm at baseline to 0.25 ± 0.50 mm at 12 months with a mean root coverage of $92.79\% \pm 14.25\%$ • Mean recession depth in ADM/CAF decreased from 2.93 ± 0.55 mm at baseline to 0.32 ± 0.46 mm at 12 months with a mean root coverage of $89.79\% \pm 14.73\%$ • PPG/CAF was found to have a perceived improvement in aesthetics
Abou-Arraj et al. (2017)	AlloDerm®, HADM Puros Dermis® Solvent-dehydrated HADM	17 patients with Miller Class I gingival recessions Randomly assigned to AlloDerm® or Puros Dermis® groups	• Both groups had predictable and sufficient root coverage • A zone of immobile connective tissue extending to the mucogingival junction was created
Cosgarea et al. (2016)	Mucoderm®, PADM	12 patients with at least two Miller Class I, II or III gingival recessions treated with a modified coronally advanced tunnel technique and then with an ADM 9 women, mean age: 34 years	• Found significant improvements in 98.15% of gingival recessions with a 2.06 ± 1.18 mm reduction • Mean root coverage was $73.20\% \pm 27.71\%$ • No significant changes in periodontal pocket depth
Chaparro et al. (2015)	Unspecified PADM	24 patients with 93 gingival recessions were treated with the tunnel procedure and ADM	• 100% root coverage in 68% of maxillary recessions and 53% of mandibular recessions • In partial root coverage, the recession went from a mean of 4.41 to 0.83 mm in the maxilla and 3.78 to 0.78 mm in the mandible • Root coverage of 100% was observed in 74.07% of Miller Class I recessions in comparison with 43.59% of Class II recessions ($P = 0.003$)

Table 7. (Continued)

Authors	Product name(s), Material	Usage, Population	Summary findings
Costa et al. (2016)	AlloDerm®, HADM	19 smokers with bilateral Miller Class I or II gingival recessions were randomly assigned to received ADM and EMD or ADM alone	• Mean gain in recession height ($P < 0.05$) and sites with complete root coverage ($P < 0.05$) were better in the ADM/EMD group • Percentage of root coverage was 60% in the ADM/EMD group and 53% in ADM alone
Mahn et al. (2015)	AlloDerm®, HADM	50 patients with Class I and II gingival recessions were treated with an ADM with a CAF	• At 52 weeks, the average recession decreased from 3.8 ± 0.9 mm to 0.2 ± 0.5 mm • There was 94.7% root coverage • Complete root coverage achieved in 80% of cases
Ozenci et al. (2015)	AlloDerm®, HADM	20 patients with 58 Miller Class I gingival recessions were divided into receiving either ADM with tunnel technique or ADM with CAF	• Mean root coverage was 75.72% in TUN/ADM and 93.81% in CAF/ADM • CAF/ADM performed significantly better in probing depth, clinical attachment level, recession height and width, keratinised tissue height, gingival thickness and complete/mean root coverage ($P < 0.05$)
Wang et al. (2015)	AlloDerm®, HADM Puros Dermis®, Solvent-dehydrated HADM	20 patients with Miller Class I and II gingival recessions were treated with either FDADM or SDADM	• At 12 months, a mean improvement in attachment level of 2.0 ± 1.08 mm for FDADM and 2.0 ± 0.70 mm for both SDADM was achieved ($P = 0.002$) • Root coverage after 12 months was $80.66 \pm 22.90\%$ for FDADM and $80.97 \pm 18.08\%$ for SDADM
De Resende et al. (2019)	AlloDerm®, HADM	25 patients with 50 recession sites were treated with either a FGG or ADM	• Probing depth and clinical attachment level showed no significant differences • Professionals thought the aesthetics were better in the ADM group • Tissue thickness was inferior for ADM vs. FGG • Histomorphometric analysis demonstrated higher percentage of cellularity, blood vessels and epithelial luminal to basal surface ratio for FGG group • ADM had a higher percentage of collagen fibres and inflammatory infiltrate
(B) Gingival fenestration			
Case series and case reports			
Breault et al. (2016)	AlloDerm®, HADM	ADM used to treat one gingival fenestration	• At 2.5 months, ADM was integrated into the soft tissue with complete resolution of gingival fenestration • Excellent aesthetics

(Continued)

Table 7. (Continued)

Authors	Product name(s), Material	Usage, Population	Summary findings
(C) Parotid fistula			
Case studies			
Blythe et al. (2016)	AlloDerm®, HADM	One patient with a parotid fistula	• A parotid fistula was successfully treated with ADM
(D) Alveolar bone grafts			
Retrospective studies			
Clavijo-Alvarez et al. (2010)	AlloDerm®, HADM	35 patients included from a retrospective review from 2005 to 2007 15 patients (4 girls) received ADM augmentation Mean age at surgery was 10 years	• No significant difference in mucosal disruption between the two groups or complete mucosal healing time (average of 4 weeks) • Exposure of bone graft occurred in 0% of the ADM group and in 30% of the control group ($P = 0.016$) • No significant difference in postoperative bone graft incorporation according to the Chelsea scale • No significant difference in canine eruption through graft site
(E) Regenerate bone/soft tissue in dental implants			
Case studies and case series			
Momen-Heravi et al. (2018)	PerioDerm®, HADM	A patient with a successful soft-tissue and bone regeneration of dehiscence in the maxillary incisor region using ADM	• There was >95% new bone formation at implant surface 5 months after soft-tissue and bone augmentation
Prospective studies			
Fischer et al. (2019)	Derma®, PADM	20 patients undergoing implant surgery with soft-tissue augmentation (24 total cases) with ADM Mean age: 50.2 ± 11.9 years	• At 6-month follow-up, there was a mean dimensional gain of 0.83 ± 0.64 mm ($P < 0.01$) • Soft-tissue shrinkage on average was averaged 34.2% ± 77.0% from T2 to T3 ($P < 0.01$) and did not change ($p = 0.39$) • No adverse events
Papi and Pompa (2018)	Mucoderm®, PADM	12 patients received a dental implant in the upper premolar area and the ADM was inserted 8 weeks later	• One month after insertion of the ADM, mean KMW was .86 ± 3.22 mm At 1 year after insertion, mean KMW was 5.67 ± 2.12 mm • No complications with wound healing occurred
Fernandes et al. (2016)	AlloDerm®, HADM	19 patients undergoing extraction of maxillary teeth were randomly assigned to	• ADM/AB showed reduced bone loss after 6–8 months ($P < 0.01$) • ADM/AB showed a higher percentage of mineralised tissue

Table 7. (Continued)

Authors	Product name(s), Material	Usage, Population	Summary findings
		ADM and mineralised AB or ADM only	and lower percentage of non-mineralised tissue ($P > 0.05$) • ADM/AB had reduced alveolar bone loss after 6–8 months
(F) Repair ora-antral fistulas			
Prospective studies			
Li et al. (2018)	Heal-all®, HADM	9 patients with oro-antral fistulas had the defects repaired with ADM and acellular bone matrix	• At 6 months postoperatively, the fistulas were well healed; no nasal congestion or runny noses • Computed tomography confirmed wound healing

AB, bone allograft; ADM, acellular dermal matrix; CAF, coronally advanced flap; EMD, enamel matrix derivative; FDADM, freeze-dried ADM; FGG, free gingival graft; HADM, human acellular dermal matrix; KMW, keratinised mucosa width; PADM, porcine acellular dermal matrix; PPG, periosteal pedicle graft; SDADM, solvent-dehydrated ADM.

innervation.[17] Increased duration of treatments raises costs associated with ADMs.[2,45,48,49] When incorporating BADM into DFU treatment, 42.9% of patients needed multiple applications with an average wait of 23 days between appplications.[45] ADM + STSG treatment is a staged process in which STSG is performed 3–4 weeks after ADM application.[34] When incorporating ADM in wound treatment algorithms, the effects of treatment duration should be considered.

Breast reconstruction. ADMs have become a popular adjunct to enhance wound healing, organised tissue regeneration and cosmesis in breast reconstruction and augmentation (Table 4).[2,50,51] While individual reports vary, aggregate data indicate that complications are rare.[52–57] A systematic review of 1039 breast reconstructions with either PADM or HADM showed low overall rates of skin and nipple necrosis (11% and 5%, respectively), infection (12%), hematoma (1%) and seroma (5%), with only 9% of patients requiring reoperation.[52] This success may be attributed to ADMs' ability to fully integrate into host tissue with neovascularisation, cell repopulation and lack of inflammatory cells observed at both short- and long-term follow-up.[56,58]

ADMs have been applied to revision augmentations, as they adequately reinforce the soft tissue and implant pocket, thereby decreasing rates of capsular contracture.[53–55] A retrospective review of 850 breast reconstructions reported that out of 450 breast reconstructions using PADM,

there was a total complication rate of 33.2%: 12.2% developed seromas; 5.2% major infections; and 6.5% minor infectons.[59] One study of 3189 breast reconstructions noted that if antibiotics were administered for <24 h after operation, the infection rate was 2.48%, whereas regimens that lasted >24 h had an infection rate of 13.21%.[60] In a prospective study of 27 patients, ultrasound detected lymphoceles in only three patients; one patient experienced infection, and all three cases of seroma resolved by 12 months.[61]

A 13-year cumulative study of 1584 breast reconstructions with ADM reported capsular contracture of 0.8% in the entire cohort and 1.9% in irradiated breasts.[53] A separate study of 455 breasts revealed minimal contracture 21 months after breast reconstruction surgery.[54] By facilitating an optimal breast pocket, ADMs help to obtain symmetrical coverage, enhance the aesthetic outcome, decrease pain from pectoralis muscle mobilisation and reduce scarring.[57,62] Limited capsule contracture and scarring may also be attributed to the decreased inflammatory response associated with ADMs.[63,64] Additionally, it is more difficult for scar tissue or capsules to develop on the ADM surface. Once revascularised, the ADM-treated tissue will exhibit improvements, such as enhanced elasticity, that minimise contracture.[65]

One case study described the use of ADM to rescue a non-ADM reconstructed breast from complications.[66] A patient undergoing radiotherapy after breast reconstruction developed a

radiation ulcer, and by utilising PADM with Becker's 50 expander as reinforcement, the breast and ulcer were resolved.[66]

While ADM appears more costly in the short term ($6686 ADM vs. $5615 non-ADM), ADM has been associated with lower total cost at two years postoperatively ($11,862 vs. $12,319).[67] ADM integration with fenestrations and perforations led to decreased risk of infection, duration of tissue draining and length of hospital stay.[68]

Thick ADM implants ($\geq$1.2 mm), compared to thin ADM implants, have been linked to increased rates of necrosis (+3.5%), seroma (+3.5%), infection (+8.8%) and need for drainage two weeks postoperatively (+15%).[60,69] This may be the result of reduced neovascularisation in thicker ADMs.[69] One study showed that implants <400 mL were 10.3 times more likely to experience capsular contracture.[53]

Implants from different manufacturers (with different processing protocols) may produce different outcomes. In two comparative studies of HADMs, FlexHD resulted in more complications than AlloDerm and Cortiva.[70,71] In studies directly comparing ADMs of different origins, results indicate that BADM may be more suitable for breast reconstruction compared to HADM and PADM.[12,71–73]

Patient lifestyle factors are known to affect outcomes in ADM procedures.[53,58,69,74,75] Smoking status, chemotherapy or radiation, and diabetes mellitus have been associated with increased risk for seroma, cellulitis, wound infection and implant failure.[53,58,69,74,75] Body mass index (BMI) has been identified as a predictor of tissue drainage time.[69]

Surgeon expertise appears to influence outcomes of ADM procedures.[70,76,77] Multiple factors must be carefully considered when performing ADM breast procedures, including the following: pectoralis muscle anatomy; flap conditions; skin excess; sentinel-node status; flap vascularity; BMI; and the type of tumour, if present.[78]

Andrology. Following application in breast reconstructions, ADM usage evolved to include penile augmentations, erectile dysfunction (ED) treatments and phalloplasties (Table 5).[79,80] Advantages of ADM include lower risk of necrosis, shorter operation time and more subtle incisions.[79–81]

One study of 69 patients described a technique in which PADM was placed circumferentially from the groove between cavernous and spongious bodies on one side to the other and secured to Bucks fascia.[79] One year postoperatively, penile circumference increased 3.1 cm while flaccid and 2.4 cm while erect.[79] A retrospective study of 78 patients who received ADM administrations as filler material also showed increased measurements (mean + 1.1 cm).[82] A pilot study assessing an acellular collagen matrix reported results varying by ADM insertion method, with a bilayer inserted through V-Y suprapubic incision producing greater circumference increases and patient satisfaction.[83]

ADMs may contribute to improved erectile function and reduced premature ejaculation in penile augmentation patients.[81,84] One study followed 39 patients seeking treatment for ED, and after six months, flaccid girth increased >1 cm, erect girth by >2 cm and intravaginal ejaculatory latency time increased by 200 s on average.[84]

PADM has been used as an adjunct in Fournier gangrene treatment.[85] In one study, average wound preparation time was 13.6 days when using PADM whereas non-PADM treatment required 22.4 days.[85] Overall hospitalisation decreased by 14 days on average. PADM was shown to promote granulation tissue growth, with maximum retention of penile and perineum function, morphology and protective features.[85]

While aphallia is a condition typically addressed by either the De Castro technique or a scrotal flap phalloplasty,[86,87] one case report has detailed usage of ADM in this procedure for an infant, with the goal of supplying additional support and girth to the phallus as well as increased vascularisation.[80] After harvesting scrotal skin flap for neophallus construction, the ADM was sutured to the pubic symphysis, then covered with a layer of tunica vaginalis. Twelve months postoperatively, the patient had no complications and good cosmetic outcome.[80] Aphallia in children, however, is a rare disease with limited published data, and further research is needed to assess efficacy of ADM in this context.

One study reported that 60.3% of patients experienced erectile discomfort and 12.8% had no obvious augmentation effects when treated with ADM.[82] Reported complications include severe penile oedema, ischemic shaft ulcers, hematomas and wound infections.[82,83] Upon suturing the ADM to Buck's fascia, microbranches of the dorsal nerve of the penis may become covered and lead to less receptor threshold.[84] Additionally, a thick ADM may affect proprioception receptors in the deep tissue and on the skin surface, leading to abnormal temperature and pressure differences.[84]

Table 8. Clinical evidence for ADMs in AWR.

Authors	Product name(s), Material	Usage, Population	Summary findings
Case reports			
King et al. (2013)	Strattice™, non-cross-linked PADM	45-year-old obese white man	• Successful repair of a giant, multiply recurrent subcostal hernia with loss of domain in a 45-year-old obese white man • Used a PADM as the floor of the repair, fixed to the costal margin using orthopaedic bone anchors and covered with a pedicled omental flap
Retrospective studies			
Begum et al. (2016)	Strattice™, non-cross-linked PADM	Paediatric AWR and chest wall reconstruction 13 patients over a 3-year period. 11 had AWR and two underwent chest wall reconstruction. 7 procedures were contaminated at the time of surgery	• Median age at insertion was 8.1 years (age range = 5 days–18 years) with a median weight of 20.6 kg (range = 1.9–99 kg) • PADM failed in one patient
Caso Maestro et al. (2014)	Strattice™, non-cross-linked PADM	Paediatric delayed closure after liver transplant 6 paediatric patients underwent delayed abdominal wall closure with a biological mesh after liver transplant	• Mean follow-up of 26 months (range = 21–32 months) • All patients had a functional abdominal wall
Clemens et al. (2013)	Strattice™, non-cross-linked PADM SurgiMend®, FBADM	234 consecutive cancer patients who underwent AWR for ventral hernia or musculofascial resection defects with underlay bioprosthetic mesh (porcine or bovine acellular dermal matrix) and complete midline musculofascial closure. 120 patients underwent a non-bridged, inlay AWR with PADM (n = 59/120) or BADM (n = 51/120).	• Mean follow-up: 21.0 ± 9.9 months • Overall complication rate: 36.6% • PADM had a significantly higher complication rate (44.9%) than the bovine matrix group (25.5%; $P = 0.04$) • No significant differences in rates of recurrent hernia (2.9% vs. 3.9%; $P = 0.99$) or bulge (7.2% vs. 0%; $P = 0.07$) • Rate of intraoperative adverse events in the PADM group (10.1%) was significantly higher than BADM (0%; $P = 0.02$)
Garvey et al. (2017)	Alloderm®, HADM	191 patients	• Median follow-up: 52.9 months • 26/191 patients had a hernia recurrence. Recurrence rates were 11.5% at 3 years and 14.6% by 5 years. In subset excluding bridged repairs and HADM patients, cumulative hernia recurrence rates were 6.4% by 3 years and 8.3% by 5 years • Factors significantly predictive of hernia recurrence: bridged repair, wound dehiscence, use of H-ADM, and coronary disease. • Component separation was significantly protective. • Crude rate of surgical site occurrence (SSO): 25.1% (48/191). Factors significantly predictive of SSO: at least 1 comorbidity, BMI ≥30 kg/m(2), and defect width >15 cm.

(Continued)

Table 8. (Continued)

Authors	Product name(s), Material	Usage, Population	Summary findings
Giordano et al. (2017)	Strattice™, non-cross-linked PADM	511 consecutive patients who underwent complex AWR using ADM. Propensity scoring done for multivariable analysis and one-to-one matching	• Mean follow-up: 31.4 months • 184 patients (36%) were elderly. Elderly and non-elderly groups had similar rates of hernia recurrence (7.6% vs. 10.1%; $P = 0.43$) and SSO (24.5% vs. 23.5%; $P = 0.82$). Bulging occurred more often in elderly patients (6.5% vs. 2.8%; $P = 0.04$). • After propensity matching of 130 pairs, these results persisted
Giordano et al. (2018)	Strattice™, non-cross-linked PADM	452 patients (mean age: 59 years) underwent AWR with ADM	• Mean follow-up: 35 months • 6.4% (29/452) were readmitted within 30 days. Most readmissions were due to SSO (44.8%) or wound infections (12.8%) • Hernia recurrence rate was higher in readmitted patients (17.2% vs. 9.9%; $P = 0.044$) • Wider defects, prolonged operative time and coronary artery disease were independent predictors of readmission
Gowda et al. (2016)	Strattice™, non-cross-linked PADM Alloderm®, HADM	87 patients who underwent hernia repair after pancreas and/or renal transplant 27 underwent ventral hernia repair with PADM, 34 patients with HADM and 26 with synthetic mesh	• Rates of wound infection: PADM: 14.8%; HADM: 14.7%; and synthetic mesh: 65.4% • Rates of recurrence: PADM: 13.3%; HADM: 23.5%; and synthetic mesh: 76.9% • Rate of mesh removal: PADM: 7.4%; HADM: 11.8%; and synthetic mesh: 69.2% • Complication rates were significantly lower in patients who received HADM or PADM compared with patients repaired with synthetic mesh ($P < 0.001$) • No significant difference in outcomes between HADM or PADM
Guerra et al. (2014)	Strattice™, non-cross-linked PADM	13 adults (mean age: 60 years; 8 women) underwent single-stage ventral herniorrhaphy involving removal of infected synthetic mesh and repair with PADM 54% (7/13) were obese and 46% (6/13) had chronic obstructive pulmonary disease/emphysema. 6 patients had undergone ≥2 previous repairs	• Most synthetic mesh infections were polymicrobial (n = 7, 46%) or associated with *Staphylococcus aureus* (n = 4, 31%) • Mean follow-up: 23 months • With single-stage herniorrhaphy using PADM, primary fascial closure was achieved in 11 patients; bridged closure was required in 2 patients • Mean duration of hospital stay was 12 days • 1 wound infection (drained surgically, PADM remained in place) and one seroma (resolved without intervention) • 2 hernia recurrences, both in patients who received PADM as bridged repair

Table 8. (Continued)

Authors	Product name(s), Material	Usage, Population	Summary findings
Guerra et al. (2014)	Strattice™, non-cross-linked PADM	44 patients (mean age: 57.5 years) with complex ventral abdominal wall hernias were repaired using PADM. 45 single-stage repairs (3 primary; 42 incisional) 17 had previously placed synthetic mesh removed. In 40 cases, primary fascial closure was achieved; in 5 cases, PADM was used as a bridge. Vacuum-assisted closure was used for 38/45 cases: 19 closed incisions, 16 cases using the 'French fry' technique, and 3 cases with open incisions	• Mean follow-up: 17 months (range = 1–48 months) • Mean hospital stay: 8.2 days (range = 3–32 days) • 4 hernia recurrences (8.9%), 3 requiring additional repair and 1 requiring PADM explantation • 6.7% (3/45) skin dehiscence, 8.9% (4/45) deep wound infections requiring drainage and 11.1% (5/45) seromas (4 self-limited, 1 requiring drainage)
Systematic reviews and meta-analyses			
Adetayo et al. (2016)	Alloderm®, HADM	AWR and breast reconstruction 53 studies for meta-analysis. Majority (68.6%) were retrospective	• Mean follow-up in in the abdominal wall cohort was 14.2 ± 7.8 months • Abdominal wall complication rates: 17% cellulitis, 3.4% implant failure, 11.8% seroma formation, 10.9% wound dehiscence, 24.6% wound infection, 27.6% hernia, 28.1% abdominal bulging

ADM, acellular dermal matrix; AWR, abdominal wall reconstruction; BADM, bovine acellular dermal matrix; FBADM, fetal bovine acellular dermal matrix; HADM, human acellular dermal matrix; PADM, porcine acellular dermal matrix.

Gynaecology and gynaecological oncology. Historically, vaginoplasties were performed using peritoneal tissue, STSGs or allogenic epidermal sheets.[88,89] However, ADM has recently been utilised to reduce postoperative pain, procedural complexity and preserve the vaginal mucosa histology.[90] In one study, 16 patients diagnosed with uterine cervix carcinoma underwent vaginal repair using ADM after radical hysterectomy and radiotherapy.[90] Two weeks postoperatively, normal epithelial tissue and vaginal mucosa histology were observed whereas histology previously revealed granulation and inflammatory cells.

Published reports suggest that vaginal length <7 cm is correlated to less sexual satisfaction with lower sexual function.[91] After vaginoplasty with ADM secondary to carcinoma resection of the cervix, vaginal length was improved to an average final length of 9.25 cm, with 75% of patients reporting improved sexual satisfaction.[90] By utilising the ADM in the cervical repair, the superior end of the vagina is preserved, thus retaining cells for future cervical screening tests.[90] Unlike biological tissue, which is at risk of defects and infections when exposed to radiation, a synthetic ADM mesh may be better suited for harsh environments and minimise

inflammation and malformations in surrounding tissue.[92–94] Of note, successful integration of ADM relies on implantation within highly vascularised tissue.[94]

Recurrent gynaecological cancer is traditionally treated with pelvic exenteration using synthetic mesh, myocutaneous flaps from the abdomen or thigh, or pedicled greater omental flaps (PGOF) to secure the pelvic floor.[95] However, a recent case report described the use of PGOF, HADM, and autologous adipose-derived cells to improve pelvic cavity support and volume.[96] Success in this case may be attributed to accelerated angiogenesis and the favourable environment for adipose-derived stem cell incorporation provided by HADM.[97] Another patient with osteoradionecrosis and recurrent vulvar squamous cell carcinoma underwent exenteration, and pelvic floor reconstruction incorporated HADM with bilateral, thigh-based tissue flaps. The carcinogenic and bacterial-infected wounds resolved without complication.[98]

Orthopaedic surgery

Foot and ankle. ADMs have been used to promote bony regrowth and periosteum replacement,

Table 9. Clinical evidence for ADMs in urology.

Authors	Product name(s), Material	Usage, Population	Summary findings
Case series and case reports			
Bonitz et al. (2016)	AlloDerm®, HADM AlloMax®, HADM	CBE 6 male patients, born with CBE, and who had abdominal wall defects. 2 children, aged 6 and 8 years, with unrepaired bladder exstrophy plates and large abdominal wall defects (8 and 12 cm wide). Both had their bladders reconstructed, placed within the pelvis, and HADM was used to replace the absent abdominal wall (bridged repair) without the use of pelvic osteotomy. In 3 other patients, HADM reinforced the native fascial repair (bolster repair). HADM also served as a filler for the abdominal depression that was present after initial staged repair. Where HAD was used for bridged or bolster repair, the edges of the allograft were extended 2–3 cm beyond the perimeter of the defect	• Follow-up: 1–3 years • All 6 patients healed without evidence of abdominal wall hernias. All regained functional level of abdominal wall strength • 2 children successfully underwent a secondary procedure through the bridged allograft repair (both required bladder neck reconstruction and bilateral ureteral reimplantation). Continence was achieved in both, with one voiding at 2-h intervals and the other at 3-h intervals • 1 patient developed a urethral-cutaneous fistula, distant to the allograft • No associated wound complications

ADM, acellular dermal matrix; CBE, classic bladder exstrophy; HADM, human acellular dermal matrix.

ultimately leading to cell proliferation, neovascularisation and resolution of bone defects (Table 6).[99,100] ADMs have gained popularity in foot and ankle procedures as they lack the disadvantages inherent in many human auto- or allografts, xenografts or synthetic grafts.[101]

Multiple case reports describe ADM augmentation of Achilles tendon repairs with no instances of tendon rerupture or complications.[101,102] ADMs have been used in interpositional ankle arthroplasty, either as a way to resurface the talus[103] or as a spacer in the first metatarsophalangeal joint.[104] Both procedures were successful, with increased ROM, decreased pain, and no complications.[103,104] ADMs have also been successfully utilised to facilitate ankle wound healing.[105] When combined with a reverse sural adipofascial flap (RSAF), ADMs led to 25% faster healing compared to RSAF alone.[34]

Shoulder and upper extremity. In both primary and revision rotator cuff repairs, incorporation of ADMs has led to improvements in pain, ROM and muscle strength.[106,107] These repairs remained intact at long-term follow-ups.[107] In irreparable rotator cuff tears, ADMs have been used to cover the exposed bone, leading to decreased pain and better functional scores.[108] ADM augmentation of distal biceps repair in a tendon-deficient model led to a stronger tendon than without ADM.[109]

ADMs have been shown to improve interface strength and decrease re-tear rates when applied at the suture-tendon interface of rotator cuff repairs.[110] Though the procedure is technically challenging, surgeons have also utilised ADMs in superior capsular reconstructions, resulting in improved pain and shoulder function.[111]

ADM use has been described in glenoid resurfacing with improved outcomes in most cases.[112] However, foreign body reactions have been reported and should be considered if there is significant postoperative pain.[112] ADMs have been interposed between the radius and ulna to prevent heterotopic ossification after a forearm injury, leading to improvements in ROM and no recurrence.[113] ADMs are also thought to be more resistant to infection than silicone and collagen-based alternatives.[113]

Hand and wrist. ADMs have been used to reconstruct ligaments in arthritic hands.[114] Historical

methods utilised donor tendon, but were associated with scarring, pain, tendon rupture, tendonitis and neuroma formation.[114] Xenografts addressed some of these disadvantages, but caused immunologic reactions in some patients.[114] In a cadaveric scapholunate reconstruction model, HADM provided tensile strength comparable to traditional techniques and may potentially decrease donor site morbidity in these repairs.[115] A study of 100 ligament reconstructions in patients with thumb carpometacarpal arthritis found that, when using ADM, there were no adverse effects, foreign body reactions or infections.[114]

When used for Dupuytren's disease, ADMs have been shown to decrease the rate of recurrence, presumably via ADM-mediated inhibition of myofibroblasts that might otherwise create contractures.[116,117] ADMs have been used in proximal row carpectomies to prevent degradation of the radiocapitate space and have been effective in treating radiocarpal arthritis.[118] ADMs have demonstrated efficacy as an adjunct in treating neuropathic wrist pain.[119] In these cases, ADM was used to cushion the nerve as an alternative to the traditional flap coverage.[119]

Hip and pelvis. ADMs have been used effectively to augment gluteus medius and minimus repairs.[120] This technique is thought to decrease re-tear rates by providing structural strength to the repair, better tendon-bone healing and increased tensile strength due to revascularisation of the graft.[120]

Capsular defects have been filled using ADMs to create hip stability in hip reconstructions.[121] ADMs have shown some utility in addressing shortcomings of common hip abductor repair methods.[122] Traditional techniques are associated with unpredictable results with extended periods of rehabilitation.[122] However, patients receiving ADM treatments had significant improvement in Visual Analogue Scale pain and Harris Hip scores across groups.[122]

Significant complications are common in pelvic reconstructions due to the complex anatomy, multi-level organ involvement and microbial environment associated with these procedures.[96] Historical attempts to improve outcomes such as synthetic meshes led to adhesions and infections, and myocutaneous flaps from the thigh were too invasive in many cases.[96] One case report described a less-invasive technique using HADM combined with a pedicled omental flap and autologous adipose derived cells that led to fewer adhesions.[96]

Other cases have described the successful use of HADM in pelvic floor reconstruction after total exenteration or cylindrical abdominoperineal resection.[96,98,123]

Oral and maxillofacial surgery

The current gold standard for the treatment of gingival recession is the bilaminar technique using subepithelial connective tissue graft (SCTG); however, this technique has limitations, including the following: lack of available grafts; need for a second surgical site; pain after the surgery; proximity to the palatine neurovascular bundle; and suboptimal aesthetic outcomes.[124] ADMs have been shown to reduce the need for donor tissue and surgical time, and increase patient acceptance (Table 7).[125]

ADMs have shown increased efficacy in treating Miller Class I, II and III gingival recessions in non-smokers[124–127] and Miller Class I and II in smokers[128] compared to non-ADM controls. ADMs were also an effective adjunct when used in conjunction with a coronally advanced flap in Miller Class I and II recessions.[129,130]

Multiple formulations of ADMs have been used in gingival recession treatment, with both freeze-dried and solvent-dehydrated ADMs successfully achieving root coverage.[131] HADMs have produced superior aesthetic outcomes when compared to autogenous free gingival graft but were associated with delayed healing.[132] Of note, one study reported complete root coverage in only 42.86% of patients using PADM.[133]

There is a growing body of research evaluating ADMs in other conditions, including gingival fenestrations,[134] persistent parotid fistulas,[135] ora-antral fistulas,[136] alveolar bone loss/grafting[137,138] and dental implants.[139–141] Generally, ADMs were used to limit donor tissue harvest,[134] promote soft tissue growth[137,139] and improve aesthetic outcomes.[141]

Craniofacial surgery

ADMs have been used in craniofacial surgery to treat soft-tissue defects secondary to congenital conditions, disease and surgical wounds.[142–150] In aplasia cutis congenita (ACC), ADMs have shown utility both as an adjunct to grafting and as a conservative treatment for scalp coverage.[142,143]

BADM has been used as a spacer graft for upper eyelid retraction procedures secondary to thyroid eye disease.[145] In a study of 32 eyelids in

26 patients, average upper margin reflex distance was lowered from 7.7 mm to 3.3 mm with 69% of patients achieving perfect results.[145] ADMs have also been used to manage nasal lining deficiency in Le Fort 1 osteotomy, prevent Frey syndrome after parotid neoplasm surgery and as an implant for dorsal augmentation in rhinoplasty.[146–148] In patients with cranial defects, ADM has been used to improve bone regeneration and closure of chronic wounds after skull defect reconstruction.[149,150]

Abdominal wall/hernia

Ventral hernias, though common, continue to present surgical challenges, and there is no consensus regarding optimal treatment (Table 8).[151,152] Biological mesh composed of ADM has recently been used in efforts to address the shortcomings of synthetic materials in abdominal wall reconstructions.[74,153,154] In 2010, the Ventral Hernia Working Group published a grading system with recommendations for use of either synthetic (Grade 1) or biological mesh (Grades 2–4), with grades designated by risk of postoperative complications.[152,155]

Compared to synthetic mesh, ADM has been associated with decreased rates of infection, extrusion, erosion and adhesion formation.[154] In studies comparing different types of ADM, PADM and BADM appear to outperform HADM.[153,154,156] While HADM may be equally effective in reducing infection, recurrence rates are higher than in PADM or BADM.[74,153,154,156,157] The high elastin content of HADM is believed to contribute to relaxation over time and may be the cause of increased reports of laxity and/or bulging.[154,156–158]

PADM has been used effectively in giant and recurrent hernias, as well as in both elderly and paediatric patients and recurrent hernias.[155,159,160] One study comparing PADM and BADM showed similar outcomes between the two formulations.[161]

The literature assessing PADM and BADM is lacking in some surgical procedures such as bladder exstrophy repair, urethral reconstruction and treatments for premature ejaculation; however, HADM has shown utility in these procedures (Table 9).[4,162,163]

Of note, one case report described a delayed type IV hypersensitivity reaction to PADM.[164] When infection is suspected after ADM placement, hypersensitivity should be considered as part of the diagnostic algorithm.[164]

Otolaryngology/ear, nose and throat (ENT)

HADM and xenogeneic ADMs have been used in laryngotracheal and pharyngeal reconstruction as they are relatively thin and flexible compared to myocutaneous flaps.[165–169] ADM grafts carry lower risk of fistula and stricture formation and avoid donor site complications associated with flap harvest.[165] Thin ADMs are more often used for partial superficial defects in the trachea, larynx or hypopharynx. Thicker sheet ADMs were typically used for complex pharyngeal fistula closure and partial pharyngoplasty for stage III–IV carcinomas.[165] Other successful uses of ADM in otorhinolaryngology include closure of hard palatal fistula and tympanoplasty.[170,171]

Discussion

The current literature indicates that there is not a single ADM that has proven superiority in every clinical context.[70,153,154,156] In burn wounds, BADMs have produced the most favourable outcomes (compared to PADM and HADM). While Integra™ is the most popular option for coverage, MatriDerm® has seen increased utilisation as it can be applied in a single-stage procedure and provides improved neovascularisation and degradation.[19] Further studies are needed to compare PADM and BADM.

In breast reconstruction, multiple studies have been performed to directly compare ADMs of different tissue origins.[12,73] There is no clear aggregate trend indicating that one tissue source consistently produces favourable outcomes.[12,72,73] However, of the available HADMs, AlloDerm® may outperform other HADMs in breast reconstruction.[71,75] In these procedures, increased implant size and/or thickness (≥1.2 mm) appears to negatively impact outcomes.[53,60,69]

In procedures such as abdominal wall reconstruction, structural components of ADM play a role in the stability of the repair. Aside from providing mechanical cues, properties that confer rigidity, such as lower elastin content, may influence the success of a repair.[154,156–158]

As previously mentioned, ADMs are frequently used to treat gingival recessions and provide improved cosmesis compared to traditional autograft techniques. HADM outcomes are generally superior to PADM, though the literature is lacking in studies with direct comparisons.[132,133] Of note, standardised ADM graft size may skew outcomes as individual patients have highly variable gingival defects.[132]

In orthopaedic procedures, ADMs have primarily been used in orthoplastic reconstructions (e.g. reverse sural flap) and in tendon repairs where limited vascularisation and/or adhesion is a concern.[120] Future applications of ADM in orthopaedic applications may incorporate more injectable formulations.

Many ADMs have been treated with different products, cells and signalling molecules.[6,7] For example, ADMs pretreated with bFGF had better recruitment of mesenchymal stem cells,[71] proliferation and differentiation compared with a matrix pretreated with BMP-2 (though both were better than controls).[6,172] Further studies are needed to assess the clinical utility of various treated ADMs.

ADMs have been produced from a variety of sources including human, porcine and bovine tissue and can be further classified by tissue source (dermis, intestinal submucosa, urinary bladder, pericardium, etc.).[173,174] The variable efficacy between different allogenic or xenogenic ADMs may be attributed to advantages and/or disadvantage of each in providing barrier function, vascular ingrowth, innervation potential, growth factors and mechanical cues to induce site-appropriate healing.[175] In addition to the origins of each ADM, products vary by type and level of processing and/or sterilisation.[176] Some studies have suggested that aseptic processing is more beneficial than sterilisation, but others have found them to be equivalent, and there is currently no consensus on optimal processing.[177,178]

In addition to efficacy considerations, practical and ethical constraints must be considered in discussions of ADM products. Xenogenic ADMs are more readily available (compared to HADMs). However, patients belonging to certain ethnic and/or religious groups may hold beliefs that preclude the use of products with certain tissue origins.[179] Patients' belief systems often require a nuanced understanding of religious and cultural norms.[179] For example, while Jewish and Islamic dietary restrictions may not translate to tissue implantation, Buddhists and Seventh-day Adventists often practice veganism, which could lead them to refuse xenogenic tissue products.[180] Furthermore, some Hindus and Sikhs are opposed to all allogenic and xenogenic products, but other Hindus allow the use of donated allogenic tissues.[179,180]

Given that ADMs represent a relatively new addition to the reconstructive ladder, datum is limited regarding the efficacy of different commercially available ADMs in specific clinical contexts. This review does not include quantitative meta-analyses and is limited by the quality and/or amount of clinical data available for some injury patterns. Additional studies are needed for direct comparison of various ADMs. While formulations and clinical uses of ADM continue to evolve, this review provides a broad overview to better define our current understanding of its clinical utility.

Conclusion

ADMs have been used in a variety of clinical contexts, utilising the properties of the ECM to aid in organised native tissue regeneration. There is clinical evidence to support ADM usage in various subspecialties and procedures, including orthopaedic surgery, breast reconstruction, burn, wound care, andrology, oral and maxillofacial surgery, craniofacial surgery, abdominal wall/hernia repair and otolaryngology. Early reports on ADMs are promising, and further research is needed to determine their place in current reconstructive algorithms.

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Supplemental material

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